CURRICULUM VITAE

PROFESSOR DHAVENDRA KUMAR

William Harvey Research Institute
Bart's and The London School of Medicine and Dentistry
Queen Mary University of London
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London
United Kingdom

January 2025

Bioprofile/ Summary ***i-iii***

Professor Dhavendra Kumar, MBBS, MD, DCH (RCPSI), MMedSci, PGCertMedEd, FRCP Ireland, FRCP London, FRCP Edinburgh, FRCPCH, FACMG, DSc.(Hon) ; The William Harvey Research Institute, Bart's and The London School of Medicine & Dentistry, Queen Mary University of London, UK

Academic positions:

- *Hon. Consultant in Clinical Genetic/ Cardiovascular Genetics, Inherited Cardiac Unit, Bart's Heart Centre, St. Bart's Hospital, Bart's NHS Foundation Trust, London, UK*
- *Consultant in Clinical Genetics & Genomic Medicine, Cardiff Spire Hospital, Cardiff, Wales, UK*
- *Senior Consultant Adviser, 'Apollo Genomics Institutes', Apollo Group of Hospitals, India.*
- *Hon. Professor of Medicine, Swansea University, Wales, UK*
- *Visiting Professor, Centre for Health Genomics, University of South Wales, UK*
- *Visiting Professor, Centre for Genomic Healthcare, University of South Wales, Pontypridd, Wales, UK*
- *Senior Faculty Adviser to the 'Centre of Precision Medicine & Health', King George Medical University, Lucknow, India*
- *Hon. Professor, Department of Medical Genetics and Genetic Counselling, JSS Academy of Higher Education (Deemed University), Mysore, India.*
- *Hon. Professor, Department of Biotechnology, Shri Mata Vashno Devi University, Katra, Jammu, India*
- *Hon. Professor, Department of Medical Genetics, Kasturba Medical College, Manipal, Karnataka, India.*
- *Visiting Professor, Centre for Advanced Research & Education, Chettinad Medical College & Health University, Chennai, Tamil Nadu, India.*
- *Honorary Visiting Professor, Faculty of Medicine, University of Colombo, Sri Lanka*
- *Visiting Professor, School of Medicine, Texas Tech University, Texas, USA*
- *External Adviser for Genomic Medicine, South Africa Medical Research Council (SAMRC), South Africa*
- *Honorary Adjunct Professor, Mahatma Gandhi University Medical Sciences Technology, Jaipur, India*
- *Honorary Adjunct Professor. Shri Guru Ramdas University of Health Sciences, Amritsar, India*
- *Fellow Faculty of Scholars, Human Genome Organization International (HUGO), USA*

Citation:

- A highly acclaimed, globally acknowledged genetic and genomic clinician with special interests in clinical genetics, cardiovascular genomics and genomic/ OMIC medicine. He is credited with landmark contributions and achievements in genetic-inherited diseases of children, hereditary familial conditions of heart and blood vessels, applications of novel genomic principles and technology in genomic-precision medicine and public and population health genomics.
- He is honoured with ***Doctor of Science, Honoris Causa*** by the alma mater, KGMU Lucknow, ***Hind Rattan*** International NRI Award, the ***GAPIO-Siemens Medical Innovation Award***, the

Glory of Georgians & Life Time Achievement Award of the King George's Medical University Alumni UK, and the ***Life Time Achievement Award conferred by GAPIO (2023***).

- He is honoured with inclusion in the ***HUGO Faculty of Scholars***, one of the highest recognition in the field of Genomics and Molecular Biology conferred by the Human Genome Organization International (HUGO). He is widely applauded for his sincere and persistent efforts for medical genetics as the integral part of medical teaching and practice across India and in low and middle income countries (LMICs).
- He serves on the panel for WHO sponsored International partnership for genomic education and training in collaboration with the NHS England Genomic Medicine Service. He founded and leads the Genomic Medicine Foundation UK that is committed to promoting and educating genomic applications in medicine and healthcare in developing countries, notably in South Asia (South Asia Genomic Healthcare Alliance- SAGHA).

Notable services, achievements and contributions:

- **Author/Editor** of several peer reviewed research papers, articles and books. Main book titles include-

Genetic Disorders of the Indian Subcontinent (Kluwer-Springer); Genomics and Clinical Medicine (Oxford); Principles and Practice of Genomic Medicine (Oxford); Principles and Practice of Clinical Cardiovascular Genetics (Oxford); Cardiovascular Genetics & Genomics- Principles and Clinical Practice (Springer-Nature); Oxford Specialist Handbook Inherited Cardiac Disease (Oxford); Medical & Health Genomics (Elsevier); Genomics and Society (Elsevier); Clinical Molecular Medicine-Principles & Practice (Elsevier); Genomic and Molecular Medicine e-book series (9 volumes), Morgan& Claypool Publishers. Advances in Genetics series (9 volumes), Academic Press by Elsevier.

- **Founding Editor in Chie**f of new bio-medical journals-

'Genomic Medicine' (Kluwer-Springer), continues as 'Human Genomics', the official journal of HUGO, BMC/Springer Nature ; 'Applied and Translational Genomics' (Elsevier); 'Genomic and Molecular Cardiology (GMF-UK); ***'Seminars in Genomic Medicine' (GMF-UK).***

Founded and leads the multi-volume book series '***Genomic and Precision Medicine in Clinical Practice***'. Authored and edited new books in this series-

1. *'Genomic Medicine Skills and Competencies'*
2. *'Cardiovascular genomic medicine' and 'Genomics, Populations and Society', Co-Editors- Prof. Perry Elliott, University College London, UK & Prof. Arthur Wilde, University of Amsterdam, The Netherlands.*
3. *'Genomics, Populations and Society', Co-editor- Prof. Ruth Chadwick, University of Lancaster & Cardiff University.*
4. *New titles in this series include- 'Clinical Nutrigenomics for Personalized Healthcare'; 'Cancer Genomic Medicine'; 'Medical and Health Genomics of South Asia'; 'Genomic and Molecular Dysmorphology'; 'Clinical Pharmacogenomics'; 'Laboratory Genomic and Molecular Medicine'.*

- **'Genomics and healthcare in low and middle income countries (LMICs)'**
  Leading ambassador for harnessing the genetic and genomic advances for improved healthcare in developing nations. This book is a unique resource for genetic-genomic status across all Low & Middle Income Countries (LMICs).

- Founded and continues to lead the ***Genomic Medicine Foundation UK*** (www.genomicmedicine.org). Main project of the Foundation- the **South Asia Genomic Healthcare Alliance (SAGHA**) to promote and enhance mutually beneficial collaboration-partnership in the fast-emerging field of genomic medicine and healthcare. The alliance has close academic and professional links all over India & South Asia.
- Established and manage key projects of SAGHA for promotion and empowering genomic healthcare in South Asia- *Genomic and Precision Medicine in South Asia; DECIPHER South Asia; South Asia Pharmacogenomics Consortium; Genomethics South Asia Consortium*
- Established close links with India's leading medical scientific academic institutions through the ***Memorandum of Understanding*** with KGMU-Lucknow, the JSS Higher Education Research Academy (Mysore, Karnataka) and Shri Guru Ram Das University of Health Sciences (Amritsar, Punjab). Main focus of MOU is to enhance and strengthen genomic and molecular elements in higher medical education and research.
- Delivered the '**Professor SS Agarwal Oration'** of the Society of the Indian Academy of Medical Genetics (SIAMG) at the 2018 annual conference held in CMC, Vellore, India.
- Served on the Panel of the **VAIBHAV** summit, Department of Science Technology, Government of India. October 2020. International scientists' advisory forum of Indian Origin.
- Funder and established the '***Young Investigator Gold Medal'*** to enhance research & academic contributions of the junior Faculty of KGMU, Lucknow.
- Founder President of the new ***Global Academy of Medical Sciences (GAMS)*** for enhancing & empowering academic medicine in 'low and middle income countries (LMICs)'.
- Consultant Advisor to the Apollo Group Hospitals, India for the Apollo Genomics Initiatives. He was instrumental for establishing and directing the ***Apollo Genomics Institutes*** in Delhi, Mumbai, Chennai, Bangalore, Hyderabad, Kolkata and Ahmedabad, with further four Institutes under development. The Apollo Genomics Institutes are prime example for delivering the 'state of the art' genomic medicine and healthcare across India with the sole aim to offer cutting edge precision genomic diagnostic and therapeutic services in rare and common diseases along with teaching, training, research and novel applications of multi-OMIC sciences and technologies.
- Served as a panelist on the ***WHO Science Council*** for promoting genomic applications in healthcare across low and middle income countries (LMICs).
- Current Chair of the Human Genome Organization International (**HUGO) Genomic Education Committee** steering the global program for enhancing genomic knowledge and skills for multi-disciplinary healthcare with particular reference to the low and middle income nations.
- Member of the **International Partnership for Genomics Education and Training** led by the NHS England Genomics in collaboration with the World Health Organization (WHO).

Updated- January 2025

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I PERSONAL

Place of Birth	Moradabad, UP, India
Nationality	British- U.K. Citizen
Defence Organisation	Medical Protection Society No. 281124
General Medical Council	Full Registration No: 2351409
	Specialist Register: Clinical Genetics, April 2006
	GP Register: March 2006

II EDUCATION & QUALIFICATIONS

II.1 Secondary Education: Government Intermediate College, Moradabad, UP, India 1960-1967

II.2 Graduate Education Hindu College, University of Agra, Moradabad, UP, India 1967-1968

II.3 Professional Education:

Medical School/College attended- King George's Medical College, Lucknow University, Lucknow, India

Undergraduate **MBBS:** August 1968 – July 1973

Postgraduate **MD Paediatrics**: January 1976 – December 1977

The Medical School, University of Sheffield, UK

Postgraduate (**MMedSci**): April 1982 – December1986

II.4 Qualifications:

M.B., B.S. 1973 (King George's Medical College, University of Lucknow, India)
MD 1977 in Paediatrics (University of Lucknow, India)
D.C.H 1979 (Royal Colleges of Surgeons and Physicians in Ireland)
M Med Sci. 1987 (University of Sheffield)
MRCPI 1990 (Royal College of Physicians, Ireland- RCPI)
DABMG American Board Certification in Clinical Genetics 1990 (ABMG)
FRCPI 1992 (Fellow Royal College of Physicians, Ireland);
MRCPCH 1996 (Royal College Paediatrics & Child Health-RCPCH, UK)
PG Cert. Med Edu , 2003 (Staffordshire University, UK)
FACMG, 2003 (Fellow American College of Medical Genetics-ACMG)
FRCPCH 2006 (Fellow RCPCH, UK)
FRCP 2008 (Fellow Royal College Physicians, London, UK- FRCP)

D.Sc. (Hon) 2015 (King George's Medical University, Lucknow, India-KGMU)
FRCPE 2024 (Fellow Royal College of Physicians Edinburgh)

III. APPOINTMENTS

III.1 Current appointments:

1. Visiting Professor, Genomic Policy Unit, Faculty of Life Sciences & Education, The Glyn Taff Campus, The University of South Wales (previously Univ. of Glamorgan), Wales, UK; 2010-To date
2. Honorary Consultant in Cardiovascular Genetics Inherited Cardiac Diseases Unit, Department of Cardiology, St. Bart's Hospital, London; 1 March 2018 to Date.
3. Honorary Clinical Professor, William Harvey Research Institute, Bart's and the London School of Medicine & Dentistry, Queen Mary University of London, UK; 1May 2019 to date.
4. Honorary Professor, Genomic Medicine Unit, Institute of Life Sciences, Swansea University, 1 November 2020 to date.
5. Consultant in Clinical Genetics & Genomic Medicine, Spire Cardiff Hospital, Spire Healthcare UK, May 2015 to date.

III.2 Most Recent Appointment:

Consultant in Clinical Genetics & Clinical Lead for Cardiovascular Genetics, All Wales Medical Genetics Service, University Hospital of Wales, Institute of Medical Genetics, Cardiff University, UK (1 November 2004 to 31 October 2017- Retirement from NHS UK duties)

III.3 Academic Appointments:

1. Honorary Senior Research Fellow, Institute of Medical Genetics, Division of Cancer & Genetics, Cardiff University School of Medicine, UK; 2007 to 2019
2. Visiting Professor, Education & Research, Chettinad Health University, Chennai, India; 2011 to 2018.
3. Adjunct Professor, Public Health/ Medical Genetics, China Capital Medical University, Beijing, China; 2010-TO Date
4. Visiting Professor, Ranbaxy Science Foundation, India; January- February 2013
5. Visiting Academic Faculty- Advanced Bio-Medical Research Centre, King George's Medical University, Lucknow, India, 2013-date
6. Distinguished Academic Visitor, 10-12 December 2015, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.
7. Visiting Academic Fellow, William Harvey Research Centre, Queen Mary University of London, UK, 15 January 2016 to 30 March 2016.
8. Adjunct Professor, Kasturba Gandhi Medical College, Manipal University, Manipal, Karnataka, India; (March 2017 to Date)

9. Adjunct Professor, Shri Mata Vashno Devi University, Katra, Jammu & Kashmir, India (June 2018 to Date)
10. Honorary Professor, JSS Higher Education Academy (Deemed University), Mysore, Karnataka, India; May 2018 to date.
11. Honorary Visiting Professor, Faculty of Medicine, University of Colombo, Sri Lanka. Jan 2022 to December 2024.
12. Visiting Professor, School of Medicine, Texas Tech University Health Sciences Center, USA. June 2022.
13. External Academic Faculty Adviser, Shri Guru Ramdas University of Health Sciences, Amritsar, Punjab, India; November 2022 to 2024.
14. Honorary Adjunct Professor, Mahatma Gandhi University of Medical Sciences and Technology, Jaipur, Rajasthan, India; December 2023 to date.
15. Honorary Adjunct Professor, Shri Guru Ramdas University of Health Sciences, Amritsar, Punjab, India; November 2024 to Date.

IV. AWARDS, DISTINCTIONS AND HONOURS

IV.1. *Awards & Honours*

i) Awarded a ***Gold Medal*** for the highest percentage of marks at the second professional MBBS examination (1971), which covered the second MBBS professional examination included pharmacology, pathology, forensic medicine, and social and preventive medicine.

ii) Awarded a ***Gold Medal*** for the first position at the final professional MBBS examination (1973): Final MBBS examination subjects included general medicine, general surgery, ophthalmology and obstetrics and gynaecology.

iii) Awarded a ***Gold Medal*** for the best successful candidate for M.D. in Paediatrics, King George's Medical College (now University), 1977.

iv) BMA Medical Book Award 2012-'**Highly Commended'** for new book '***Oxford Handbook- Inherited Cardiac Disease'***, Oxford University Press, Oxford, UK.

v) Conferred ***Doctor of Science Honoris Causa (DSc HC)*** by the King George's Medical University, Lucknow, UP, India; December 2015.

vi) 'Guest of Honour' at the ***Convocation and Foundation Day*** of the King George's Medical University, Lucknow, India; 20-21 December 2015.

vii) BMA Medical Book Award 2017-'**Highly Commended'** for new book '***Medical and Health Genomics'*** (Elsevier)

viii) Awarded '***Hind Rattan (Jewel of India)***' at the **Pravasi Bharatiya (Global Non-Resident Indians) Conference**, Bangkok, Thailand. 9 -10 January 2018.

ix) Athena Swan Oration 2018, Cardiff University School of Medicine **''The Helical Path**

of Clinical Genetics- Climbing the DNA Ladder', 8th November 2018.

x) '**Dr. S.S. Agarwal Oration'**, awarded at the Annual Conference of the Society of the Indian Academy of Medical Genetics (SIAMG), held In CMC, Vellore, TN, India; 12-15 December 2018.

xi) 'VAIBHAV SUMMIT', served as a 'Panelist' in this prestigious project on invitation from the Principal Scientific Adviser to the Prime Minister of India, Shri Narendra Modi. November 2020.

x) 'Genomics and Global Health', served on the Advisory Panel on this project initiated and led by the WHO Science Council, World Health Organization. November 2021.

xi) 'HUGO Education Committee', appointed the Chair of the genomics education & committee initiative led by the Human Genome Organization (HUGO). December 2021.

xii) 'GAPIO Life Time Achievement Award 2023', from the Global Association for Physicians of Indian Origin, 11 February 2023, Ahmedabad, India.

xiii) 'Fellow HUGO Faculty of Scholars', Human Genome Organization International (HUGO), September 2024.

xiv) 'Guest of Honour', November 2024, Mahatama Gandhi University of Medical Sciences and Technology, Jaipur, Rajasthan, India

xv) 'Guest of Honour', December 2024, Aligarh Muslim University, Aligarh, India

IV.2. ***External higher Doctoral degrees examiner- PhD & DSc***

- Queen's University, Belfast, Northern Ireland, UK
- Cardiff University, Cardiff, Wales, UK
- All India Institute of Medical Sciences, New Delhi, India
- Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India
  Guru Nanak Dev University, Amritsar, India.
- University of Cape Town, South Africa
- Shri Mata Vashno Devi University, Katra, Jammu & Kashmir, India
- Punjab University, Lahore, Pakistan

IV.3. ***External advisor for Higher academic awards, promotions & appointments:***

- University College London, The University of London, UK
- King's College, The University of London, UK
- The University of Leicester, Leicester, UK
- The University of Glasgow, Glasgow, Scotland, UK
- Johns Hopkins Medical School, Baltimore, USA
- King George Medical University, Lucknow, India
- The University of Jordan, Amman, HK Jordan
- The University of Colombo, Sri Lanka

- The University of Cape Town, South Africa
- Apollo Hospitals Education and Research Foundation, India

IV.4. ***Independent External Research Grants Reviewer***

- Medical Research Council (UK)
- Wellcome Trust (UK)
- European Union Rare Diseases Research Consortium
- Belgian Research Council
- South African Research Council
- Heart Research (UK)
- Netherlands Research Council, The Netherlands
- British Heart Foundation, London, UK
- Tenovus Cancer Charity, Wales, UK
- Albert Einstein Foundation, Berlin, Germany
- UK Research and Innoovations (UKRI)

V. ACADEMIC ACHIEVEMENTS AND CONTRIBUTIONS

V.1 External higher Doctoral degrees examiner- PhD & DSc:

- Queen's University, Belfast, Northern Ireland, UK
  Doctor of Science (DSc)
  "Systems approaches for elucidation of molecular mechanisms of disease"
- Cardiff University, Cardiff, Wales, UK
  Doctor of Philosophy (PhD)
  "Genetic Testing for Sudden Arrhythmic Death Syndrome and the Coroners' System of England and Wales"
- All India Institute of Medical Sciences, New Delhi, India
  Doctor of Philosophy (PhD)
  "Molecular genetic studies in Indian families with autosomal recessive non-syndromic hearing loss'
  "Testicular germ cell arrest (maturation arrest): Phenotype-Genotype correlation"
- Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India
  Doctor of Philosophy (PhD)
  "Characterization of exonic and splice site variations in ATP8B1, ABCB11 and ABCB4 genes in Indian patients with progressive familial intrahepatic cholestasis."
- University of Cape Town, South Africa
  Doctor of Philosophy (PhD)
  "Clinical and genetic studies in Lynch syndrome"
- Shri Mata Vashno Devi University, Jammu & Kashmir, India

Doctor of Philosophy (PhD)
"**Genetic susceptibility in Esophageal carcinoma patients from Jammu and Kashmir"**

- Faculty of Medicine, The University of Colombo, Sri Lanka
  Doctor of Philosophy (PhD)
  "A Study of the Genetic Aetiology of Rare Inherited Conditions in the Sri Lankan Population"
- Punjab University, Lahore, Pakistan
  Doctor of Philosophy (PhD) 'Genetic studies in congenital heart disease in Pakistan'

V.2 Research awards

Established endowment for the 'Young Investigator Award' at the King George's Medical University, Lucknow, Inida. This award aims at promoting quality research amongst junior Faculty within 10 years of first academic appointment and under 45 years of age. It consists of a gold medal, citation and opportunity to deliver the key note address at the annual 'KGMU Research Sowcase'.

VI. CURRENT ACTIVITIES AND CONTRIBUTIONS IN CLINICAL GENETICS/GENOMICS

This section includes all to date current roles and activities since 1 November 2017 following my retirement from the UK National Health Service on 31 October 2017. There is clear overlap with contents of the section 7 as some current roles continue to date.

VI.1. Clinical commitments

i) Consultant Clinical Genetics & Genomic Medicine- Cardiff Spire Hospital, Wales, UK

I hold practice privileges with the Spire Healthcare UK (www.spirehealthcare.com). The Genome Clinic is held in the Spire Cardiff Hospital and as well as virtually through the online web link.

The current practice includes-

a) Comprehensive clinical genetics service covering wide-ranging specialist areas:

- Genetic disease diagnosis with diagnostic genetic testing
- Detailed assessment of birth anomalies
- In depth review and analysis of the family history
- Specialist advice on cousin marriages (consanguinity)
- Genetic counselling
- Genetic risk review and assessment (for example breast/ovarian & bowel cancer)
- Specialist service for Inherited heart and blood vessel diseases
- Predictive or pre-symptomatic genetic testing
- Genetic & genomic screening for life style and health counseling
- Prenatal screening and testing for chromosomal abnormality or specific genetic disease
- Pre-implantation genetic diagnosis for preventing recurrence of high risk genetic disease
- DNA testing for disputed paternity or identity
- Medical-legal review and Expert Witness reports related to genetic or possible genetic condition

b) Laboratory genetic and genomic diagnosis

Genetic/Genomic Tests (by Accredited Genetic Laboratories in UK/Europe)

- **Chromosome test** including Fluorescent In situ Hybridization (**FISH**)
- Array Comparative Genomic Hybridization (**aCGH**)
- **Single gene mutation testing** for specific gene(s) (for example Cystic Fibrosis, Duchenne Muscular Dystrophy, Hypertrophic Cardiomyopathy and many more)

- **Multi-Gene panel testing** for complex undiagnosed possible genetic conditions, for example familial cardiomyopathy, breast/ ovarian cancer, colorectal cancer, diabetes/obesity, infantile epilepsy, inherited blindness, floppy child etc.
- **New generation genome sequencing** – targeted clinical exome sequencing, whole exome sequencing and whole genome sequencing; for in-depth analysis of life time genetic risk analysis and advice for life style modification and health enhancement
- **Tumour genomic profiling** for confirmation of diagnosis, staging of cancer, targeted selection of anti-cancer drug, and prognostication.
- **Prenatal diagnosis including the non-invasive prenatal testing (NIPT)**
- **Preconception/Prenatal screening** for carrier status of common genetic diseases in ethnic groups, for example metabolic diseases in Jewish people, recessive genetic diseases in first cousin marriages etc.

c) Medico-Legal service

Medico-Legal Genetics expert- Genome Clinic UK Ltd.

- Independent and as member of consortium
- Expert Witness for all three sectors – Family Court proceedings, Civil proceedings and Criminal Crown Court
- Individual expert reviews and reports on wide ranging Paediatric and Adult genetic conditions on instructions from Solicitors and Barristers in UK and Ireland
- Expert reviews and reports including expert witness presentation and cross-examinations in Family, Civil related to genetic predisposition for fractures, soft tissue injuries, clinical negligence in the diagnosis and/or treatment, and paternity disputes.
- Expert review, report and Crown Court witness evidence in Criminal cases related to serious injuries and child's death on behalf of both criminal prosecution service and defence team alleging related to possible underlying genetic or inherited medical condition mitigating circumstances and evidence.

ii) Honorary Consultant Cardiovascular Genetics, Inherited Cardiac Diseases Unit, Bart's Hospital NHS Foundation Trust, London, England, UK

iii) Senior Consultant/ Adviser- Clinical Genetics & Genomic Medicine

Apollo Genomics Institutes, Apollo Group Hospitals, India;

- Indraprastha Apollo Hospitals, Delhi, India
- Other Apollo Hospitals in Navi Mumbai, Chennai, Bangalore, Hyderabad, Ahmedabad and Kolkatta.

VI.2 Academic commitments

a) Recent new books (see Section 9 for details)

i) 'Cardiovascular Genetics and Genomics: Principles and Current Practice', Eds. Dhavendra Kumar & Perry Elliott

ii) 'Clinical Molecular Medicine: Principles and Practice', Ed. Dhavendra Kumar

iii) 'Inherited Cardiac Disease', Oxford Specialist Handbook, Eds. Perry Elliott, Pier Lambiase & Dhavendra Kumar

iv) 'Tryst with the Double Helix- An Autobiography', Kindle books, Dhavendra Kumar

v) 'Genomic Medicine Skills and Competencies', Elsevier, Ed. Dhavendra Kumar

b) New book series- '**Genomic and Precision Medicine in Clinical Practice'**, commissioned by the Elsevier, world's leading bio-medical and life sciences publishers. (see Section 9 for details)

1. *Fundamentals of genomic and molecular medicine*
2. *Clinical Bioinformatics and Digital Genomic Medicine*
3. *Laboratory Genomic and Molecular Medicine*
4. *Infectious diseases and Pathogenomics*
5. *Clinical genomics and genetic counselling*
6. *Genomic and molecular medicine of rare diseases*
7. *Cancer genomic and molecular medicine*
8. *Cardiovascular genomic and molecular medicine*
9. *Reproductive and fetal medicine*
10. *Ophthalmic genomic and molecular medicine*
11. *Neurology and Neuropsychiatric genomic and molecular medicine*
12. *Immunogenomics and Clinical Immunology*
13. *Genomic and Molecular Therapeutics*
14. *Epigenomics in Clinical Medicine*
15. *Nutrition and Nutrigenomics in health and disease*
16. *Pharmacogenomics and Targeted Pharmacotherapy*
17. *Genomic Medicine–Skills and Competencies*
18. *Genomics, Populations and Society*

VI.3 Genetic and Genomic Education & Training

i) Director Postgraduate Diploma Genomic Medicine & Healthcare, University of South Wales, UK

ii) Faculty- MSc Genomic Medicine, Swansea University, UK

iii) Founding Chair- Indo-UK Genetic Education Forum

iv) Founding Chair- Global Consortium for Genomic Education (GC4GE)

v) Chair- HUGO- Education Committee

vi) Director/ Faculty- Teaching and Training Courses in genetics and genomics
vii) Faculty- Conferences/ Symposia/ Seminars/ Lectures

Details on these activities are included in respective sections.

VI.4 Genomic Medicine & Healthcare

i) Honorary Clinical Professor, Cardiovascular genomic medicine, William Harvey Research Institute, Bart's and the London School of Medicine & Dentistry, Queen Mary University of London, UK (from August 2019 to date)

ii) Senior Faculty Adviser, The Centre of Precision Medicine, King George's Medical University, Lucknow, India. (From November 2018 to date)

iii) International Assessor/Adviser to the South Africa Medical Research Council for Genomic Medicine & Healthcare Centre, the University of Cape Town (From October 2022 to date)

iv) Chair- UK India Genomic Medicine Alliance, The Genomic Medicine Foundation (UK) (From October 2011 to date)

v) External Faculty adviser for genomic medicine & healthcare- all current and active roles:

a. University of Colombo, Sri Lanka
b. King George's Medical University, Lucknow, UP, India
c. JSS Academy Higher Education (Deemed University), Mysore, Karnataka, India
d. Kasturba Medical College, University of Manipal, Karnataka, India
e. Shri Mata Vashno Devi University, Katra, Jammu & Kashmir, India
f. Shri Guru Ramdas University of Health Sciences, Amritsar, Punjab, India
g. Apollo Group of Hospitals & Apollo Hospitals Research and Education Foundation, India.
h. International collaboration for Cardiovascular Genomic Medicine- UK, India & Egypt, William Harvey Research Institute, Queen Mary University of London, UK
i. Biennial International Cardiovascular Genomic Medicine conferences, Genomic Medicine Foundation, UK
j. Biennial Genomic and Precision Medicine Conferences, Genomic Medicine Foundation UK.
k. Invited key note speaker- genomic medicine conferences- several institutions in India, Egypt, South Africa
l. Member- Scientific Committee for several other genomic conferences

VI.5 Editorial responsibilities (see Section 9 for details)

i) Founding Editor in Chief- 'The HUGO Journal', continues as 'Human Genomics', BMC/Springer-Nature

ii) Serial Editor- 'Advances in Genetics', Academic Press, Elsevier

iii) Founding Editor-in-Chief- 'Genomic and Molecular Cardiology, Genomic Medicine Foundation UK (GMF-UK)

iv) Founding Editor-in-Chief- 'Current Trends in Genomic Medicine', GMF-UK.

v) Editorial Board Membership-several genetic and genomic journals
vi) Peer review/ Referee for many high impact journals

VI.6 Global genomic health developments

i)Founder/ Medical Director/ CEO- 'The Genomic Medicine Foundation UK'

THE GENOMIC MEDICINE FOUNDATION (UK)
FELLOWSHIP, SCHOLARSHIP, EDUCATION AND PROMOTION OF GENOMIC APPLICATIONS IN MEDICINE, HEALTHCARE AND SOCIO-ECONOMIC PROGRESS

www.genomicmedicine.org

Independent organization promoting application and translation of ***Genomics*** and other ***OMICS*** sciences in the current and future practice of clinical medicine, personalized healthcare & socio-economic progress

The Genomic Medicine Foundation in the United Kingdom (GMF-UK) is an independent 'not for profit' organization committed to application and translation of *Genomics* and related *OMICS* sciences and technologies in medicine, personalized health care and socio-economic progress. Patrons of GMF-UK include the Late Professor Sir David Weatherall followed by Professor Sir Munir Pirmohamed. Priority sectors of the GMF-UK include global genomic education, birth defects, rare genetic diseases, precision & personalized healthcare and harnessing genomic applications to enhance health status in developing World. This article introduces the GMF-UK with its objectives, current projects and status in pursuit of the genomics led medicine and healthcare.

ii) Global Familial Heart Challenge (GFHC)

Familial and inherited cardiovascular diseases are global and affect all irrespective of geographic and ethnic origin. It is a global phenomenon and requires a worldwide high-level strategic health approach. The whole group of conditions poses a major global challenge. The Global Familial Heart Challenge (GFHC) is a new international initiative for raising awareness and developing regional and country specific health information, data resource and targeted specialist health service provision on ICCs. I set up and lead GFHC to deal with medical and health challenges of the familial / inherited heart disease.

Main Objectives of GFHC include-

1. To assist clinicians, health professionals, laboratory scientists and patient & family support groups to on the key health challenges of familial and inherited heart disease- clinical diagnosis, laboratory genetic/genomic diagnosis, multi-disciplinary care and health surveillance, prevention and support.

2. To develop a fully accessible clinically oriented database to include fully validated evidence-based information for clinical applications.
3. To set up on-line access for the consumer (professionals, partners, patient and public) on qualified and validated information related to the key familial heart health challenges.
4. To encourage and engage in applied research on management and treatment of familial/ inherited conditions in a cost-effective manner, including prevention; providing data for bio molecular research for a 'cure'.
5. To strengthen the emphasis in public health to make sure that it encompasses some aspects of mapping genetic mutation and genomic variant patterns across various populations, and from this being able to provide some evidence to service providers regarding public health messages as opposed to individual case treatment.

The project includes setting up dedicated cardiovascular genomic medicine centres in India, Egypt, South Africa and Brazil. All these centres will be centrally coordinated by the International Centre based in Queen Mary University of London, UK. The network of the Cardiovascular Genomic Medicine Centres would focus on setting standards, developing protocols and the database with information on phenotype and associated genomic variants.

iii) **The Global Consortium for Genomic Education (GC4GE)**

In keeping with my passion for genomic education, I set up the Global Consortium for Genomic Education (GC4GE). It is a major new initiative to bring together many committed scientists, clinicians, professionals, institutions, laboratories and organizations for developing a concerted program for genomic education and training delivered globally with a particular focus on developing and less developed nations.

The main aim is to organize, coordinate and steer a global consortium for the integrated genomic education and training programs.

Objectives include-

1. To identify and engage with major Professionals, Institutions and Organizations involved with genetic/genomic education and training.
2. To develop the core framework for the consortium in collaboration with participating groups.
3. To develop a network for the consortium working on the 'hub and spoke' model.
4. To develop the bespoke integrated genomic education and training program incorporating major components of genome science and technology.
5. To develop mechanisms for delivering the integrated genomic education program on regional and country basis.

This project is now closely linked with the genomic education and training initiatives of the Human Genome Organization International (HUGO), Global Genomic Medicine Collaborative (G2MC) and the Global Partenership for Genomic Education jointly led by the Genomics Services of the UK National Health Service and the WHO Science Council.

iv) **Founder/ Chair- 'UK India Genomic Medicine Alliance- UKIGMA'**

The 'Indo-UK Genetic Education Forum' is the flagship programme to steer ahead he education and training initiatives of the Genomic Medicine Foundation UK. I largely included series of workshops, dedicated seminars and biennial conferences held in different locations across India including Sri Lanka. This project became very popular with members representing distinguished academic and clinical units-

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Indo-UK Genetic Education Forum *cont...*

The programme was largely focussed on genetics and genomics in clinical medicine with particular reference to cardiovascular disorders. The symposiums collectively attracted 22 hours of CPD credits from the Royal College of Physicians, London. The Faculty travelled to the Post Graduate Institute of Medical Education and Research, Chandigarh; Himalayan Institute of Medical Sciences and Hemwati Nandan Bahuguna Medical University, Dehradun and King George's Medical University, Lucknow. In total around 1000 participants took part including senior and junior medical practitioners, resident trainee doctors, medical students, research scientists and laboratory personnel. Feedback has been consistently excellent with encouraging comments from wide ranging audience. The Forum has been invited by at least three leading Indian academic institutions to host similar programme in 2016.

1. **Current Trends in Genetics of Heart Failure and Cardiac Arrhythmias**
   30 Jan-1 Feb 2015, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

Overseas faculty- Professor Dhavendra Kumar (Cardiff), Professor Perry Elliott (London), Professor Mary Porteous (Edinburgh), Professor Andrew Read (Manchester), Dr Alan Fryer (Liverpool), Dr Pier Lambiase (London), Dr Mieke van Haelst (Uttrecht), Dr Lorenza Monstraat (A-Coruna, Spain) and Dr. Paul van Haelst (Sneek, Holland)

This two day conference focussed on a number of inherited cardiovascular conditions encountered in clinical cardiology, emergency medicine and clinical genetics practice. Apart from the visiting overseas Faculty a number of distinguished cardiologists and cardiovascular scientists delivered the programme (See Figure 1). An account of the prevalence and challenges of inherited heart and blood disorders in India was provided by Professor KK Talwar, (Professor of Cardiology, Former Director PGI, Chandigarh and Director of Max Heart Hospital, New Delhi). The highlight of the conference was plenary lecture on *Clinical Cardiology in the Genome Era* delivered by Professor Perry Elliott, The Heart Hospital, UCL, London, UK (See Figure 2).

Figure 1 (Left): Professor Kumar with Professor Talwar (next on left) Inaugurating the Cardiac Genetics Symposium in PGIMER, Chandigarh, India.

Figure 2: Professor Elliott (UCLH) delivering the Key Note Lecture in PGIMER, Chandigarh, India.

2. **The genetic and genomic practice of clinical medicine and cardiology**
   3 Feb 2015, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India.

Overseas faculty- Professor Dhavendra Kumar (Cardiff), Professor Perry Elliott (London), Professor Mary Porteous (Edinburgh), Professor Andrew Read (Manchester), Dr Alan Fryer (Liverpool), Dr Pier Lambiase (London), Dr Mieke van Haelst (Uttrecht), Dr Lorenza Monstraat (A-Coruna, Spain) and Dr Paul van Haelst (Sneek, Holland)

This one day high profile scientific symposium focused on rapidly evolving and emerging applications of genetics and genomics in the current and future practice of Clinical Medicine (See Figure 3, and 4). A team of international genetic & genomic practitioners and scientists presented key topics with real time examples providing a clear landscape for the benefit of junior and senior secondary and tertiary medical practitioners of India. The seminar was approved by the Royal College of Physicians (London) for continued medical education & professional development.

Figure 3: Professor Anita Sharma, Head of Medicine, Himalayan Institute of Medical Sciences, Chief Convenor of the Conference

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Table 1: List of seminars and conferences organised by the Forum 2010-2014

Seminar/Conference	Date and Place	Overseas Faculty
Short course on clinical cardiovascular genetics	30-31 January 2010; Bangalore, India	Professor Dhavendra Kumar (Cardiff), Dr Perry Elliott (London), Dr Bronwyn Kerr (Manchester) and Dr Rob Hastings (Bristol and Oxford).
Current trends in Clinical Genetics & Genomic Medicine	21-24 March 2011; Chettinad Health City, Chennai, India	Professor Dhavendra Kumar (Cardiff), Professor Frances Flinter (London), Dr Leema Roberts (London) and Dr Robert Elles (Manchester)
Current practice of genetic and genomic medicine	26-27 March; Apollo Hospital, New Delhi, India	Professor Dhavendra Kumar (Cardiff), Professor Frances Flinter (London) and Dr Robert Elles (Manchester)
Genes and Human Malformations- Indian Birth Defects Conference	27-29 February 2012; Bangalore, India; part of the Indo-UK Genetic Education Forum, jointly supported by CGS/BSHG and hosted by the Centre for Human Genetics, Indian Institute of Science, Bangalore, India	Professor Dhavendra Kumar (Cardiff), Professor Jill Clayton-Smith (Manchester), Professor. Ruth Newbury-Ecob (Bristol), Dr Andrew Jackson (Edinburgh) and Dr Peter Turnpenny (Exeter)
The First Indian Cancer Genetics Conference	23-25 January 2013, Advanced Center for Treatment, Research and Education for Cancer (ACTREC), Tata Memorial Cancer Trust, Mumbai, India; jointly organised by the Indo-UK Genetic Education Forum and ACTREC.	Professor Shirley Hodgson (London), Professor Eamon Maher (Birmingham/Cambridge), Professor Gareth Evans (Manchester). Professor Diana Eccles (Southampton), Professor Meena Upadhyaya (Cardiff) and Professor Dhavendra Kumar (Cardiff)
The Next Revolution of Genetics and Genomics	27-29 January 2013; Postgraduate Education Centre, Ram Manohar Lohia Hospital, New Delhi; jointly organised by the Indo-UK Genetic Education Forum with the Indian Academy of Medical Genetics and the Centre for Genetic Medicine, Sir Ganga Ram Hospital, New Delhi, India.	Professor Shirley Hodgson (London), Professor Eamon Maher (Birmingham/Cambridge), Professor Gareth Evans (Manchester). Professor Diana Eccles (Southampton), Professor Meena Upadhyaya (Cardiff), Professor Sian Ellard (Exeter), Dr Bert de Vries (Nijmegan) and Professor Dhavendra Kumar (Cardiff)
Current Trends in Genetic and Genomic medicine	31 January 2013; Dr Ram Manohar Lohia Post Graduate Institute of Medical Sciences, Gomti Nagar, Lucknow; jointly organised by the Indo-UK Genetic Education Forum	Professor Shirley Hodgson (London), Professor Meena Upadhyaya (Cardiff), Professor Sian Ellard (Exeter), Dr Bert de Vries (Nijmegan) and Professor Dhavendra Kumar (Cardiff)
Gains of Genomic Research for Medicine and Biology	4 February 2013; The Ranbaxy Science Foundation Symposium, Institute of Immunology, New Delhi, India.	Professor Dhavendra Kumar (Cardiff)
International Birth Defects Conference	9-11 February 2014; Jointly organised on behalf of the Indo UK Genetic Education Forum, Wales Gene Park and the Human Genetics Unit, The University of Colombo, Sri Lanka	Professor Dhavendra Kumar (Cardiff), Professor Philip Beales (London), Professor Daniela Pilz (Cardiff), Dr Sarah Smithson (Bristol)and Dr Trevor Cole (Birmingham)
Ophthalmic Genetics Seminar	11 February 2014; Jointly organised on behalf of the Indo UK Genetic Education Forum, Wales Gene Park and the Human Genetics Unit, The University of Colombo, Sri Lanka.	Professor Graeme Black (Manchester), Professor Veronica van Heyningen (Edinburgh/London), Dr Trevor Cole (Birmingham), Dr Georgina Hall (Manchester) and Professor Dhavendra Kumar (Cardiff)
Indian Ophthalmic Genetics Conference	15-16 February 2014; Jointly organised on behalf of the Indo UK Genetic Education Forum, Wales Gene Park and Narayana Nethralaya, Bangalore. India.	Professor Graeme Black (Manchester), Professor Veronica van Heyningen (Edinburgh/London), Dr Georgina Hall (Manchester), Dr Trevor Cole (Birmingham), Professor Daniela Pilz (Cardiff) and Professor Dhavendra Kumar (Cardiff)
Genes and Genome	21 Feb 2014; Organised by the Dept. of Human Genetics, Guru Nanak Dev University, Amritsar, Punjab, India.	Professor Dhavendra Kumar (Cardiff)

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Indo-UK Genetic Education Forum *cont...*

Figure 4: Dr Lorenzo Monstraat, Consultant Cardiologist/ Cardiac Genetics from Spain at the Genomic Medicine Symposium in Sahu Ram Health University, Dehradun, India.

3. **Our genes and genomes in Health and Disease**, 4 February 2015, Open seminar hosted by Hemwati Nandan Bahuguna Medical University, Dehradun;held in the Indian Council for Forest Research and Education.

One day seminar aimed at young secondary and graduate science students provided basic introduction to genetics and genomics with its wide ranging applications. The seminar was attended by around 300 high school and university students from local and nearby science schools and colleges (See Figure 5).

Figure 5: Professor Andrew Read delivering Public Lecture in Dehradun at the 'Our Genes & Genomes' Open Seminar

4. **Genetics and Genomics in Modern Clinical Medicine**
9-10 Feb 2015, King George's Medical University, Lucknow, UP, India.

Overseas faculty- Professor Dhavendra Kumar (Cardiff), Professor Mary Porteous (Edinburgh), Professor Andrew Read (Manchester), Dr Alan Fryer (Liverpool)

The two day symposium in the historic city of Lucknow provided the audience and participants clinically oriented introduction to genetics and genomics. Local researchers and postgraduates presented their research as posters. The visiting Faculty went through all posters and the best two were given prizes sponsored by the Research Cell of the King George's Medical University.

Figure 6 (left):The Faculty of the Genetic and Genomic Medicine Conference, from left Professor Mary Porteous, Dr Alan Fryer, Professor Andrew Read, Professor Dhavendra Kumar, Professor Ravi Kant (VC, KGMU), Professor Ravinder Garg (Research Dean, KGMU) and Professor Mahboob Khan (Dean-Dental Faculty, KGMU)

Figure 7 (right): The UK Faculty visiting KGMU Campus- from right Professor Read, Professor Porteous, Professor Ravi Kant (VC, KGMU), Dr Alan Fryer, Professor Kumar and Professor Khan (Dental Faculty).

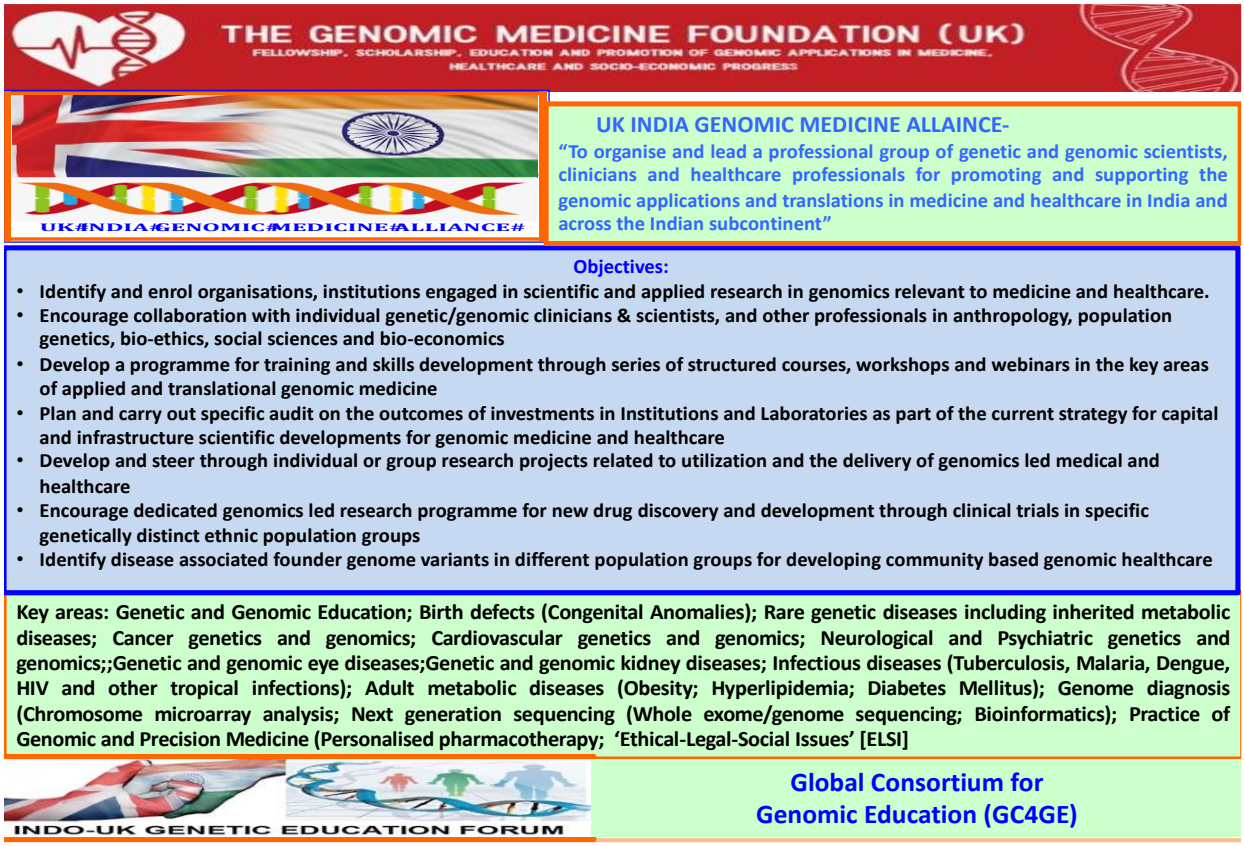
Figure 8: The UK visitors in the historic KGMU Campus- from left Dhavendra Kumar, Alan Fryer, Mary Porteous and Andrew Read.

In addition to the above engagements, Professor Dhavendra Kumar, Dr. Alan Fryer and Dr. Peter Turnpenny (Exeter) participated as invited Faculty to the Second National Paediatric Genetics Conference, held on 13-15 February in the Dinanath Mangeshkar Hospital Medical School & Research Centre in Pune, Maharashtra, India. Professor Dhavendra Kumar visited Chennai, Tamil Nadu as the Visiting Professor to the Chettinad Academy for Research and Education of the Chettinad Health University. All events and seminars were highly successful with excellent feedback from Indian colleagues and participants.

The Forum is invited to organise future genetic and genomic educational and research events in 2016. The highlight for the 2016 round will be the *Third Biennial International Birth Defects Conference* in New Delhi jointly convened by the Forum with the Indian Academy of Medical Genetics. Anyone interested to join the Faculty and/or leading a particular seminar is invited to contact Professor Dhavendra Kumar for informal discussion and further information.

kumard1@cf.ac.uk;
dhavendra.kumar@southwales.ac.uk ;
Dhavendra.kumar@wales.nhs.uk

The success of the Indo-UK Genetic Education Forum led to the UK-India Genomic Alliance to include organisation and delivery of genomic medicine and genomic healthcare across the Indian subcontinent-



This is one of the flagship projects of the Genomic Medicine Foundation (UK). It. Was founded and led by Dhavendra Kumar supported by the International Advisory Board. Several genome scientists and clinicians with interest in clinical genomics and genomic medicine have joined the Alliance. The new alliance between leading human genetic and genomic organizations and institutions in the UK and Indian subcontinent aims to foster new links and partnerships focused on next generation genome sequencing methods and applications in medicine and healthcare. The UKIGMA has initiated series of Memorandum of Understanding (MOU) with key academic and teaching Institutions across India and Sri Lanka. This programme continues with a broader remit to include whole South Asia overlapping Asia-Pacific and neighbouring regions.

V) 'The Centre for Precision Medicine', King George's Medical University, Lucknow, India.

I am an alumnus of the above leading prestigious medical institution of India. It is one of the very few institutions with heritage of British Raj in India. Under the leadership of Professor Kumar, The Genomic Medicine Foundation UK has signed the MOU for developing the academic, research and teaching base for *Genomic and Molecular Medicine*. This unique arrangement is

supported by massive investment made in creating the infra structure for the advanced bio-medical research facility, one of the finest in north India. I was fortunate to be involved in planning and setting up the '*Centre for Advanced Research'*. The University has now agreed in principle to establish the state of the art '*Centre for Precision Medicine'* that I am advising and actively pursuing as the Senior Faculty Adviser.

The Centre of Precision Medicine
King George's Medical University, Lucknow, UP, India

Infection

Rare Diseases KGMU **Metabolic**

CPM

Cancer **Inflammation**

"Joint KGMU- UKIGMA Project"

UK INDIA GENOMIC MEDICINE ALLIANCE

THE GENOMIC MEDICINE FOUNDATION (UK)

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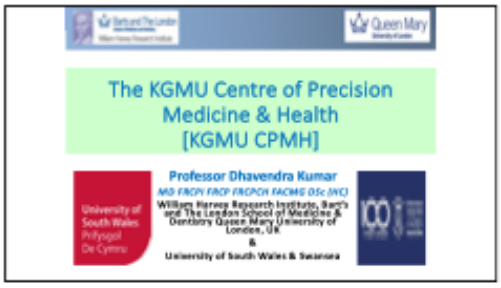
The KGMU Centre of Precision Medicine & Health [KGMU CPMH]
Professor Dhavendra Kumar
University of South Wales
Prifysgol De Cymru

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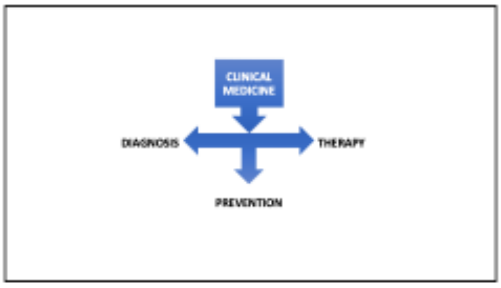
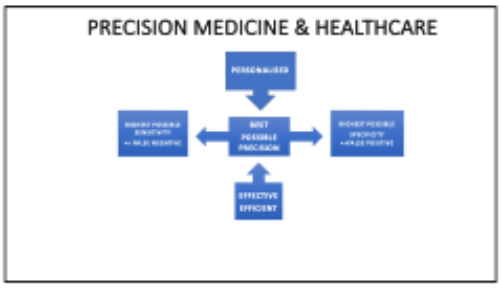

CLINICAL MEDICINE
DIAGNOSIS
THERAPY
PREVENTION

2

New Paradigms of Clinical Medicine: The P's of Medicine
• Personalized
• Precision
• Predictive
• Preventive
• Preemptive
• Participatory

3


PRECISION MEDICINE & HEALTHCARE

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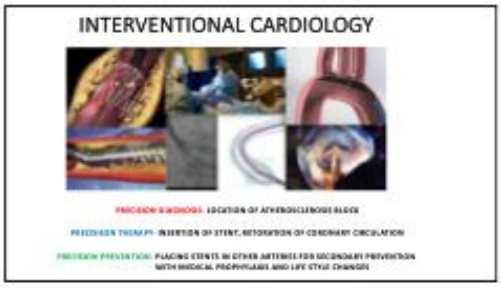
INTERVENTIONAL CARDIOLOGY

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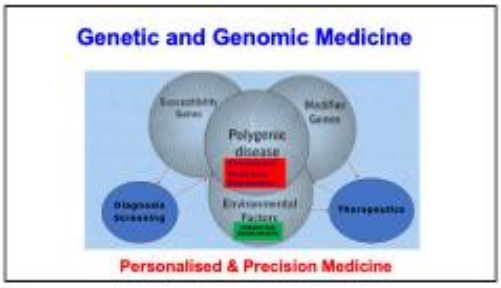
Genetic and Genomic Medicine
Polygenic disease
Personalised & Precision Medicine

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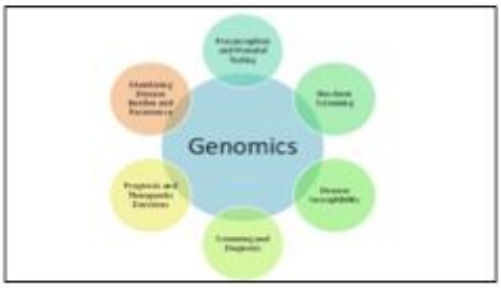
Genomics

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Translational genomics and precision medicine: Moving from the lab to the clinic.

Zeggini et al., Science 365, 1409–1413 (2019) 27 September 2019

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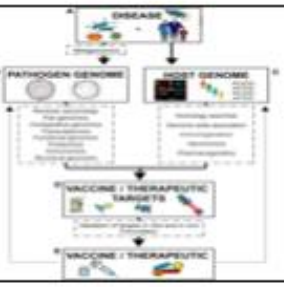

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Genotype driven cardiac arrhythmias management

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DENTAL MEDICINE

Yu et al: Genome editing- a new horizon for oral and cranio-facial research. J. Dent. Res. 98(1):36-45

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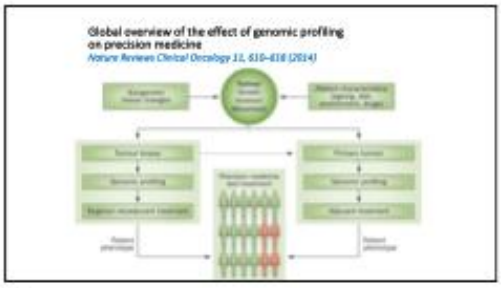

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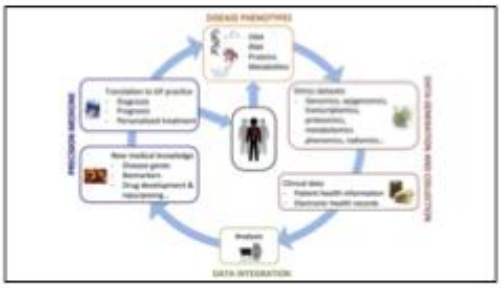

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KGMU CPMH STRATEGIC AREAS

- **Fetal Medicine-** High risk pregnancy/ fetal precision diagnosis/ targeted interventions
- **Rare diseases-** phenotype/genome profiling
- **Infection-** sepsis, tuberculosis, malaria & viral (Covid-19; Dengue & others)
- **Cancer-** genotype profiling & targeted therapy
- **Diabetes mellitus/ Hyperlipidemia-** genetic/genomic vs. other biomarkers
- **Inflammation-** biomarkers/ cytokines/ interleukins/ HLA/SNPs & CNVs etc. & genome profiling
- **Precision Dentistry-** Oral health; Cranio-facial genetics; Implants etc.
- **Age related degenerative-** dementia/ neuro-muscular/ macular- retinal degeneration, osteoarthritis etc.
- **Pharmacogenomics/ Precision pharmacotherapy-** genotype profiling for best drug selection to *'maximise effect with minimal risks'*
- **Family and Community Medicine-** Targeted screening; health surveillance and personalized intervention/ prophylaxis

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ACTION PLAN

- Physical existence- location/ space/administration
- CPMH Governance team- leadership/people/protocols
- Individual field sub-committee
- Training program- generic and specific/ postgraduates/ external
- Skills and Competencies support for the current staff
- Revisit / review current research projects
- Proposals for new research projects/ grant applications
- External collaboration- national and international
- PhD research projects- short list for starters
- MD/MS/DM/Mch new topics for dissertation work

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Questions and Comments

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In addition to raising awareness and prmoting organised/ structured research, the KGMU CPMH is also engaged in undergraduate medical education as per the guidance and recommendations of the National Medical Commission of India. The outcome of this mini-project was presented at the Global Genomic Summit held in November 2023 at the prestigious Sanger Genome Centre, Hinxton, Cambrdige, UK.

Students' perception about Medical Genetics as an Elective for Undergraduate Medical training at KGMU, Lucknow, India

Amita Pandey Mishra[1], Nitu Nigam[2], Renu Singh[1], Dhavendra Kumar[3]
1.Department of Obstetrics & Gynaecology, King George Medical University (KGMU); 2.Centre for Advanced Research KGMU; 3.Bart's & The London School of Medicine & Dentistry, Queen Mary University of London, UK

Introduction

Medical Genetics is not a separate subject in Undergraduate Medical (MBBS) curriculum in India. Modification in Graduate Medical Education Regulation (GMER) in 2020[1] allowed opportunity to MBBS students to undertake 2 Electives of their choice to diversify experience, explore future interests & discover learning beyond specified core curriculum. Hence, option of Medical Genetics as an Elective (4 weeks) for Phase III MBBS students was introduced in K G Medical University in 2023.

Aims & Objectives

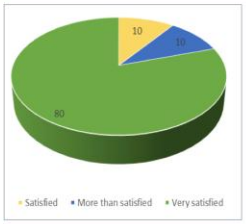
- To assess students' perception about usefulness of Medical Genetics as an Elective
- To assess their satisfaction at the end of Elective

Methods

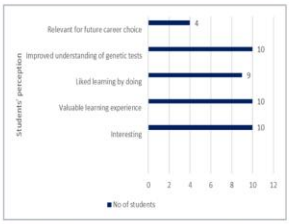
- Students introduced to basic principles of Medical Genetics & modes of inheritance.
- They learnt systematic evaluation of patients with suspected genetic disorder by detailed history, relevant examination, construction of a 3 generation pedigree to determine possible mode of inheritance & finally come to a differential diagnosis.
- They were taught steps of Genetic counselling & how to effectively communicate genetic information to patients & families.
- They were also introduced to genetic tests & technologies and allowed to spend time in genetic labs learning DNA extraction, observing PCR, Microarray, karyotyping & FISH.
- Assessment was done on basis of assignments, case presentations, reflections on self-directed learning and log book.
- At the end of the course students were made to fill an online feedback form regarding their perception about usefulness of the Elective and their level of satisfaction on a 5 point scale.

Key findings

- 10 students opted for Elective in Medical Genetics- the maximum that is allowed in any Elective at a time highlighting their preference & interest for the course.
- All students (100%) found the Elective to be interesting, a valuable learning experience & thought it improved their understanding of Genetic tests.
- 90% students felt it met their expectations
- Satisfaction (CSAT) score – 90%
- 20% students gave a feedback that increasing the time for lab exposure and more hands-on opportunity would have made the Elective more interesting & useful



Students' satisfaction with Elective



Students' perception about Elective

Conclusions

- Analysis of Feedback is an effective tool to assess students' perception
- To achieve the educational potential of an Elective, it is important to determine if the topic is of interest to the students, useful for them and if it meets their expectations & satisfaction.
- A positive students' perception and improved satisfaction is associated with higher learning effectiveness and provides an opportunity to improve the teaching-learning experience.

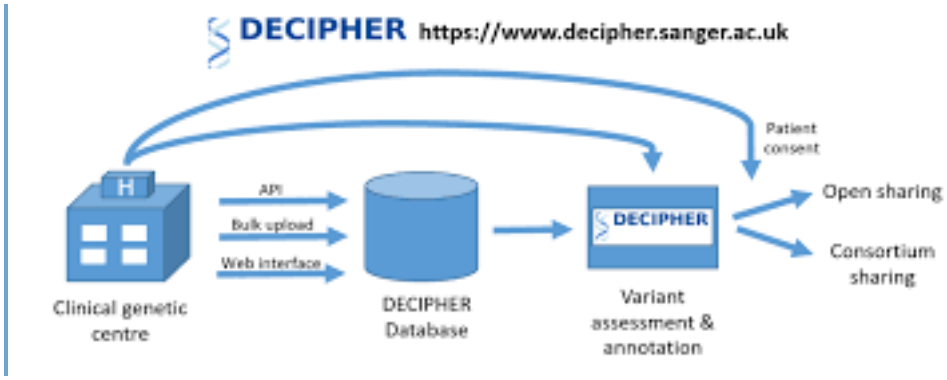
Reference:
1. Medical Council of India. Electives for the Undergraduate Medical Education Training Program, 2020: p 1- 30.

vi) Lead- DECIPHER India Consortium, Wellcome Sanger Genome Centre, UK

The **DECIPHER INDIA CONSORTIUM** represents a linked group of DECIPHER projects in the Indian subcontinent comprising genomic clinicians and scientists engaged in genome diagnosis and management of developmental disorders and many other rare genetic or genomic conditions.

The DECIPHER India consortium is part of the **UK India Genomic Medicine Alliance (UKIGMA)** on behalf of the Genomic Medicine Foundation UK Ltd., a not-for-profit organisation registered in England and Wales. (www.genomicmedicine.org) The consortium will have access and permission to store, retrieve, analyse and interpret phenotype and genotype information shared by individual or member clinical genomic units within the DECIPHER India Consortium. All members and users of the consortium will be able to use and benefit from the 'state of the art' advanced computational and genome informatic tools. In addition, individual clinicians or scientists would also be part of the wider DECIPHER community acknowledged and appreciated globally through high impact disseminations and publications (https:decipher.sanger.ac.uk).

DECIPHER is used by clinical geneticists, genomic clinicians and clinical scientists to share and compare phenotypic and genotypic data. The DECIPHER database contains open data from around 40,000 patients who have given consent for broad data-sharing. It also supports more limited sharing between trusted partners via consortia. Currently, there are just under 300 projects across the globe and 6 consortia. Anyone can browse openly-available patient data on DECIPHER and request to be put in contact with the responsible clinician. This approach benefits everyone with the ability to explore DECIPHER's genome browser and delve into the Human Phenotype Ontology Search portal.



Projects affiliated to DECIPHER can deposit and share variants, and phenotypes to invite collaboration and facilitate diagnosis. DECIPHER is a live database and once a variant is deposited, you can use DECIPHER to aid interpretation and to identify and prioritise potential matches. As well as influencing individual patient outcomes, use of DECIPHER has contributed to over 2500 peer-reviewed high impact published original papers and articles. As an academic resource, it is free to use and submitters remain in control of what data to make open, share within the DECIPHER India Consortium or retain privately within their own centre. As a member and

participant of the DECIPHER INDIA CONSORTIUM you can manage all phenotypic and genotypic data without compromising the identity of the patient and family. The phenotype entered would be structured as per the DECIPHER format. Plausibly pathogenic variants from genotypic data (array comparative genomic hybridisation, clinical or whole exome sequencing, and whole genome sequencing) would be systematically entered. Each and every mutation or variant would be associated with phenotype and classified and annotated using the tools in DECIPHER that support variant interpretation. Each consortium member and all users would be offered full in-house training to use the DECIPHER browser. In addition, there will be opportunity for free and open interpretation of all mutations and genome variants irrespective of the genetic or genomic laboratory. Each DECIPHER record has an internal ID (e.g. consortium member ID) which is only visible to members of the depositing centre; therefore no other users of DECIPHER are able to identify the patient. Consent is required for open sharing. The patient information sheet and consent form for DECIPHER can be downloaded to obtain and record informed consent.

vii) Founding member- 'The Human Variome Project'/ Member- International Scientific Advisory Committee (ISAC)/ Member- HUGO Scientific Advisory Committee - HUGO-SAC HUGO Forum.

I am closely associated with the Human Variome Project (www.humanvariomeproject.org) since it was founded in 2005 by the Late Professor Dick Cotton, the Professor of Genetics in the University of Melbourne, Australia. Its sole purpose is to ensure that all information on genetic variation and its effect on human health can be collected, collated, curated, interpreted and shared freely and openly. I have served this organization in different roles, particularly as member of the International Scientific Advisory Committee (ISAC). It now represents the **Global Variome** group, a non-governmental organization (NGO) recognised by the United Nations Educational, Scientific and Cultural Organisation (UNESCO). The Global Variome provides support services to the international coordination work of the Human Variome Project, now amalgamated with the

Human Genome Organization International (HUGO) and the Human Genome Variation Society (HGVS). I continue to serve on the newly structured HUGO International Scientific Advisory Committee (HUGO-ISAC).

viii) Chair- HUGO Education Committee

This new professional body was created following the merger of the three major global genomic organizations. These include the Human Genome Organization International (HUGO), Human Variome Project (HVP) and the Human Genome Variation Society (HGVS). The consortium is known as the Global Variome. I am the first Chair of the newly established HUGO- Education Committee. It includes 21 other members from different nations, particularly from the emerging low and middle income countries (LMICs). This committee would be responsible for setting standards, curriculum and advising on all matters related to the genomic education and training. Emphasis is given on developing and/or enhancing genomic skills and competencies. Selected areas include current global genomic educational / training activities, and design and implementing the teaching and training programs.
The HUGO Executive Board has approved the Charter of the HUGO- Education Sub-committee.

Aims and Objectives include-

1. Courses and seminars incorporating new knowledge and advances genome science and technology.
2. Aiming to incorporate and enhance the skills and competencies across the worldwide diagnostic genomic laboratories.
3. Develop mechanisms for delivering the integrated and comprehensive genomic education and training programs employing the 'state of the art' digital and artificial intelligence methods.
4. Emphasis on empowering and enhancing skills and competencies required for specific sector, for example laboratory genomics, computational genomics, clinical genomics, genetic/ genomic counselling etc.
5. Explore and liaise with current global genomic educational / training activities and programs
6. Identify and develop good working relationships with national and international human genetic and/or genomic organizations and institutions, for example ASHG, ACMGG, ESHG, BSGM, NHGRI, SIAMG, APHG, AGSHG, H3Africa and Country Node (s) of the Human Variome Project extending to the Latin America.
7. Lead role in designing and implementing genomic education teaching and training programs for students/ trainees, non-genetic physicians and healthcare professionals, general public and continued adult education etc.
8. Explore and develop courses/ guidance related to bioinformatics, digital and artificial intelligence in diverse human genomic applications.

9. Identify and develop close links with established course leaders/ teachers, for example the Harbor Genetics Course, European Diploma in Medical Genetics, Masters Genetic Counselling Programs (UK, USA, Canada, South Africa, Australia, India, Philippines etc.) and many other courses and degree programs.
10. Identify and support human genomic education and training targeted at specific areas and gaps in developing and under-resourced nations.

Achievements and Impact of the HUGO Education Committee

Summary:

'The HUGO Education Committee, with its six sub-committees, comprising numerous highly active members from many countries including many low-middle income nations. Major achievements include global template for genetic counselling, multi-disciplinary genomic healthcare applications, targeted training for variant interpretation, and development of online HUGO genomic education portal accessible to 100 countries worldwide. HUGO EdComm currently works and continues to develop close working relationship with GGNET and other global organisations committed for global genomic healthcare mission.'

The HUGO Education Committee, with its six sub-committees, comprising numerous highly active members from many countries around the worldwide, has been particularly busy in 2024. Co-chaired by Profs Dhavendra Kumar (DK, London, UK), Angela Solano (AS, Buenos Aires, Argentina) and now also Edward Tobias (ET, Glasgow, UK), the committee has been represented at many events around the world. These have included talks (by Dhavendra Kumar, Edward Tobias, Charles Wray, Angela Solano, Alison McEwen, Carolyn Applegate, Julie Makani and Andreas Laner) at the committee's educational pre-conference workshop at the Human Genome Meeting 2024 in Rome, Italy; an invited talk by ET at the BGC-I Conference, Bengaluru, India; and an invited presentation by AS, ET & DK at the ALAG Conference in Guadalajara, Mexicoin October. Additionally, the VEPTC 2024 course was (again) successfully led by Andreas Laner, in Palermo, Italy, in October 2024.

Through its active and geographically widespread international members, the HUGO Education Committee maintains strong direct links to several other international genomics education committees. For example, ET is a member of the ESHG EduComm and both DK and ET are members of the Global Genomics Network in Education and Training (GGNET) Partnership Board. Both DK and ET were invited to speak at GGNET's most recent international summit meeting at the Sanger Institute, Cambridge, UK.

Perhaps as a consequence of the committee's many activities, the HUGO Education web pages continue to receive an increasing frequency of visits and return-visits. In fact, the pages have now been visited from over 100 countries, worldwide. Amongst many activities of the HUGO Education Committee, there is emerging evidence of its impact in Low and Middle Income Countries as recommended by the WHO Science Council on Genomics. In this context, DK leads the South Asia Genomic Healthcare Alliance, initiated by the Genomic Medicine Foundation UK, and in collaboration with several academic institutions and healthcare providers across South Asia. The genomic education remains central to its many objectives. Several human genetic and genomic units have set up dedicated courses for genetic counselling, birth defects, rare diseases, cancer genetics and laboratory genomics.

It is anticipated that 2025 will be an equally busy year for the committee. A pre-conference educational workshop (to be chaired by ET) is being prepared for 12th March at HGM2025 in Durban, with several speakers representing the committee. In addition, in 2025, preparation and submission of several manuscripts, resulting from the committee's work, is planned. These will include papers discussing: the results of the recently conducted global survey of educational needs of healthcare professionals; DNA variant interpretation in molecular diagnostics; genetic counselling training (GC) in LMICs; GC in Southern Africa; GC for DSDs in LMICs; and a comprehensive new international-consensus GC curriculum.

Pre-Conference Workshop

Organised by- **HUGO Education Committee**

Date: **12th March 2025**

Time- **0830-1230 (local time)**

Title: **'Skills and Competencies for Multi-Disciplinary Genomic Healthcare'**

Aim: **'Genomic knowledge and skills of nursing and allied healthcare professionals"**

Objectives:

1. Identify and develop knowledge and skills of the genomic professionals (clinical geneticist, genetic counsellor, genome scientist) as potential educators/trainers.
2. Select and include general and specific aspects of genomic healthcare in the training program.
3. Format of training- formal didactic, tutorial/interactive, case-based/hands on, virtual, written document/ training manual.
4. Case-based training (malformation syndrome; metabolic disorder; neurology; cardiology; oncology)
5. Evaluation and assessment

Human Genome Organisation (HUGO International) Education Committee: development of greater worldwide access to genomic educational resources, training and courses.

Edward S. Tobias[1,2] on behalf of the HUGO International Education Committee & its sub-committees (SCs)

HUGO Education Committee: Dhavendra Kumar[1] (Chair), Angela Solano[2] (Co-chair), Charles Wray[3] (SC1 Lead), Andreas Laner[4] (SC2 Lead), Christian Gilissen[5] (SC3 Lead), Sherifa Ahmed Hamed[6] (SC4 Lead), Zilfalil Bin Alwi[7] (SC5 Lead), Edward S. Tobias[1,2] (SC6 Lead), Carolyn Applegate[10], Qasim Ayub[11], Anna Benet-Pages[12], Huy Phuoc Do[13], Sultana Faradz[14], Maria Gil[15], Ada Hamosh[16], Vincent Harley[17], Annie Qurratulain Hasan[18], Luz Berenice Lopez Hernandez[19], Punyaram Kharbuja[20], Iscia Lopes-Cendes[21], Alison McEwen[22], Julie Makani[23],Kelly Ormond[24], Milena Paneque[25], Peter Robinson[26], Tilak R. Shrestha[27], Catherine Lynn T. Silao[28], Nara Sobreira[29], Narazah Mohd Yusoff[30]

[1]Academic Unit of Medical Genetics & Clinical Pathology, University of Glasgow (UofG), UK. [2]Clinical Genetics, West of Scotland Centre for Genomic Medicine, Queen Elizabeth University Hospital, Glasgow, UK. [3]Queen Mary University of London & St. Barts Hospital, London, UK. [4]Departamento de Análisis Clínicos, CEMIC, Buenos Aires, Argentina. [5]The Jackson Laboratory, USA. [6]Medical Genetics Centre, Munich, Germany. [7]Radboud University, Nijmegen, Netherlands. [8]Faculty of Medicine, Assiut University Hospital, Egypt. [9]Universiti Sains Malaysia. [10]Johns Hopkins School of Medicine, USA. [11]School of Science, Monash University, Malaysia. [12]Medical Genetics Centre, Munich, Germany. [13]Vietnamese Organization for Rare Diseases, Vietnam. [14]Faculty of Medicine, Diponegoro University, Semarang, Indonesia. [15]University Agostinho Neto, Luanda, Angola. [16]Department of Genetic Medicine, Johns Hopkins University, Baltimore, MD, USA. [17]Center for Endocrinology & Metabolism, Hudson Institute of Medical Research, Melbourne, Australia. [18]Kamineni Hospital, Hyederabad, India. [19]Universidad Autónoma de Guadalajara, Mexico. [20]Bhaktapur Cancer Hospital, Nepal. [21]University of Campinas, São Paulo, Brazil. [22]University of Technology Sydney, Australia/New Zealand. [23]Muhimbili University of Health and Allied Sciences, Tanzania. [24]ETH Zurich, Switzerland. [25]University of Porto, Portugal. [26]The Jackson Laboratory, USA. [27]Tribhuvan University, Kathmandu, Nepal. [28]Institute of Human Genetics, NIH Philippines, Manila, Philippines. [29]Johns Hopkins University, USA. [30]Universiti Sains Malaysia (USM), Malaysia.

SUMMARY

The new Human Genome Organisation (HUGO) Education Committee, was established in 2021, to facilitate state-of-the-art human genomic education and training, worldwide, including in low- & middle-income countries (LMICs) (1). The current international members of the committee are each active members of other national and international genetic & genomic organisations & stronger links are currently being formed to ESHG & the Latin American network, RELAGH. The committee, led by DK & AS, now comprises 6 active sub-committees, led by CW, AL, CG, SAH, ZBA & EST, respectively. We report on the wide range of recent & ongoing global activities undertaken by the HUGO Education Committee.

New HUGO web pages: worldwide resources, societies & courses

Three new custom-designed HUGO educational web pages have been launched, providing access to numerous free genetic & genomic educational resources worldwide, to up-to-date links to the major professional genetic societies worldwide and to online courses. The pages can be visited at https://www.hugo-international.org or by using the QR code below. These pages, in approx. one year since launch, have been accessed from 85 countries worldwide, including many LMICs. The number of returning visits to the new web pages has increased by 2.7-fold over the first 12 months. Please email Prof Ed Tobias at edward.tobias@glasgow.ac.uk with any suggestions or feedback.

Figure 1: The new HUGO Education web pages, with links to over 100 genetic and genomic educational resources, to the major professional genetics societies in each continent and to online courses on genetics and genomics.

Figure 2: Map showing the 85 countries (including, for example, at least 7 in South America) from which the new HUGO Education web pages have been accessed, since launch in February 2022. Shading intensity is indicative of the proportion of total visits.

Survey to identify genomics-related educational needs, worldwide

The HUGO Clinical Genomics and Genomic Medicine education sub-committee is seeking input on the use of genetic and genomic data and resources from practising physicians worldwide. The detailed survey is intended for a wide range of physicians (other than clinical/medical geneticists). The anonymised survey data will assist in the development of appropriate clinical & general education resources for healthcare providers across the globe. The survey, hosted by The Jackson Laboratory, USA, is now underway & can now be accessed via the QR code below.

Figure 3. One of the approximately 20 questions in the HUGO survey, designed to determine the genomics-related educational needs (and attitudes) of healthcare providers, across medical specialties including primary care, worldwide. Please share the survey across your professional network of (non-geneticist) physicians or appropriate professional societies.

Links with other international organisations

The international members of the committee are each active members of other national and international genetic and genomic organisations. These include: the European, African, Australasian, Asia Pacific, & American Societies of Human Genetics; the European Certificate in Medical Genetics & Genomics (ECMGG) examination; Human, Heredity and Health in Africa (H3Africa); & the Genomic Medicine Foundation UK.

Ongoing HUGO Education sub-committee activities

The six sub-committees are jointly generating a catalogue of genomics training modules that could be delivered upon request, in addition to other individual activities that are summarised in the table below.

Sub-committee	Members	Main current activities (in addition to contributing to a catalogue of educational content, modules & presentations for future training by the Education Committee)
Genome sequencing and technology	**Charles Wray, USA (Chair)** Anna Benet-Pages, Germany; Iscia Lopes-Cendes, Brazil; Peter Robinson, USA; Nara Sobreira, USA	Creating a survey of Education Committee members on their perception of genomics training needs worldwide. Collating and analysing the data resulting from that survey. Also: hosting the worldwide survey (below)
Variant interpretation and genome databases	**Andreas Laner, Germany (Chair)** Iscia Lopes-Cendes, Brazil; Vincent Harley, Australia; Sherifa Hamed, Egypt; Bin Alwi Zilfalil, Malaysia; Tilak Shrestha, Nepal; Huy Do, Vietnam	Running the popular Variant Effect Prediction Training Course (VEPTC).
Computational genetics/genomics & bioinformatics	**Christian Gilissen, Netherlands (Chair)** Anna Benet-Pages, Germany; Charles Wray, USA	Running the ESHG/CEUR course on Clinical Genomics & next-generation sequencing (NGS). Running the ESHG Clinical NGS Data Interpretation course
Clinical genomics and genomic medicine	**Sherifa Ahmed Hamed, Egypt (Chair)** Edward Tobias, UK, Qasim Ayub, Malaysia; Ada Hamosh, USA; Iscia Lopes-Cendes, Brazil; Luz Berenice Lopez Hernandez, Mexico	Developing the detailed worldwide survey of physicians' genomics educational needs & attitudes, including under-represented communities (see Fig. 3). Analysing the resulting data from that survey.
Genetic and genomic counselling	**Zilfalil Bin Alwi, Malaysia (Chair)** NM Yusoff, Malaysia; S Faradz, Indonesia; TR Shrestha, Nepal; P Kharbuja, Nepal; CLT Silao, Philippines; C Applegate, USA; M Gil, Angola; AQ Hasan, India; A McEwen, Australia/New Zealand; M Paneque, Portugal; K Ormond, Switzerland.	Developing core curriculum guidelines for Genetic Counselling training, worldwide. Organising and running the genetic counselling workshop at HGM2023.
Genomic education for the general public	**Edward Tobias (Chair)** Qasim Ayub, Malaysia; Maria Gil, Angola; Sherifa Hamed, Egypt; Iscia Lopes-Cendes, Brazil; Narazah Yusoff, Malaysia; Huy Phuoc Do, Vietnam	Developing & maintaining HUGO's Education Committee's web pages. Forming links to ESHG & RELAGH. Compiling up-to-date lists, links & guide to worldwide educational resources (& patient-centered genomics organisations) for non-geneticists and the public. Co-running massive open online courses (MOOCs) on genetics, genomics & cancer genomics, suitable for wide range of audiences, with University of Glasgow Medical Genetics & Genomics team

Table 1: The activities of the 6 sub-committees of the HUGO Education Committee.

Conclusions & future development

In conclusion, several activities aiming to identify worldwide educational needs worldwide and also to facilitate the delivery of genomics education globally, including LMICs, have already been completed. Further work of the committee currently includes: distributing and running the international survey to identify the genomic education needs of non-genetics health professionals globally; the development of an international curriculum for training in genetic counselling; the creation of a catalogue of genomics training modules for worldwide education; running the Variant Effect Prediction Training Course (VEPTC) and Human Genome Variation Society (HGVS) nomenclature training; and the development of links with other genetic and genomic organisations worldwide.

References

1. Lee C., Antonarakis, SE, Hamosh A, Burn J. (2021). Three decades of the Human Genome Organization. Am J Med Genet A. 185(11):3314-3321.

Acknowledgements

The author is hugely grateful to all of his university, hospital, HUGO Education Committee & ESHG Education Committee colleagues for their assistance & support.

Comments please

Please email Prof. Tobias at Edward.Tobias@glasgow.ac.uk with any comments or suggestions.

ix) Panelist- Global summit of overseas Indian scientists and technologists, Government of India- The VAIBHAV project, convenor The Prime Minister of India Shri Narendra Modi

I served on the Panel of the prestigious global summit of the Indian origin overseas scientists and technologists convened by the Honourable Prime Minister of India Shri Narendra Modi. It was coordinated and steered by the eminent Indian Scientist Prof. Raghavan, the Principal Scientific Advisor to the Prime Minister's Office, New Delhi, Government of India.

I participated with two sessions-

1. **"Making medicine preventive, predictive, personalized and participatory" , Moderator: Dr. Anurag Agrawal, Director IGIB, CSIR, New Delhi, India; held on 19th October 2020.**

2. "Predictive and Therapeutic Genomics", 20th October 2020; Moderator, Dr. K. Thangaraj, Director- Centre for DNA Fingerprinting and Diagnostics (CDFD) & Deputy Director- Centre for Cell & Molecular Biology (CCMB), Hyderabad, Telangana, India.

x) **International Genomics Education and Training Summit**

As a member of the Global Partnership for Genomic Education, I have actively participated and contributed to the International genomics education and training workshops. The first training summit was held in November 2023 hosted by the Sanger Genome Centre. The second one is held in Athens, jointly organised by WHO Science Council and the UK NHS Genomic Medicine group. Aims and objectives of this programme include-

1. Promote genomics education and training globally and share experiences, opportunities and challenges;
2. Discuss and agree the purpose and structure_of a global genomics education and training network as related to the healthcare workforce;
3. Explore alignment to work being done through other international organisations and by industry;
4. Consider global and inclusive education and training themes and resource needs, with particular emphasis on patient/clinician partnerships, and considering gender, ethnic, language and geographical diversities;

5. Consider global research projects aligned to genomics education and training;
6. Develop an informed and collaborative plan for action.

xi)South Asia Genomic Healthcare Alliance (SAGHA)

"To organise and lead a professional group for promoting and supporting the genomic applications and translations in medicine and healthcare across South Asia"

THE GENOMIC MEDICINE FOUNDATION (UK)
FELLOWSHIP, SCHOLARSHIP, EDUCATION AND PROMOTION OF GENOMIC APPLICATIONS IN MEDICINE, HEALTHCARE AND SOCIO-ECONOMIC PROGRESS

www.genomicmedicine.org

Independent organization promoting application and translation of ***Genomics*** and other ***OMICS*** sciences in the current and future practice of clinical medicine, personalized healthcare & socio-economic progress

South Asia Genomic Healthcare Alliance (SAGHA)

Amongst the key projects of the Genomic Medicine Foundation UK (GMF-UK), the UK India Genomic Medicine Alliance (UKIGMA) has been one of the most popular initiatives of GMF-UK. It was set out with the aim of promoting and implementing the genomic applications in medicine and healthcare in India and neighboring regions through collaboration and partnership with clinical and academic institutions and organizations across the whole South Asia. Apart from the UK, many genomic professionals and scientists from other nations have also contributed. In view of the current vastly expanded collaborations, this alliance is now known as the South Asia Genomic Healthcare Alliance (SAGHA) effective 1st January 2024.

The SAGHA has many objectives as shown in the Table-1:

Table-1: Objectives of the South Asia Genomic healthcare Alliance

- Identify and recruit organisations and institutions engaged in scientific and applied research in genomics relevant to medicine and healthcare.
- Encourage collaboration with individual clinicians, scientists, and other professionals in population genetics, ethical & social issues and health economics.
- Develop a programme for training and skills development through series of structured courses, workshops and webinars in the key areas of applied and translational genomic medicine.
- Identify and develop partnerships to steer the multi-disciplinary specialist genomic healthcare with the sole objective of integration with the mainstream medical practice.

- Plan and carry out specific audit on the quality and outcomes of investments in Institutions and Laboratories as part of the current strategy for capital and infrastructure scientific developments.
- Develop and steer through individual or group research and innovations projects on related to utilization and the delivery of genomics led medical and healthcare, particularly in therapeutic interventions and new drug and devices development.

Collaborators and partners of the SAGHA have identified and agreed to work in several diverse fields relevant to the South Asia (Table-2):

Table-2: Fields of Interest to the UK India Genomic Alliance

- Genetic and Genomic Education
- Birth defects (Congenital Anomalies)
- Rare developmental disorders
- Cancer genetics and genomics
- Cardiovascular genetics and genomics
- Pharmacogenomics
- Genomic and Precision & Personalised Medicine
- Ethical, Legal & Social Issues

Many institutions, hospitals and independent organizations in the region (Figure-1) are committed to work together and deliver many projects (Table-3).

Table-3: Current projects of the SAGHA

- Indo-UK Genetic Education Forum
- Biennial South Asia Birth Defects Conference
- Indian cancer genetics interest group
- South Asia cardiovascular genomics consortium
- Decipher India (South Asia) consortium
- South Asia Pharmacogenomics Consortium
- South Asia Genome Ethics consortium

JAMMU- JAMMU & KASHMIR
AMRITSAR- PUNJAB
CHANDIGARH (UNION TERRITORY)
NEW DELHI- DELHI
DEHRADUN- UTTARAKHAND
LUCKNOW- UTTAR PRADESH
JODHPUR- RAJASTHAN
GWAUHATI- ASSAM
DIBRUGARH- ASSAM
MUMBAI- MAHARASTHRA
HYDERABAD- TEALNGANA
BANGALORE-KARNATAKA
MANIPAL-KARNATAKA
MYSORE-KARNATAKA
KOCHI- KERALA
CHENNAI- TAMIL NADU
VELLORE- TAMIL NADU
COLOMBO- SRI LANKA

Figure-1: SAGHA collaborators & partners across the South Asian subcontinent

In view of rapidly growing genomics awareness and interests across the entire South Asian region (Figure 2), the scope and remit of the UKIGMA is expanded to the entire South Asia. This is considered more relevant and well timed given the role and importance of genomics during and after the Covid-19 pandemic. Large majority of the South Asian inhabitants are aware of the importance of RT-PCR genome testing and the prevention offered by the mRNA vaccines (Pfizer and Moderna). In addition, parents and patients acknowledge the power of precision genomic diagnosis and specific treatment for rare genetic diseases, cancers, heart diseases and many other systemic diseases.

Figure-2: The current political map of the South Asia region; the South Asia includes Afghanistan, Pakistan, India, Nepal, Bhutan, Bangladesh and Sri Lanka (shown in red).

The new expanded UKIGMA includes neighboring nations (Figure-2). In the northwest sector, the scope and remit are broadened with the inclusion of Afghanistan and Pakistan. In the northeast, Nepal, Bhutan, Bangladesh and possibly Myanmar are included. It is anticipated that in future other nations from the Western Asia and the Southeast Asia might also be included. All these Low and Middle Income Countries (LMICs) have very basic infrastructure and healthcare facilities to cater diverse and distinct ethnic peoples. Work has already commenced by setting up the northwest and northeast genomics consortia. Initial response is overwhelmingly positive and very encouraging. However, major challenges and hurdles are likely due to inevitable intra-regional political and socio-economic variations.

The current projects are included in the newly structured SAGHA. In addition, the work has commended for developing a multi-author edited book (Editors-Dhavendra Kumar & Kumarsamy Thangaraj), the '***Medical and Health Genomics of South Asia***' commissioned by Elsevier, the leading life sciences publisher.

Advisory Council of the South Asia Genomics Alliance

Professor Dhavendra Kumar, The Genomic Medicine Foundation UK (Chair)
Professor Amarjit Bhanwer, Chair- North West India Genomics Consortium
Prof. Madhulika Kabra, Delhi & NCR Region
Prof. Amita Pandey, UP & Central India
Dr. Kumarsamy Thangaraj, Telangana & South India
Dr. Saswati Mukhoupadhyaya, West Bengal & South East India
Mrs. Reena Trivedi, Gujarat & & South West India
Dr. Gayatri Gogoi, Chair- North East India Genomics Consortium
Professor Vajira Dissanayake, Sri Lanka Genomics & South East Asia
Dr. Nilam Thakur, Nepal Clinical Genomics Centre, Kathmandu, Nepal
Dr. Thinley Dorji, Bhutan Genomics Centre, Thampa, Bhutan

The alliance is very keen and open to include collaborators from Afghanistan, Pakistan, Bangladesh, Myanmar and the South East Asia.

Draft prepared by-

Professor Dhavendra Kumar,
Chair- South Asia Genomic Healthcare Alliance
CEO/ Medical Director- Genomic Medicine Foundation UK Ltd.

xii) 'Global Genomics', Science Council, World Health Organization (WHO)

The newly established Science Council of the World Health Organization (WHO) organised series of workshops aimed at accelerating access to genomic technologies for global health. This initiative is led by Professor Soumya Swaminathan, the Chief Scientist for WHO. I have had the privilege to participate in the second workshop focussed on 'technical and financial considerations'.

World Health Organization | Health Topics | Countries | Newsroom | Emergencies | Data | About WHO

World Health Organization

Home / Newsroom / Events / Detail / WHO Science Council Workshop Series: Accelerating access to genomic technologies for global health

WHO Science Council Workshop Series: Accelerating access to genomic technologies for global health

5 November – 2 December 2021

Workshop 1: Global health benefits of genomics
Friday, 5 November 2021, 14:00 – 18:00 CET

Workshop 2: Technical and financial considerations
Thursday, 18 November 2021, 13:30 – 17:30 CET

Workshop 3: Historical, ethical, legal, regulatory and related considerations
Thursday, 2 December 2021, 13:30 – 17:30 CET

About this event

Advances in science and technology hold great promise for new and improved ways to address global health and to support healthier populations worldwide. Achieving the World Health Organization's (WHO's) traditional goals, as well as more recent and more explicit objectives such as the triple billion targets, will require foresight and careful consideration of how new technologies support and align with WHO's mission and purpose. To this end, the WHO Science Council, a group of distinguished scientists from around the world, was formed to work with WHO's Chief Scientist, Dr. Soumya Swaminathan, on priority issues and to advise the WHO on scientific breakthroughs and new technologies that can help the WHO achieve its goals.

Genomics Technologies

The Science Council has identified genomic technologies as having significant implications for public health, given their broad applications across health and disease states and throughout the human lifespan, as abundantly documented in wealthy countries and during the Covid-19 pandemic.

The Science Council is organizing a series of three workshops to better understand the significance of accelerating access to genomics technologies and the difficulties of doing that, especially in low- and middle-income countries.

Objectives of the workshop series are:

- To gather information about the benefits and use of genomic technologies for low- and middle-income countries
- To discuss the impediments to implementation, and brainstorm on possible solutions
- To gain perspective on approaches and lessons learned from both successful and failed implementations
- To engage communities of experts and stakeholders in developing recommendations based on understanding diverse needs, applications, and considerations of low- and middle-income countries

Related

World Health Organization

WHO Science Council Workshop Series
Accelerating Access to Genomics Technologies for Global Health

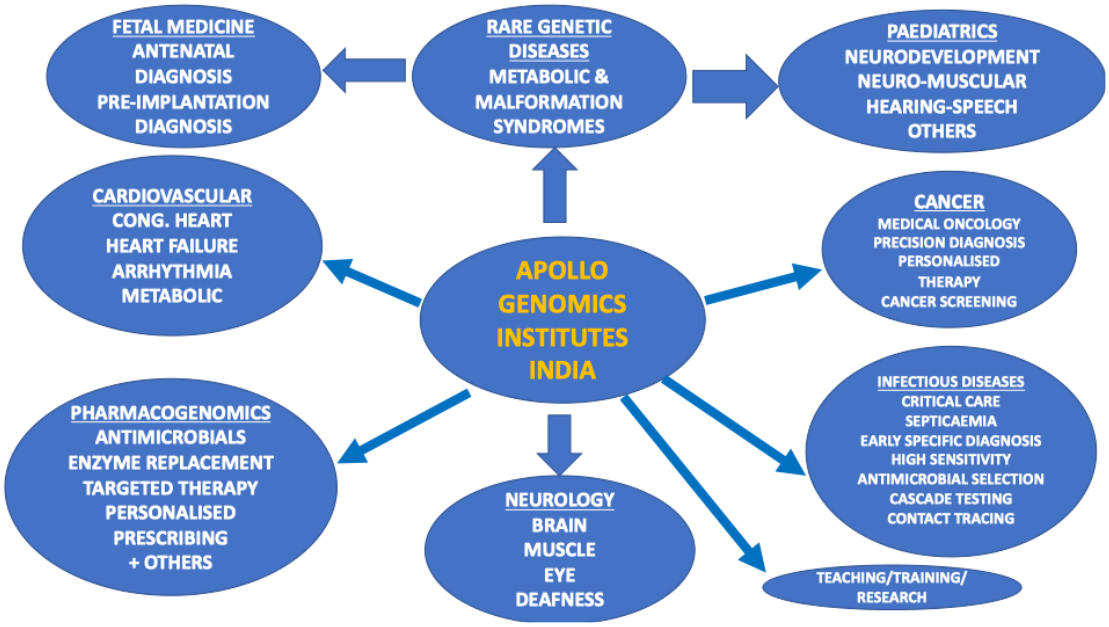
Workshop 2: Technical and Financial Considerations
1330-1730h CET Thursday, November 18, 2021

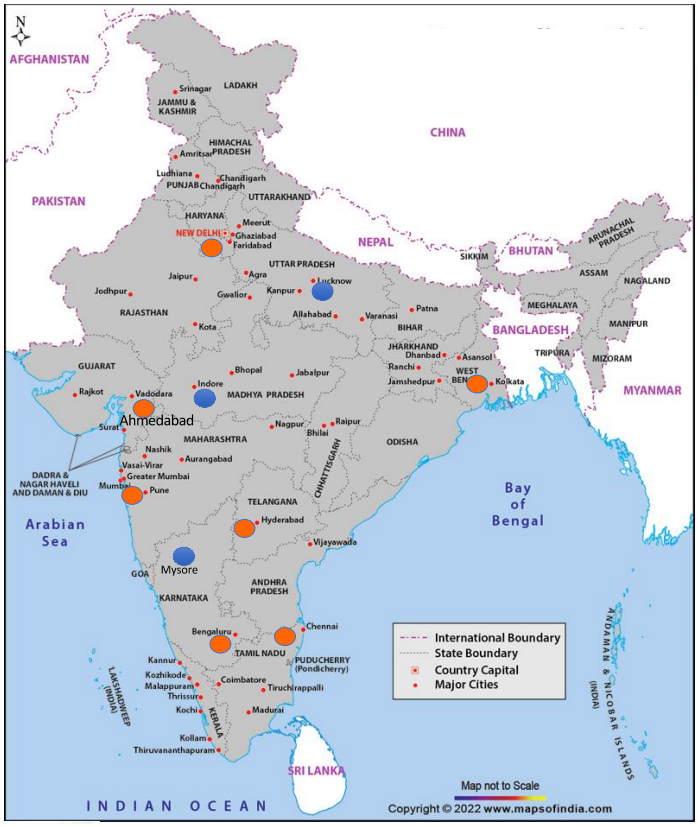
Workshop agenda

Workshop flyer

xiii) Senior Consultant Adviser- Apollo Genomics Institutes, Apollo Group of Hospitals, India

a)Organisation





ESTABLISHED:

DELHI, MUMBAI, AHMEDABAD, KOLKATTA, HYDERABAD, BANGALORE, CHENNAI

UNDER DEVELOPMENT:

LUCKNOW, MYSORE, INDORE

CLINICAL GENOMICS; GENOMIC COUNSELLING; MULTI-DISCIPLINARY GENOMIC HEALTHCARE; GENETIC AND GENOMIC SPECILIAST COURSES; GENOMIC RESEARCH & DEVELOPMENT; CONTINUED MEDICAL/PROFESSIONA/ PUBLIC/MEDIA EDUCATION

b) Scope and Remit

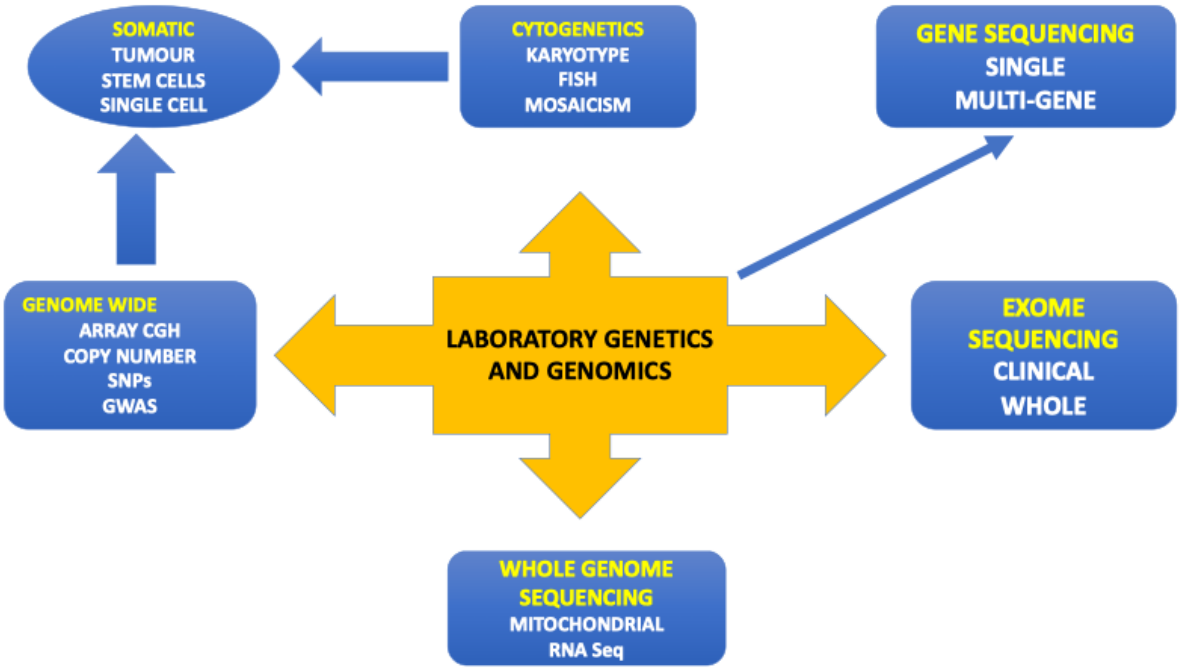
- CLINICAL GENOMICS- PRECISION DIAGNOSIS AND PERSONALISED MANAGEMENT OF GENETIC AND GENOMIC DISEASES
- GENOMIC COUNSELLING- PERSONALISED GENETIC AND GENOMIC ADVISORY AND SUPPORT TO PATIENTS, PARENTS AND FAMILIES
- MULTI-DISCIPLINARY GENOMIC HEALTHCARE- CLOSE LIAISON WITH MULTI-DISCIPLINARY TEAMS FOR EFFECTIVE / AFFORDABLE CARE & PREVENTIVE-PERSONAL GENOMIC HEALTHCARE
- GENETIC AND GENOMIC SPECILIAST COURSES- CLINICAL GENOMICS, GENOMIC COUNSELLING, SPECIALIST GENOMICS
- GENOMIC RESEARCH & DEVELOPMENT- JOURNAL CLUB/ PROJECTS/PUBLICATIONS/ PROTOCOLS/ DISSEMINATION/ DATABASE
- CONTINUED MEDICAL/PROFESSIONAL EDUCATION- APOLLO GENOMIC HEALTHCARE SEMINARS FOR MEDICAL, NURSING, ALLIED HEALTH PROFESSIONALS, NGOs, GENERAL PUBLIC-MEDIA

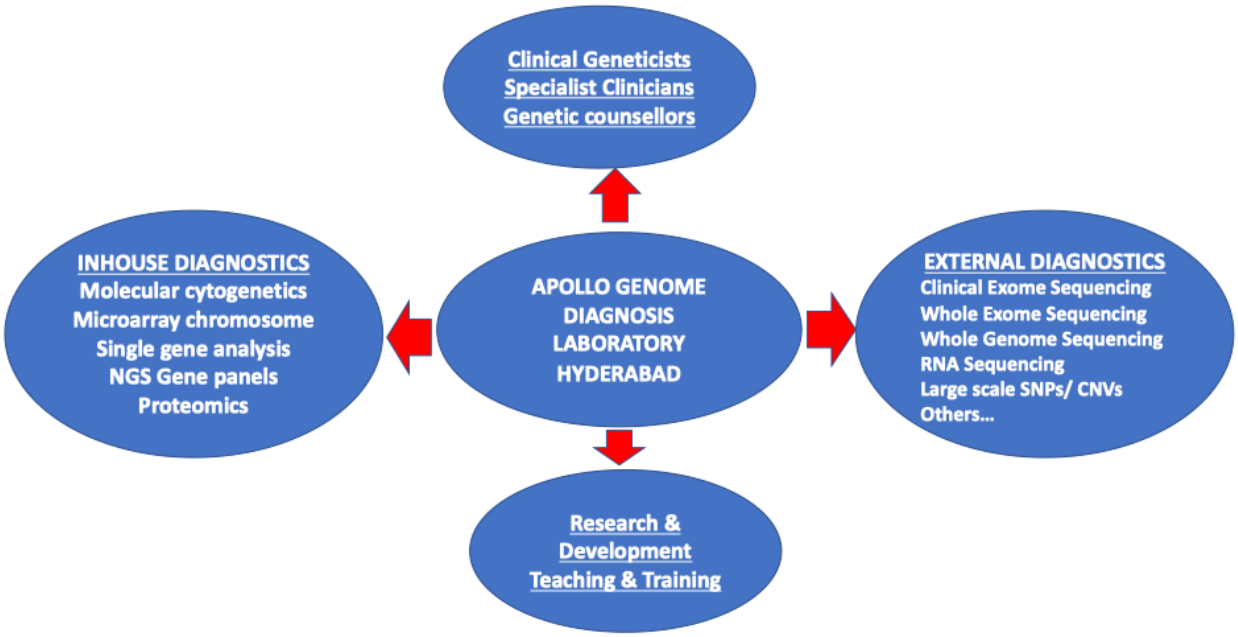
c) Apollo genetic and genomic services

Comprehensive clinical genetics and genomic medicine service covering wide-ranging specialist areas:

•Genetic disease diagnosis with diagnostic genetic testing
•Detailed assessment of birth anomalies
•In depth review and analysis of the family history
•Specialist advice on cousin marriages (consanguinity)
•Genetic and genomic counselling
•Genetic risk review and assessment (for example breast/ovarian & bowel cancer) •Predictive or pre-symptomatic genetic testing
•Genetic & genomic screening for life style and health counselling
•Prenatal screening and testing for chromosomal abnormality or specific genetic disease
•Pre-implantation genetic diagnosis for preventing recurrence of high risk genetic disease
•DNA testing for disputed paternity or identity
•Medical-legal review and Expert Witness reports related to genetic or possible genetic condition

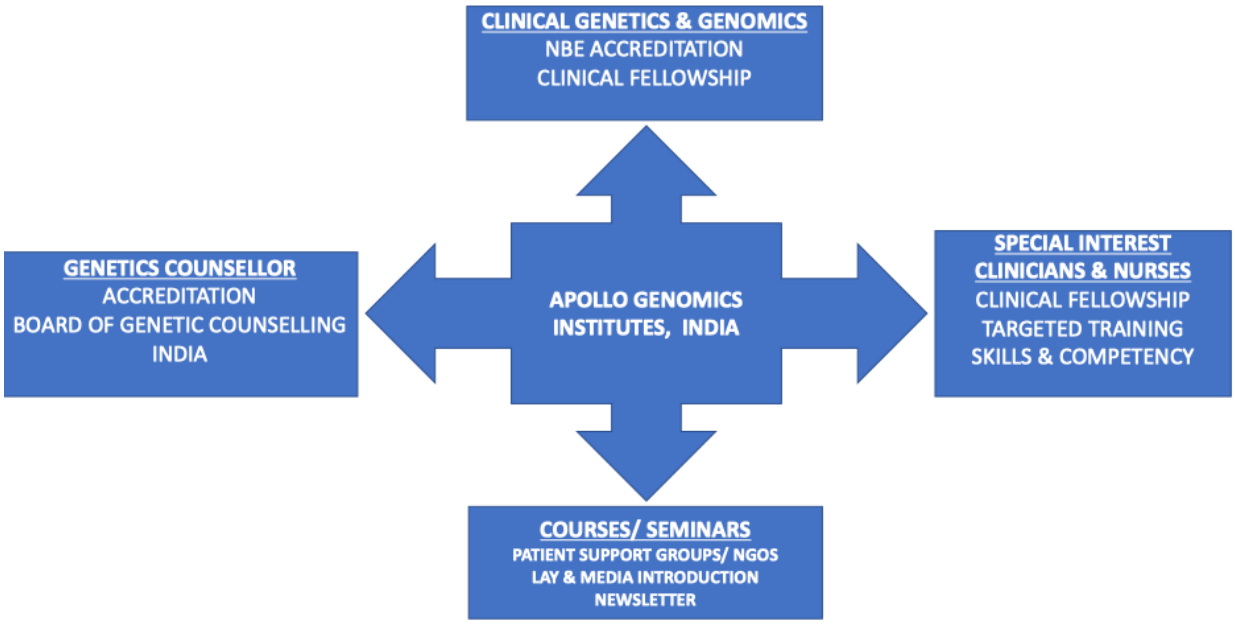
d)Apollo Genome Diagnosis Laboratory



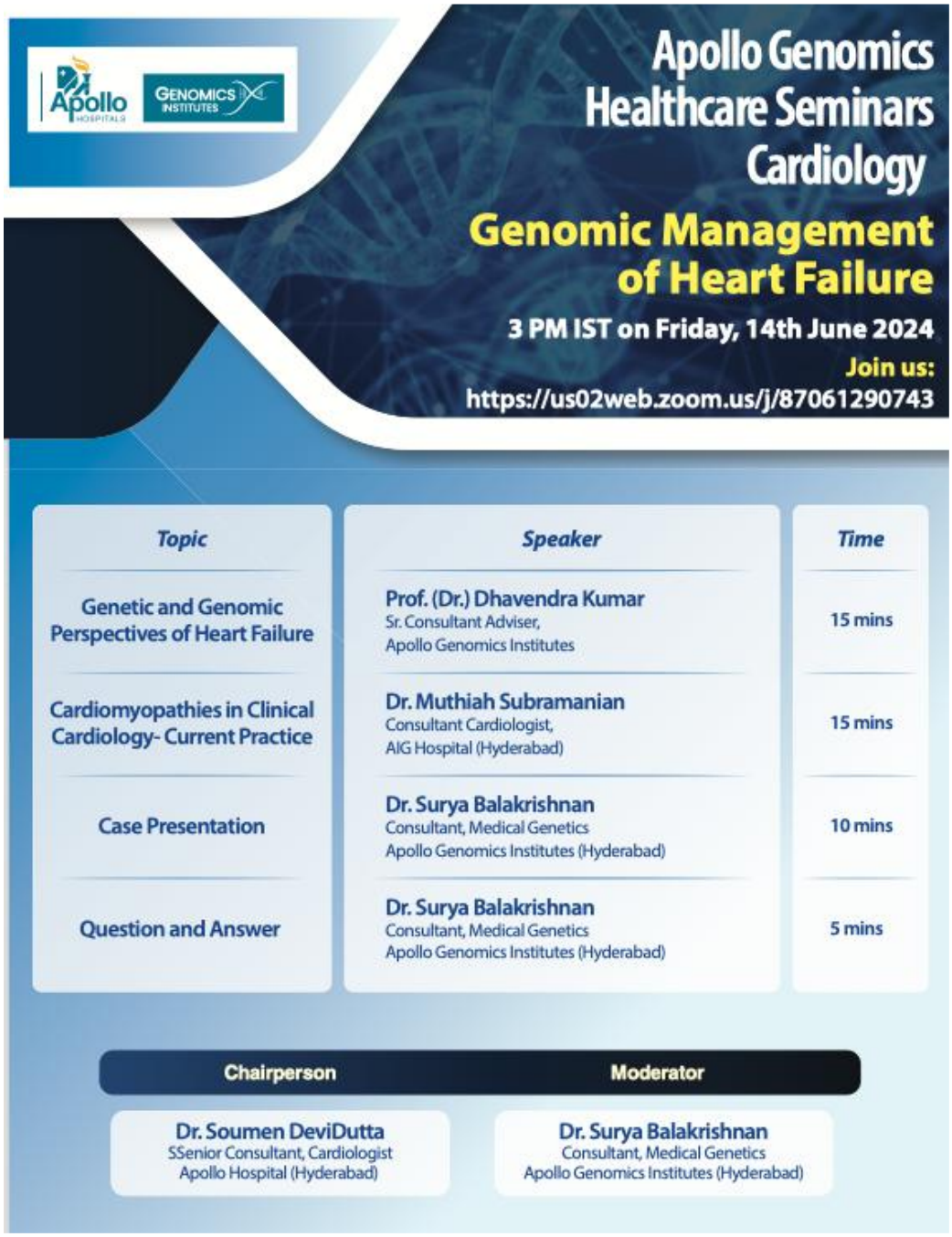


e) Apollo Genomics Academy

- Clinical case presentations (weekly)
- Continued professional development / Grand rounds (monthly)
- Journal club (monthly)
- Interactive seminars with other clinical specialty teams
- Informative discussions on key and topical issues with families, patient support groups, NGOs, Medial and general public. These could be via tele links, virtual online discussions, journalists interviews, and briefings for TV including other digital channels.



- Apollo genomic healthcare seminars (monthly)



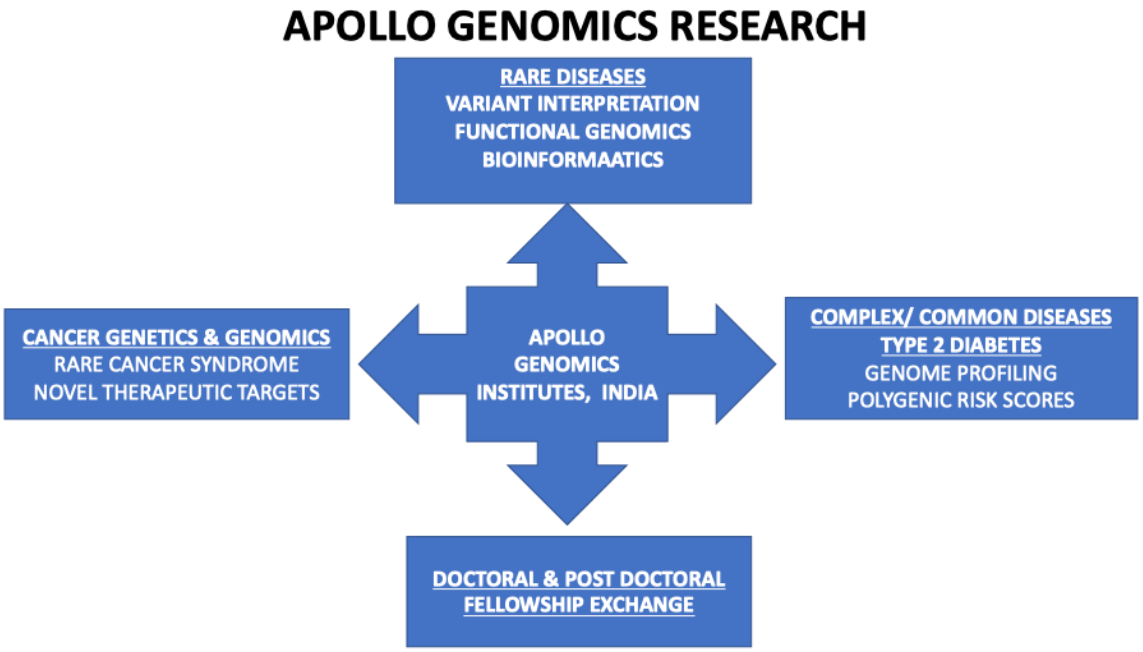
Monthly online seminars on selected areas of clinical genomics and genomic medicine delivered by invited external speakers along with relevant clinical case presentations by the Apollo Genomics Academy team. Each event has a specific theme delivered by a team of experts including an invited renowned guest speaker.

Session	Date	Department	Speakers	Chairperson	Moderator	Topic
1	14th Dec-22	Cardio	Prof. (Dr.) Dhavendra Kumar	Prof. (Dr.) S. K. Agarwal	Dr. Divya Agarwal	Genomic Perspectives Of Chronic Heart Failure
2	20th Jan-23	Cardio	Prof. (Dr.) Dhavendra Kumar	Dr Arun Aggarwal	Dr. Divya Agarwal	Inherited Arrhythmia Syndromes- Diagnosis and Management'
3	17th Feb-23	Oncology	Prof. (Dr.) Dhavendra Kumar Dr Surya	Dr Manish Singhal	Dr. Divya Agarwal	1. Current Clinical Cancer Genomics in Practice 2.Genetic paradigm of Cancer
4	17th Mar-23	Pediatrics	Prof. (Dr.) Dhavendra Kumar Dr Dipanjana Datta	Dr. Vijay Yewale	Dr. Divya Agarwal	1.Molecular diagnosis in rare malformation syndromes in clinical pediatrics 2.Multi-disciplinary care of rare malformation syndromes
5	**26th May-23**	Nephro	Prof. (Dr.) Dhavendra Kumar Prof. Shivaram Hegde Dr. Sanjay Maitra	Prof. Sanjiv Jasuja Dr. Mragank Gaur	Dr Surya Balakrishnan	1.Genomic Insights of Clinical Nephrology 2.Genomic Approach to the Child with Acute Renal Disease 3.Role of Genomics in Kidney Transplantation
6	**28th July-23**	Fetal Medicine	Prof. (Dr.) Dhavendra Kumar Dr Akshata	Dr Anita Kaul	Dr Snehal	Genomic Fetal Medicine- Opportunities and Limitation Fetal Medicine - Bridging the Gap
7	**8th September-23**	Cardio	Prof. (Dr.) Dhavendra Kumar Dr Soumen Devi Dutta	Prof. (Dr.) Narendra Nath Khanna	Dr. Saswati Mukhopadhyay	'Genomics input for Precision Clinical Cardiology- Dealing with the Sudden Cardiac Death' 'Cardiac surveillance for the 'at-risk' family'
8	**22nd September**	Pediatrics Ortho	Prof. (Dr.) Dhavendra Kumar Dr. Divya Agarwal	Dr Bipin Puri	Dr Surya Balakrishnan	Congenital bone diseases in clinical Orthopaedics". Utility of Genomic evaluation in management of Pediatric skeletal disorders- case illustrations".
9	**27th October-23**	Multi OMICS	Prof. (Dr.) Dhavendra Kumar	Dr. Ajaya Kumar	Dr Priya	Integrated multi-OMICS Medicine- the emerging paradigm for precision and personalised medicine'
10	**17th November-23**	Oncology	Prof. (Dr.) Dhavendra Kumar Prof. Rajiev Saran Dr. Arti Sharma Dr. Alec Correa	Dr Rakesh Jalali	Dr Indumati	'Genetic and Genomic Perspectives of Cancer' Clinical cancer genetics- the outcomes of Tata Memorial Cancer Hospital Genetics Clinic' 'BRCA in Ovarian Cancer- the UK protocol' Genomics driven Cancer Therapy'
11	**12th January-24**	Gastro	Prof. (Dr.) Dhavendra Kumar Dr. George Mells Dr. Asif Jah	Dr. Aabha Nagral	Dr Snehal	'Genetic Hepato-Biliary Disorders in Clinical Medicine' 'Genetic Influences in Liver Disease 'Surgical Consideration in Genetic Liver Diseases
12	**16th February-24**	ENT	Prof. (Dr.) Dhavendra Kumar Dr. Divya Agarwal Dr Sunil Narayan Dutt	Dr Ravi Meher	Dr. Parag Tamhanker	'Clinical Genetics Approach to Hereditary Deafness' 'Genetic Management of Hereditary Deafness Syndromes' 'Challenges of Cochlear Implantation in Genetic Deafness'
13	**29th February-24**	Rise for the Rare "Rare Disease Day"	Apollo Genomics team	Dr Rohit Bhojraj	Dr Dipanjana/ Upasana	Case presentations on Rare Diseases

14	**22nd March-24**	Genetic Dermatology	Prof. (Dr.) Dhavendra Kumar *Professor John McGrath* Dr Saswati Mukhupadhyay	Dr. Ravi K Joshi	Dr Snehal	Scope and Spectrum and of Genodermatoses- an Introduction' Molecular perspectives of clinical dermatology' Epidermolysis Bullosa- case presentations'
15	**26th April-24**	Genetic Opthalmology	Prof. (Dr.) Dhavendra Kumar Dr Saswati Mukhupadhyay	Dr. Shalini Shetty	Dr Surya Balakrishnan	'Current practice of genetics in clinical ophthalmology' Case presentations
16	**11th May-24**	ENT	Dr Diya Aggarwal Dr. Priya Jain Dr. (Prof) Ameet Kishore	Dr. Arun Agrawal, Dr. Shambhavi Seth, Dr. Ambika Gupta	Kriti Menon	Harmonizing Voices: Navigating the Spectrum of Speech and Communication Disorders
17	**14th June-24**	Cardio	Prof. (Dr.) Dhavendra Kumar Dr. Muthiah Subramanian Dr. Surya Balakrishnan	Dr. Soumen DeviDutta,	Dr. Surya Balakrishnan	Genomic Management of Heart Failure
18	**12th July-24**	Fragile X	Prof. (Dr.) Dhavendra Kumar Mrs Shalini N Kedia Dr.Dipanjana Dutta	Mrs Shalini N Kedia	Dr. Indhumathi N	Management of the Fragile X Syndrome'
19	**27th September-24**	Neurology	Prof. (Dr.) Dhavendra Kumar Dr. Ann Agnes Mathew Dr. Divya Agarwal	Dr. Jyotsna A.S	Upasana Mukherjee	Genetics and Genomics of Cerebral Palsy- New Clinical Dimensions'
20	**18th October-24**	Dental	Prof. (Dr.) Dhavendra Kumar Prof. Angus Clarke, Dr Surya Balakrishnan Dr. Divya Agarwal	Dr. Prema Yadav	Dr. KATHIRVEL.M	Dental Anomalies in Rare Disorders
21	**26th Nov-24**	Integrated Medicine	ACIG and Apollo Genomics Team	Dr Rajiv Vasudevan Prof N. K. Ganguly	Dr Anjali Arya	Integration of Multi-Disciplinary Medicine for Future Healthcare
22	**20th Dec-24**	Immune Deficiency Disorders'	Prof. (Dr.) Dhavendra Kumar Dr Nita Radhakrishnan Dr Ambika Gupta	Dr Umair Bargir	Ms Shilpa Kamble	Primary Immune Deficiency Disorders'
23	**31st Jan-25**	Hyper mobility syndromes	Prof. (Dr.) Dhavendra Kumar	**Prof. Dhavendra Kumar**	**Dr.ShibiKanan**	**Clinical and genetic heterogeneity of hypermobility disorders**

- Applied clinical research

The Apollo Genomics Academy is actively pursing and developing a strong collaborative research programme as shown in the Figure. The governance of this initiative is managed by the Apollo Hospitals Research and Ethics Group. Academic affiliations are offered by the Apollo University. It is a multi-specialty programme managed by like-minded clinicians who are keen to develop and conduct quality clinical applied research to enhance patient care harnessing new diagnostic and therapeutic avenues.



APOLLO GENOMICS RESEARCH CONSORTIUM

Professor Dhavendra Kumar, Senior Consultant Adviser, Apollo Genomics Institutes, Apollo Group, India

Introduction

During the last three years, the Apollo Group has invested in setting up the Genomic Healthcare network across major Apollo Hospitals. This network, designated as Apollo Genomic Institutes, is the only comprehensive and integrated genomic healthcare services provider in the whole country including neighbouring South Asia regions (see Figure-1). This network is supported by the AHEL Laboratories in Hyderabad. All Institutes have qualified clinical geneticists, genetic counsellors and supporting managerial professionals. In addition, there are physicians, surgeons, nurses and counsellors from other specialties closely working with the genomics team. The whole genomics team work together under the umbrella of Apollo Genomics Academy.

Main objectives of the Apollo Genomic Healthcare is to offer 'state of the art' clinical genetic/ genomic services supported by experienced and board certified genetic counsellors. Many other multi-disciplinary clinicians and allied healthcare professionals work closely with the core genomics team. There are weekly case presentations along with monthly journal club and the grand round. In addition, the Apollo Genomic Healthcare Webinars are offered to the whole Apollo Group, and including external audience. There is active collaboration for DNB training programs and research based projects.

Figure-1: Apollo Genomics Institutes across India

Contd…Page 2

One of the objectives of Apollo Genomics Institutes includes 'Research and Development (R&D). So far limited progress has been made in this context, largely due to being a new service development, limited skilled manpower and lack of targeted funding. It is proposed to organise the Apollo Genomics Research Consortium within the remit of the Apollo Research and Innovations (ARI) organisation. Main objectives of the Consortium include to plan and carry out applied research for developing precision diagnostics and targeted therapy protocols to enhance standards of multi-disciplinary specialist healthcare across the Apollo Hospitals Group. In addition, the Consortium shall carry out pilot projects for the prevention of common and uncommon genetic diseases.

Key Research Areas

1. Validation of genome sequencing in rare genetic disease.
2. Evidence based protocols for genomic interventions in foetal medicine.
3. Pharmacogenomics analysis of drugs response and safety including drug repurposing.
4. Genomic analysis for the outcomes of acute cardiovascular events- myocardial infarction, sudden collapse, chronic heart failure, and stroke.
5. Genomic analysis for selected targeted/personalised cancer therapy.
6. Pre-conceptional genomic testing for the prevention of genetic disease

Location

Apollo Genomics Institutes in various places
Collaborative centres- other laboratories including research units in IITs etc.

Funding

Initial 'start up' funding from ARI leading to external funding from governmental (ICMR, DBT, CSIR Labs like CDFD & CCMB, DBT-Wellcome Alliance) and non-governmental (NGOs, Pharma & Tech Companies and other philanthropic organisations).

Governance

Jointly through Apollo Genomics Institutes and Apollo Research and Innovations. Ethical aspects would be governed on the basis of current guidelines and international standards.

Membership

All members of the Apollo Genomics Academy representing Apollo Genomics Institutes.

Dhavendra Kumar, 20th May 2024.

- Publications

a) Special issue 'Genomic Medicine' for the 'Apollo Medicine', official journal of Apollo Hospitals, India

Vol 20 | April-June 2023 | Issue 2

Apollo MEDICINE

ISSN: 0976-0016

Genomic Medicine

Apollo Medicine

Volume 20 ¦ Issue 2 ¦ April-June 2023

Guest Editor : Dhavendra Kumar
Editorial Advisor: Divya Aggarwal & Kriti Menon

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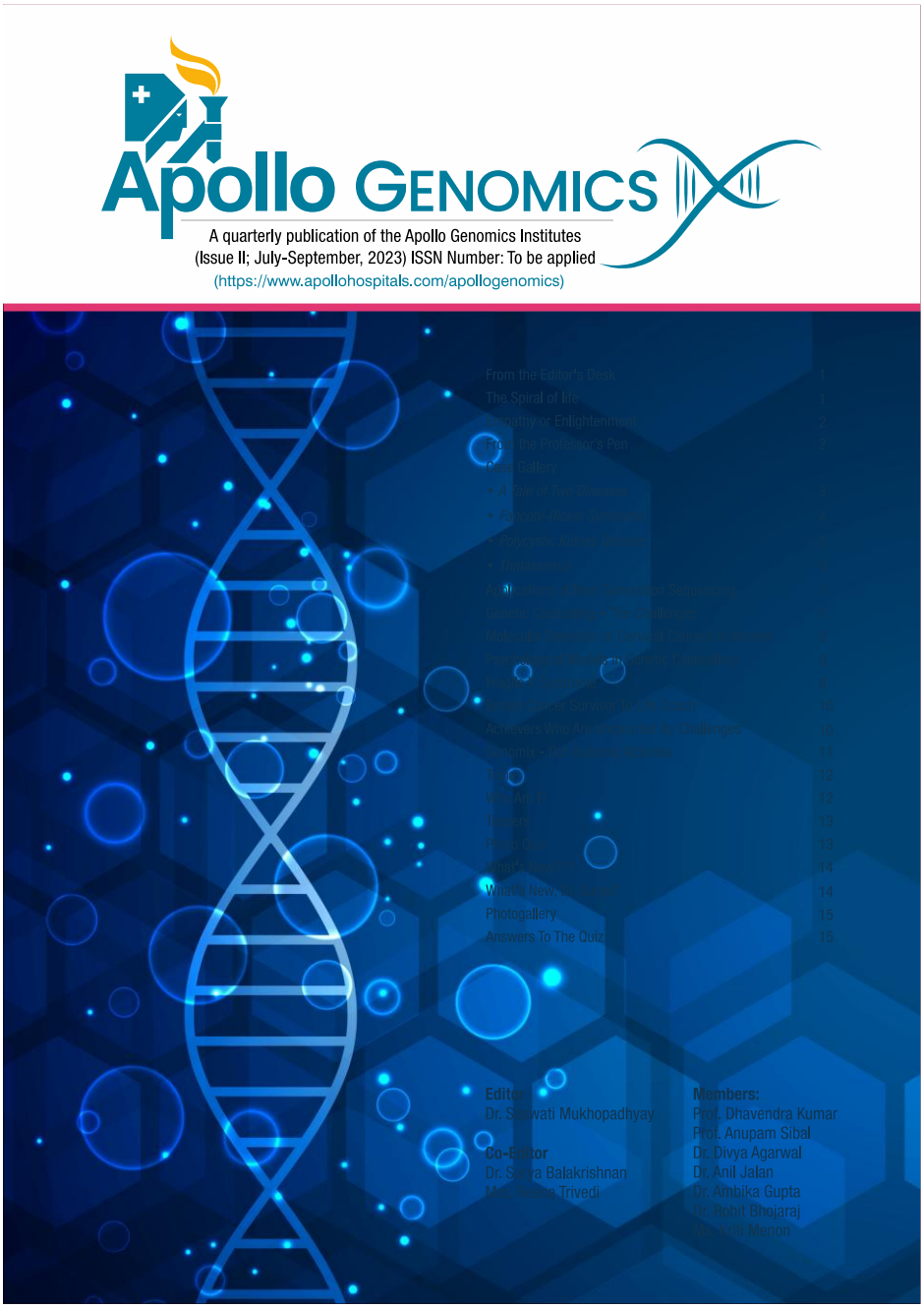
b) Quarterly Newsletter of Apollo Genomics Academy



c) Apollo Clinical Genomics Manual-

‘‘THE CURRENT PRACTICE OF CLINICAL GENETICS AND GENOMIC MEDICINE’ Editor-in-Chief: Professor Dhavendra Kumar

Preface

Since the completion of the incredible and highly ambitious Human Genome Project, the field of medical genetics has transformed in unprecedented manner. Genome sequencing and related technologies have massively enhanced the power of precision diagnosis, targeted therapy and personalised holistic healthcare. The genomic medicine is now a reality moving ahead with faster pace alongside advances and developments in related OMIC sciences. The field of genomic medicine and healthcare is now visible on the landscape of may leading specialist healthcare providers. There is thus urgent need for continued genomic education and skills development of all healthcare providers and other professionals to serve patients, families and the community with most effective, efficient and ethical approaches and interventions.

The Apollo Genomics Institutes offer this new clinical resource developed by the Apollo Genomics Team for the benefit of all clinicians, nurses and allied healthcare professionals. It is intended to inform and enhance understanding of the healthcare community, lay people, public at large and the media about the current and emerging practice of clinical genetics and genomic medicine.

The core areas include common and rare genetic diseases, conventional and new emerging genomic laboratory diagnostic methods, interpretation of the family history, assessment of individual and family's genetic risks based on comprehensive analysis of available information and outcomes of laboratory genetic testing, genetic counselling for explanation and discussion of available options, management of the pregnancy at high genetic risks, selection of patients for targeted precision-personalised medical and surgical treatment, health surveillance of 'at risk' close family members, safe drug prescribing using pharmacogenomic testing and prevention of genetic or genomic disease or risk using genome testing combined with precision intervention.

The manual is comprehensive designed on the model of integrated genomic healthcare. All contributors have included only the factual and unambiguous information supported with pertinent academic and professional references. The manual is regularly reviewed and updated in keeping with new knowledge and advances.

xiv) Member- Advisory Board, the 'Board of Genetic Counselling in India'

Board of Genetic Counseling
BGC
BOARD OF GENETIC COUNSELING
Registration No. 231 of 2015, Govt of Telangana, India

Genetic counsellors around the world are acknowledged to be important member of the clinical genetics and genomic medicine teams. In developed western nations including Australia and

South Africa, there are formally structured training programs leading to professional accreditations. These academic courses also offer qualifications like Masters and/or Diploma in Genetic Counselling. There is acute shortage of such courses and training programs in genetic counselling across most low and middle income countries (LMICs). In most of these countries there is no recognition of genetic counselling as a distinct healthcare discipline.

The Board of Genetic Counselling in India (BGCI) is a non-governmental organisation (NGO) that offers structured teaching and training in genetic counselling. It also accords 'certification in genetic counselling' to successful trainees. Most of these are now part of the clinical genomics/ genomic medicine teams. As an external advisory member of BGCI, I have actively contributed to the curriculum development in line with the UK Genetic Counselling criteria. It led to successful recognition from the Skills Board advising Government of India on new emerging healthcare disciplines.

xv) Founding President- 'The Global Academy of Medical Sciences'

The Global Academy of Medical Sciences (The Academy) is an independent 'not-for-profit' organization promoting applications and translational of advances in bio-medical sciences in the current and future practice of clinical medicine, precision and preventive healthcare and socio-economic applications. The Academy aims **''to promote and contribute to educational, teaching, academic and professional development of excellence in medical teaching, research and healthcare practice'.** The main focus shall be the '**Low and Middle Income Countries**- **LMIC**'.

<u>Objectives of the Academy</u>-

1. Acknowledgement and recognition of academic excellence and achievements of the international community of the academic medical and healthcare professionals.

2. Empowering Doctors , Nurses, and other Health professionals in the 'low and middle income' countries in keeping with national statutes and governance.

3. Guidance and protocols development for excellence in medical, dental, nursing and healthcare education and training.

4. Promoting and supporting development of technology for delivering the effective and efficient evidence-based integrated healthcare.

5. Advising and supporting innovative research planning, grants application, governance,

assisting in report writing, presentation and publication.

6. Advising and/or participation in development of new teaching, research and healthcare infrastructure.

7. Promoting and assisting collaborative applied and translational bio-medical and bio-technological research.

8. Promotion and technology development for digital healthcare, particularly utilization of artificial intelligence (AI).

9. Promotion of the traditional health practices and socio-cultural customs within the modern medicine based on the concept of 'Integrative Medicine'.

10. Assisting and encouraging mutually beneficial collaboration with the pharmaceutical and healthcare industry for vaccine and novel drugs, appliances and establishing and improving current or future resources.

The Academy is constituted by multi-specialist Faculty of Members (MGAMS) and Fellows (FGAMS) who serve and deliver its aims and objectives. Proposed Faculty structures include Bio-Medical Sciences, Medicine, Surgery, Laboratory Medicine, Women and Child Health, and Community and Public Health. The Academy works closely and constrictively with other national and international academic medical and healthcare sciences.

VII SCIENTIFIC CONFERENCES, SYMPOSIA AND SEMINARS- LEADERSHIP ROLES

- Co-organiser for the Asian Genetics 2017 conference held in Kochi, Kerala, India- 9-12 Nov. 2017.
- Chief Convenor for the 4th International Conference on Birth Defects and Workshops (Cancer Genetics; Cardiovascular Genetics; Genetic Counseling in Rare Genetic Diseases, held in Vellore, India- 12-15 December 2018.
- Chief Convenor for the 4th Indian Cancer Genetics Group conference held in ACTREC, Mumbai, India; 8-10 December 2018.
- Chief Convenor for the First Indo UK Training Workshop for Genomic & Molecular Medicine, King George Medical University, Lucknow, India; 19-21 November 2018.
- Chief Convener for the GC4GE '***Global Genomic Education'*** seminar in collaboration with the Human Genome Meeting, part of the Annual Conference of the Human Genome Organization (HUGO), held in Seoul, South Korea; 24-26 April 2019.
- Co-Convenor and Chair of the Scientific Committee for the 'Impact of Human Genomics in Clinical Practice', held in the JSS Medical College, JSS Higher Education Academy (Deemed University), Mysore, Karnataka, India; 31 October 2019.
- Chief Guest at the Genomic and Molecular Medicine Seminar for signing the Memorandum of Understanding (MOU) between the Genomic Medicine Foundation (UK) and the King George's Medical University, Lucknow, UP, India; 7 November 2019.

- Convenor and Chair of the Organising and Scientific Committees for the 7th International Cardiovascular Genomic Medicine Conference, on behalf of the GMF UK, held in York, England, UK; 4-5 December 2019.
- Convenor and Chair of the Organising and Scientific Committees for the 8th International Cardiovascular Genomic Medicine Conference, 11-12 September 2021 (Virtual).
- Convenor- Oxford Genomic Medicine Conference, Genomic Medicine Foundation (UK) Ltd. 11th November 2020 & 10th May 2022
- Convenor- 'Multi-disciplinary care for Inherited metabolic disease', 27th November 2021, Apollo Hospitals, New Delhi, India.
- Convenor- 'International Rare Diseases Conference', 5th March 2022, Apollo Hospitals Genomics Network, India.
- Chair- 'IXth International Cardiovascular Genomics Conference, 23-24 October 2023, Royal College of Surgeons, Edinburgh, Scotland, UK
- Covenor: 'Symposium on Integrated Medicine', 26th November 2024, Indraprastha Apollo Hospital, Delhi, India.
- Co-Chair: 'Sixth International Conference of Birth Defects', 27-30 November 2024, Mahatma Gandhi University of Medical Sciences and Technology, Jaipur, India.
- Co-Chair: "International symposium Breakthroughs in Genomics and Genetics- Shaping Maternal and Fetal Health', December 3-4, 2024, Aligarh Muslim University, Aligarh, India
- Chair- '3rd Genomic Medicine Symposium', 12th February 2025, Queen Mary University of London, London, UK.

VIII PRESENTATIONS- SCIENTIFIC AND LEARNED SOCIETIES (FROM 2017 TO DATE)

2017

- '**Unravelling the complexity of Chronic Heart Failure- Lessons from Rare Inherited Cardiovascular Diseases',** Invited Lecture, 42nd Annual Conference of the Indian Society of Human Genetics, held in Indian Institute of Science, Bangalore, India. 1-3 March 2017.
- **GENETICS AND GENOMICS IN PERSONALISED CLINICAL CARDIOLOGY, 'DNA IN HEART',** Seminar on Cardiovascular Genetics, Christian Medical College, Vellore, TN, India. 3 March 2017.
- **'Targeted Molecular Therapy for Inherited Heart Diseases',** 'DNA IN HEART', Seminar in Cardiovascular Genetics, Christian Medical College, Vellore, TN, India. 3 March 2017
- '**Clinical and Molecular Basis of Cardiomyopathies: The Paradigm of Hypertrophic Cardiomyopathy',** Guest Lecture at the Seminar on Inherited Cardiomyopathies, Dr. KM Cherian Heart Foundation, Chennai, TN, India. 8 March 2017.
- **'New Paradigms of Genomic and Precision Medicine',** Invited Guest Lecture, Institute of Genomics and Integrative Biology, CSIR, New Delhi, India, 3 Nov. 2017

- **'Targeted molecular therapy for Inherited Cardiovascular Disorders',** Invited Guest Lecture, Department of Cardiology, Post Graduate Institute of Medical Education and Research, Chandigarh, India. 6 Nov. 2017.
- **'Genomics in Clinical Medicine',** Invited Guest Lecture, Shri Guru Ram Institute of Medicine and Health Sciences, Dehradun, Uttarakhand, India. 7 Nov. 2017
- **'Contributions of genomics in improving health and socio-economic progress of emerging economies of the developing world',** Invited presentation at the 'The Landscape of Genetic Variants in Asian Founder Populations from Near to Far East', 2nd International Conference on Founder Populations. 9-12 November, 2017, Kochi, Kerala, India.

2018

- '**New emerging paradigms of targeted molecular therapy for Inherited cardiovascular conditions'** International Conference on Cardiovascular Medicine and Cardiopathy', 7 January 2018, Bangkok, Thailand.
- **'Clinical and Genetic 58eterogeneity of Down Syndrome',** Paediatric Undergraduates Study day, Cardiff University School of Medicine, 22 January 2018.
- **'Role of Cardiac Nursing in the Multi-Disciplinary Care for Inherited Cardiac Conditions', Key note Lecture,** Global Nursing Conference, 1-3 March 2018, London, UK
- **'Inherited Cardiovascular Conditions in Clinical Genetic Practice',** Lecture to BSc Intercalated (Medical Genetics), Cardiff University School of Medicine, 9 March 2018.
- **Key note address- 'Inherited cardiovascular conditions in the Genome era',** International Paediatric Cardiology Conference, 12 April 2018, Cairo, Egypt
- Guest Lecture- '**Inherited cardiovascular conditions- the global familial heart challenge'**, 16 April 2018, Aswan Heart Centre, Aswan, Egypt
- International Genomics Conference, 2-5 October 2018, Haifa, Israel
- Invited lecture- **'Sudden cardiac death in children and young adults- Genetic & Genomic perspectives'**, Heart Rhythm Congress, 8-10 October 2018, Birmingham, UK
- **Athena Swan Lecture, 'The helical path of clinical genetics- climbing the DNA ladder'**, 8 November 2018, School of Medicine, Cardiff University, UK
- **Invited lecture- 'Next generation sequencing in Clinical Practice'**, 9 November 2018, International Conference on Single Cell Genomics & Next Generation Genome Sequencing, 8-9 November 2018, London, UK
- **'Current trends in genomic and molecular medicine',** First Indo-UK Training workshop, 19-21 November 2018, King George's Medical University, Lucknow, India.
- **'Genomic applications in Medicine & Healthcare' at the 'Advances and new developments in Bio-technology',** 27-28 November 2018, Uttaranchal University, Dehradun, Uttarakhand, India.

- **'Next generation sequencing in clinical genomics',** 29-30 November 2018, Next generation sequencing in Clinical Genomics- Advances and Applications', symposium organized by the Select-Bio, Bangalore, Karnataka, India.
- **'The challenges of Rare diseases',** Tech Summit, 30 November 2018, Government of Karnataka, Bangalore, India
- **'Current practice of cancer genetics in medical practice',** 2 December 2018, Gwauhati, Assam, India
- **'Genetic diagnosis in primary immune deficiency syndromes',** Seminar on Advances in Primary Immune Deficiency Syndromes, 6 December 2018, Super Specialty Paediatric Hospital, Noida, UP, India.
- **'Large scale population genome sequencing for effective healthcare',** Wellcome Trust-DBT India Seminar on 'Development of Physician Scientists', 7 December 2018, Institute of Genomics and Integrative Biology, New Delhi, India.
- **'Genomic skills and competencies for Multidisciplinary cancer genetics service',** 4th Indian Cancer Genetics Conference, Indo-UK Genetic Education Forum, 8-10 December 2018, ACTREC, Navi Mumbai, India.
- **'Inherited cardiovascular conditions in clinical genetics',** 4th International Birth Defects Conference, Indo-UK Genetic Education Forum & Society of the Indian Academy of Medical Genetics, 12-15 December 2018, Vellore, TN, India.
- **'Heterogeneity in Clinical Genomics and Medicine', Dr. S. S. Agarwal Oration,** 4th International Birth Defects Conference, Indo-UK Genetic Education Forum & Society of the Indian Academy of Medical Genetics, 12-15 December 2018, Vellore, TN, India.
- **'Inherited cardiovascular development disorders & aortopathies',** Cardiovascular Genetics Workshop, 15 December 2018, Christian Medical College, Vellore, TN, India.
- **'The challenges of sudden cardiac death',** Cardiovascular Genetics Workshop, 15 December 2018, Christian Medical College, Vellore, TN, India.
- **'Therapeutic advances for Inherited cardiovascular conditions',** Cardiovascular Genetics Workshop, 15 December 2018, Christian Medical College, Vellore, TN, India.
- **'Inherited arterial and aortic diseases- the TGF Betapathies',** International Cardiovascular Genetics Conference, 18-19 December 2018, Frontline Hospital & Dr. Cherian Heart Foundation, Chennai, TN, India.
- **'Genetic and Molecular approach to chronic heart failure',** The current practice of Clinical genetics & genomics, 20 December 2018, Kaminini Postgraduate Medical Institute, Hyderabad, Telangana, India.

2019

- **"The Global Status of Genetic/Genomic Education", delivered at the "Genomic Education and Training for Healthcare" seminar** Sponsored by the 'Global Consortium

for Genomic Education (GC4GE)' in collaboration with the HUGO/HGM 2019, Seoul, South Korea; 24-26 April 2019

- **"Cardiovascular Genomic Medicine in Clinical Cardiology- Applications in chronic heart failure"** delivered at the 'Human Genomics in Clinical Practice' seminar held in JSS Medical College, Mysore, Karnataka, India; 31 October 2019.
- **"Targeted Molecular Cancer Therapy",** delivered at the 'Human Genomics in Clinical Practice' seminar held in JSS Medical College, Mysore, Karnataka, India; 31 October 2019.
- **"Genome Diagnosis of Disorders of Genome Architecture",** delivered at the 'Human Genomics in Clinical Practice' seminar held in JSS Medical College, Mysore, Karnataka, India; 31 October 2019.
- **'Targeted molecular diagnosis and therapy- applications of recent genomic advances',** Invited Lecture delivered at the International Conference of the Applied Biology & Society of Biologists, 4-6 November 2019 held in Shri Mata Vashno Devi University, Katra, Jammu & Kashmir, India.
- **'Cardiovascular Medicine in the Genome Era',** Welcome lecture at the VIIth International Conference of the Cardiovascular Genomic Medicine, held in York, England, UK; 4-6 December 2019.

2020

- **'Global Genomic Education- Challenges for Developing Nations',** Workshop at the International Birth Defects and Prevention of Developmental Disabilities', March of Dimes & WHO Conference, held in Colombo, Sri Lanka, 23-25 February 2020. Co-Convenor, Chair and Faculty of the Multi-Disciplinary Workshop.
- **'Neoplasms complicating multiple malformation syndromes',** Indian Cancer Genetics and Genomics Conference, All India Institute of Medical Sciences, New Delhi, 20-21 November 2020.

2021

- 26-27 February- AHPI-GAPIO Annual Conference
  'Next generation genomic diagnosis and precision medicine and healthcare'
- 5th – 8th November- NextGen Omics UK: In-Person- Oxford Global
  'Emerging dynamics of genome sequencing in clinical practice'
- 19th November- Inaugural symposium- 'The KGMU Centre of Precision Medicine'
  'The landscape of Precision Medicine'
- 24th November – Shri Guru Ram Das University Health Sciences, Amritsar, India
  'Genomic Perspectives of Precision Medicine and Healthcare'
- **'Multi-disciplinary care for Inherited metabolic Disease- Introduction',** 27th November 2022, Apollo Hospitals, Delhi, India.

- 5th December- ;Symposium in Advanced Genomics', Indian Academy of Paediatrics & Kamalnayan Bajaj Hospital, Aurangabad, Maharashtra, India
  "Keynote address: Next generation genome sequencing in clinical practice- scope, limitations and challenges"

2022

- The Festival of Genomics and Biodata, 25-28 January, 2022
  'Genomics led precision medicine and healthcare- where is the evidence?'
- Key note presentation at the 'International Rare Diseases Symposium- Emerging new trends in diagnosis and management', 5th March 2022, Apollo Hospitals, Delhi, India.
  'Common and complex issues in rare diseases'
- 'Board of Genetic Counselling in India', 7th International Conference, 1-3 July 2022
  "Genetic counselling in Cardiovascular Emergencies"
- 'II EINSTEIN INTERNATIONAL SYMPOSIUM ON PRECISION MEDICINE', Sao Paulo, Brazil, 20 October 2022
  "Genomic medicine skills and competencies"
- 'II EINSTEIN INTERNATIONAL SYMPOSIUM ON PRECISION MEDICINE', Sao Paulo, Brazil, 20 October 2022
  "Genomics and Society: Ethical, Legal, Cultural and Socioeconomic Implications"
- **'**Symposium- Communicable and Non-Communicable Diseases', Session XI 'Art of War Against Cardiovascular Disease: Progression and Outcomes', Dr. B.R. Ambedkar Centre for Biomedical Research, University of Delhi, India; 4th November 2022
  "Molecular aspects of cardiovascular diseases'
- 'The 5th International Birth Defects Conference' (ICBD-2022), JSS Academy of Higher Education (Deemed University), Mysore, Karnataka, India; 21-23 November 2022
  -21 November 2022: "Precision Medicine- from concept to reality'
  -22 November 2022: "Neoplasia and Malformation syndromes"
- 'Genomic Medicine in Clinical Practice', Pharmacogenomics and Targeted Therapy, 25 November 2022.;
  Invited Lecture- " Cardiovascular pharmacogenomics'
- 'Genomic Medicine in Clinical Practice', Multi-disciplinary genomics in clinical medicine, 26 November 2022.
  "Multi-disciplinary care team management of selected genetic disorders- the UK model"
- Department of Clinical Genetics, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India; 3rd December 2022
  Invited Guest Lecture- 'Multi-OMICS Medicine- the future of Clinical Medicine'
- 'Second Annual Symposium- Centre for Precision Medicine, Center for Advanced Research (CARE), King George's Medical College, Lucknow, UP, India; 7th December 2022'
  Key note Lecture- "Precision Medicine- Facts and Fantasies"

- '7th Annual Conference- Society of Indian Academy of Medical Genetics, Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGI), Lucknow, UP, India; 8-11 December 2022.
  -10 December 2022: "Novel therapies for inherited cardiomyopathies'
  -11 December 2022: Chief Guest Lecture- 'Future of Fetal and Neonatal Genomic Medicine', Symposium 'From Womb to Cradle- Genomic perspectives of Prenatal diagnosis, Perinatology and Neonatology'.
- 'GUT, LIVER AND GENES- WHAT A PAEDIATRICIAN NEEDS TO KNOW', Indraprastha Apollo Hospital, Delhi, India; 11 December 2022.
  "Future of Clinical Genetics"
- 'Apollo Genomic Healthcare Seminars', CME seminar on Cardiology, 14th December 2022, Indraprastha Apollo Hospital, Delhi, India.'
  "Genomic perspectives of Chronic Heart Failure'

2023

- **"Genomics led Precision Cardiology in clinical practice",** Festival of Genomics, London, 25-26 January 2023
- **"Multi-OMICS led precision clinical cardiology- the model of heart failure",** Invited talk at the 'Precision Medicine conference 2023', 9-10 March 2023, Earls Court, London, UK
- **" From the double helix to the precision genomic medicine and healthcare',** Key note/ Invited speaker, 'Celebrating the 70 years of Double Helix', 23-26 April, Apollo Genomics Institutes, Chennai and Hyderabad, India.
- **"Genomics in Clinical Nephrology & Renal Transplantation",** 30th June 2023, Genomic Healthcare Seminars, Apollo Group of Hospitals, India.
- **" Emerging ethical issues of genomic diagnosis & counselling- the role of the genetic counsellor,** 7-8 July 2023, Annual Conference, Board of Genetic Counselling, Hyderabad, Telangana, India.
- **" Fetal and Neonatal Genomics- new horizons",** 28th July 2023, Genomic Healthcare Seminars, Apollo Group of Hospitals, India.
- **"'Genomics input for Precision Clinical Cardiology- Dealing with the Sudden Cardiac Death'**, 8th September 2023, Apollo Genomic Healthcare Seminar, Apollo Genomics Institutes, Apollo Group of Hospitals, India.
- **"Congenital bone diseases in clinical orthopedics**", 22nd September 2023, Apollo Genomic Healthcare Seminar, Apollo Genomics Institutes, Apollo Group of Hospitals, India.
- **"Integrated multi-OMICS Medicine- the emerging paradigm for precision and personalised medicine',** 27th October 2023, Apollo Genomic Healthcare Seminar, Apollo Genomics Institutes, Apollo Group of Hospitals, India.
- **"Genetic and Genomic Perspectives of Cancer",** 17th November 2023, Apollo Genomic Healthcare Seminar, Apollo Genomics Institutes, Apollo Group of Hospitals, India.

- "**Genomics led Precision and Personalised Medicine**", 26th December 2023, Mahatma Gandhi University of Medical Sciences and Technology, Jaipur, India
- "**'Emergence of precision and personalised genomic healthcare',** 29th December 2023, Postgraduate Institute of Medical Sciences, University of Health Sciences, Rohtak, Haryana, India.

2024

- **"Indigeous genome databases for genomic healthcare**", Festival of Genomics, London, 24-25 January 2024.
- **"Precision and personalized clinical cardiovascular genomic medicine- the way forward",** 28th February 2024, International symposium on genomics in cardiovascular health, hosted by the Era University, Lucknow, India.
- **"MultiOMICS in Integrated Clinical Medicine: Scope, Limitations and Challenges",** 2nd August 2024, Texas Tech University of Health Sciences, Luback, Tx, USA.
- **"Integrated multi-OMICS for patient diagnosis and management",** 25th October 2024, NextGen Genomics Conference, Oxford Global, London, UK.
- **"Genomics and multi-OMICS in Medicine",** 10th November 2024, 'New Horizons of Medicine through Genomics', Manipal Hospitals, Bangalore, India.
- **"Key Note Lecture- Genomics and OMICs Paradigm of Integrated Medicine", Sympsoium on Integrative Healthcare, Apollo Hospital, Delhi, India. 26th November 2024**
- **"Integration of Genomics in Maternal-Fetal Medicine",** 3rd December 2024, Aligarh Muslim University, Aligarh, UP, India.
- **" Genomic Healthcare in South Asia",** Invited Guest Lecture, South Asia University, Delhi, India. 13th December 2024.

2025

- **"Integrated multi-OMICS for precision diagnosis and treatment",** 7th January 2025, Division of Cancer and Genetics, School of Medicine, Cardiff University, UK

IX PUBLICATIONS

A)INDEX

ORCID ID: HTTPS://ORDIC.ORG/0000-0001-9928-0476

	All	Since 2014
Citations	25011	15854
h-index	68	50
i10-index	513	348

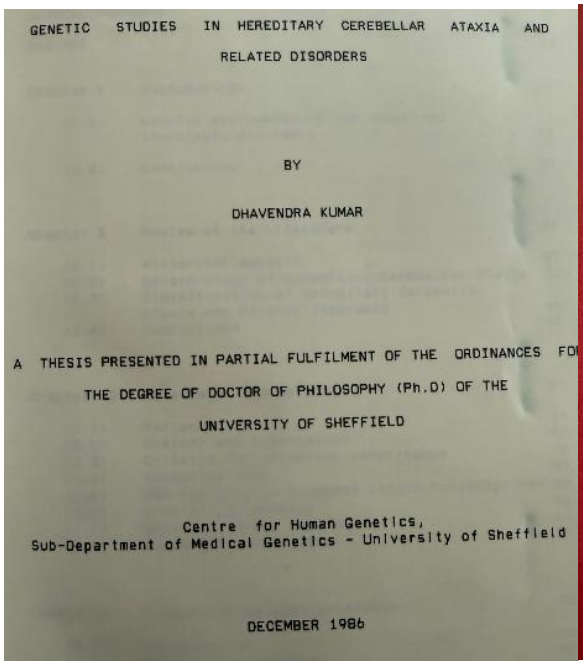
Google-scholar:
https://scholar.google.com/scholar?hl=en&as_sdt=0%2C5&q=dhavendra+kumar&oq=dhavendra

B) Theses (Total=3)

1. MD (Paediatrics), King George's Medical College, University of Lucknow, India 1977.

"**A study of plasma and cerebrospinal fluid electrolytes in certain childhood neurological disorders with special reference to magnesium"**

2. PhD, University of Sheffield, UK, 1986.
"Genetic studies in hereditary cerebellar ataxia and related disorders"


GENETIC STUDIES IN HEREDITARY CEREBELLAR ATAXIA AND RELATED DISORDERS

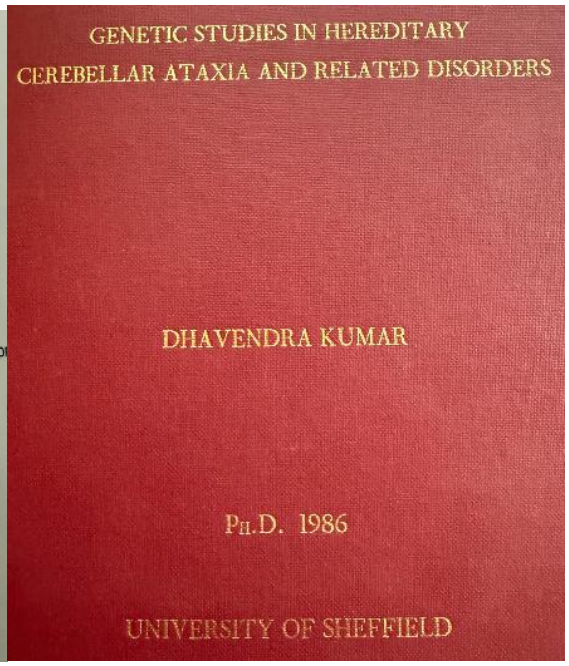
BY

DHAVENDRA KUMAR

A THESIS PRESENTED IN PARTIAL FULFILMENT OF THE ORDINANCES FO
THE DEGREE OF DOCTOR OF PHILOSOPHY (Ph.D) OF THE
UNIVERSITY OF SHEFFIELD

Centre for Human Genetics,
Sub-Department of Medical Genetics - University of Sheffield

DECEMBER 1986

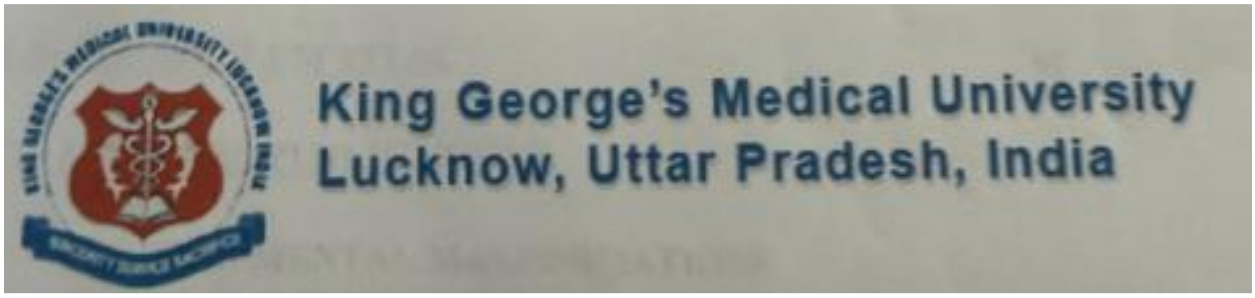

GENETIC STUDIES IN HEREDITARY
CEREBELLAR ATAXIA AND RELATED DISORDERS

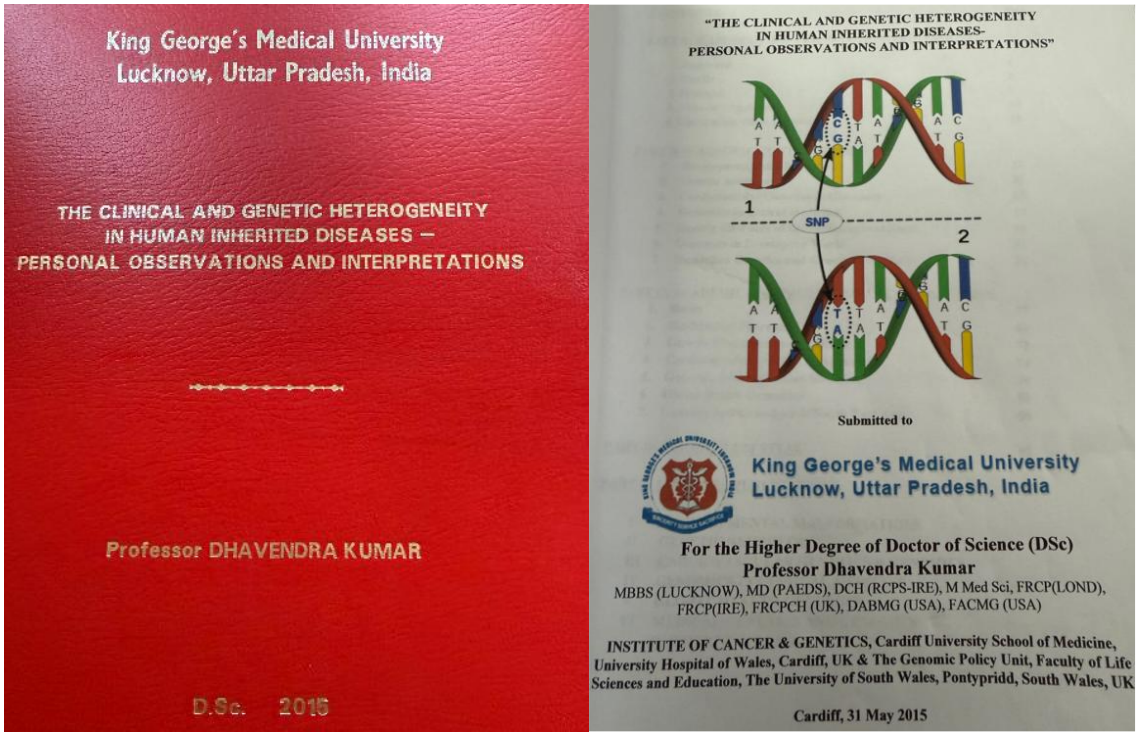
DHAVENDRA KUMAR

PH.D. 1986

UNIVERSITY OF SHEFFIELD

3. DSc, King George's Medical University, Lucknow, UP, India, 2015
"Clinical and Genetic Heterogeneity of Human Inherited Disease- Personal Observations and Interpretations"


King George's Medical University
Lucknow, Uttar Pradesh, India



C) Book chapters (Total=64)

1. "***Genetic Disorders of the Indian Subcontinent***", ***Amsterdam, Kluwer-Springer Academic, The Netherlands, 2004 (Total=6)***

I compiled and edited this reference book to cover various aspects of genetic variation and genetic diseases among people from the Indian subcontinent. Several authors from India, UK and other countries have contributed various chapters.

In addition to editing the book, I wrote the following chapters:

- Kumar D: 'The Indian subcontinent and genetic disorders: An introduction'.
  Ishwar C Verma and Dhavendra Kumar: 'Epidemiology of genetic diseases in the Indian Subcontinent'
- Kumar D: 'Congenital developmental anomalies'.
- Dhavendra Kumar, Michael Patton, Ajith Kumar: 'Genetic neurological and psychiatric disorders'.
  Sanjay S Madan, James A Fernandes and Dhavendra Kumar: 'Inherited skeletal dysplasias and collagen diseases'.
- Dhavendra Kumar, Carani B Sanjeevi, V. Radha and V. Mohan: 'Diabetes mellitus and related disorders'.
- Kumar D: 'Genetic counselling for families from the Indian subcontinent'.
- Kumar D: 'The genetics of cancer-the Indian subcontinent perspective'

2. ***"Genomics and Clinical Medicine"***, ***New York, Oxford Univ. Press, 2007. (Total=6)***

This is a multi-author edited text book largely focussing on applications of genome science and technology in clinical medicine and population/public health.

The book includes sections on general genomics, clinical genomics and health genomics. Several leading experts have contributed chapters. My own contribution in the book includes the following chapters/ sections. The book offered my excellent opportunity for editing the book.

- Genomic perspectives of human development
- A taxonomy for human disease- genetics and genomics approaches
- Clinical medicine in the genomic era- an introduction
- Neuropsychiatric diseases II: Affective disorders
- Genomics and global health (Co-author, Prof. David Weatherall)
- Glossary (compiled from various sources)

3. "***Principles and Practice of Clinical Cardiovascular Genetics***", ***New York, Oxford Univ. Press, 2010 (Total=3)***

This is a joint project with Dr. Perry Elliott, Reader/Consultant in Inherited Heart Disease at the Heart Hospital, University College Hospital, London. Apart from planning and editing, I co-authored the following chapters in this book:

- Challenges of clinical cardiovascular genetics- an Introduction
- The classification of inherited cardiovascular conditions
- Thoracic and abdominal aortic aneurysms

4. "***Oxford Handbook of Inherited Cardiac Disease"***, ***London, Oxford Univ. Press, 2011 (Total=6)***

- Introduction to clinical cardiovascular genetics
- Genetic testing and genetic screening
- Congenital Heart Disease
- Cardiovascular manifestations in chromosomal abnormalities
- Inherited connective tissue disorders
- Mitochondrial heart disease

5. ***"Genomics and Health in Developing World***", ***New York, Oxford Univ. Press, 2012 (Total=6)***

- The genomic map of population diversity in Asia
- Transcultural perspectives of genetics and genomics
- Transgenic foods and the nutritional status of developing countries
- The burden of congenital anomalies on global health
- The Indian subcontinent and its people
- Familial cancer and cancer genetics in the Indian subcontinent

6. "Genomic and Molecular Medicine", Morgan and Claypool, CA, USA (Total=1)

- The molecular biology of chronic heart failure

7.***"Genomic Medicine- Principles & Practice***", ***Oxford University Press, NY, 2014 (Total=7)***

- Genes, genome and human health- Introduction
- Genes, genome and human malformations
- Mendelian and mitochondrial genetics

- Genetic and genomic basis of clinical practice: an introduction
- Genetic and genomic basis of the classification of human Disease
- Genomic applications in Clinical Pediatrics
- The genetic and genomic practice of reproductive medicine

8. "Medical and Health Genomics", Elsevier, 2016 (Total=6)

- Preface
- The Human Genome
- Medical and Health Aspects of Genetics and Genomics
- Genetics and Genomics of Reproductive Medicine and Health
- Stratified and Precision Medicine
- Glossary: Medical and Health Genomics

9. ***"Genomics and Society", Elsevier, 2016 (Total=3)***

- Preface- Introduction to Social and Economic Genomics
- Socioeconomic outcomes of genomics in the developing world
- Glossary: 'Genomics and Society"

10. "Cardiovascular Genomics- Principles and Clinical Practice", **Springer Nature, 2018 (Total=3)**

- Preface
- Introduction to genes, genome, genetics, and inheritance patterns
- Glossary- Cardiovascular Genomics

11. *"Clinical Molecular Medicine-Principles and Practice",* Academic Press, Elsevier, December 2019 (Total=5)

- The human genome and molecular medicine
  - Molecular medicine of diabetes mellitus
  - Molecular biology of acute and chronic inflammation
  - Gene, genome, and molecular therapeutics
  - Integrated genomic and molecular medicine
  - Glossary—molecular medicine

12. '***Genomic Medicine Skills and Competencies", Academic Press, Elsevier, March 2022 (Total=1)***

- Global perspectives of genomic education and training

13. " ***Genomic and Molecular Cardiovascular Medicine', Elsevier, July 2023 (Total=3)***

- Introduction to genomic and molecular biology
- Genetic and molecular profiling in clinical cardiology
- Cardiovascular precision and personalized medicine

14. **"** ***Genomics, Populations and. Society", Elsevier, November 2024 (Total=2)***

- Introduction to genes, genomes and genomics
- Genomic and Precision Medicine

15. "Clinical Nutrogenomics in Personalised Medicine and Healthcare", Elsevier, 2025

- Nutritional management of monogenic inherited disorders
- Metagenomics in personalised nutrition

16. Chapters in other books (Total=3)

1. **Kumar D**, Clark J W, Blank C E: Acrocephalosyndactyly and fragile site 12q13 segregating in the same family. In 'Recent Trends in Medical Genetics'(Eds.K.M.Marumuthu, P.M. Gopinath) Pergaman Press, Oxford1986
2. **Kumar D**: Grebe Syndrome. In "BirthDefects Encyclopaedia". Ed. Mary Louise Bruyse. Alan R. Liss Inc. New York, 1990.
3. **Kumar D:** Moebius syndrome In "Congenital Malformations" Eds.D.Donnai and R.Winter, Chapman and Hall, London, 1995.

d)Peer-reviewed articles & papers (Total=66)

1. Gray R G F, **Kumar** D, Whitfield A E, Glycogen Phosphorylase b Kinase deficiency in three siblings. J. Inherited Metabolic Disease 1983, 6, 107
2. **Kumar** D, Curtis D, and Blank C E, Grebe Chondrodysplasia and Brachydactyly in a family. Clinical Genetics 1984, 25(1), 68-72
3. Blank C E, **Kumar** D, Johnson M. Multivitamins and prevention of Neural Tube Defects: A need for detailed counselling. Lancet 1984, February 4, 291
4. **Kumar** D Genetics of Indian Childhood Cirrhosis. Tropical and Geographic Medicine 1984, 36, 313-316
5. Barnes ICS, **Kumar** D, Bell R J M. A child with recombinant of chromosome 8 inherited from her carrier mother. Journal Medical Genetics, 1985, 22(1), 67-70
6. Gray RGF and **Kumar** D. Mitochondrial Malic enzyme in Friedreich's Ataxia – Failure to demonstrate reduced activity in cultured fibroblasts. J.NeurNeurosurgPsych.Jan1985, 48(1),70-74.
7. **Kumar** D, Blank C E, Griffiths B L. Cornelia de Lange syndrome in several members of the same family. Journal Med Genet 1985, 22:296-300
8. **Kumar** D, Blank C E, Gelsthorpe K. Hereditary Cerebellar Ataxia and Genetic Linkage with HLA. Human Genetics 1986, 72: 327-332
9. **Kumar** D and Blank C E. Hereditary Spinocerebellar Ataxia and genetic linkage with HLA. Journal Medical Genetics, 1984, 21, 301
10. **Kumar** D, Clark J W, Blank C E, Patton M A. A family with Craniofrontonasal dysplasia and fragile site 12q13 segregating independently. Clin Genetics, 1986, 29(6): 530-537
11. **Kumar** D, Levick R K. Autosomal dominant onychodystrophy and anonychia and brachydactyly type 'B' with ectrodactyly. Clin Genetics, 1986, 30: 219-225.
12. **Kumar** D, Heath P R and Blank C E. Clinical manifestations of trisomy 5q J.Medical Genetics, 1987, 24(3): 180-184

13. **Kumar** D, Papiha S S, Gelsthorpe K. Cell mediated immunological status and association of genetic markers in Hereditary Cerebellar Ataxia. Disease Markers 1987, 5: 31-41
14. **Kumar** D. Genetic aspects of congenital cerebellar ataxia: Ind. J. Pediatrics 1986, 53: 761-773
15. **Kumar** D, Timperley W R. Neurilemmomatosis and Neurifibromatosis Syndrome Ind. Journal Pediatrics 1985, 52:523-526
16. **Kumar** D, Timperley W. Late onset sporadic Cerebellar Ataxia: The clinical, genetic and pathological aspects of some observations on a series of ten patients. Acta Neurol. Scand. 1988 77:181-186.
17. Hurst J, Mankiewicz M, **Kumar** D, Winter R M. Hirschsprung's disease,microcephaly and Iris coloboma. A new syndrome of defective neuronal migration Journal Med. Genetics, 1988,25: 494-500.
18. **Kumar** D Syndrome of the Month: Moebius syndrome J.Med Genet 1990, 27:122-126
19. Nour S, **Kumar** D, Dickson J A. Anorectal malformations with sacral bony abnormalities. Archives of Disease in Childhood, 1989, 64: 1618-1620
20. **Kumar** D Late onset Spinocerebellar Ataxia of possible X-linked recessive inheritance Brain dysfunction, 1989,2(5): 268-272
21. **Kumar** D, Blank C E. Early onset Spinocerebellar Ataxia with retained tendon reflexes: an autosomal recessive disease distinct from Friedreich's Ataxia. Indian Pediatrics, 989, 26: 1014-1019
22. Priestley L, **Kumar** D, Sykes B Amplification of COL2A1variable region used for segregation analysis in a family with the Stickler syndrome Hum Genet, 1990,85: 525-526
23. **Kumar** D, Mueller RF, Duggan MB, Brocklebank T. Familial aplasia/ hypoplasia of pelvis, femur, and ulna with abnormal digits in an inbred Muslim family: an example of autosomal recessive disorder with overlapping features of syndromes of Fuhrmann, Al-Awadi, and Raas-Rothschild. Am. J.Medical Genetics 1997; 70:107-113
24. **Kumar** D, Garcia-Minaur S, Quarrell OWJ, Landa G and Garazar C. A distinct syndrome of familial cleft lip and palate with prominent eyes and characteristic facies in two unrelated families. Clinical Dysmorphology, 1996;5:295-301.
25. **Kumar** D, Moss G, Primhak R, Coombs R: Congenital renal tubular dysplasia and skull ossification defects similar to teratogenic effects of the angiotensin-1 converting enzyme [ACE] inhibitors J Med Genet 1997;34:541-545
26. **Kumar** D, Masel J A new multiple malformation syndrome of Mullerian Dysgenesis, facial hypoplasia, bilateral limb deformity brachydactyly, spinal stenosis and scoliosis. Clinical Genetics July 1997; 52: 30-36.

27. **Kumar** D, Rittey C, Cameron A, Variend S: A recognizable inherited syndrome of progressive central nervous system degeneration and intra cranial calcification with over lapping features of Aicardi-Goutieres syndrome. Am J Medical Genetics 1998;75:508-515.
28. **Kumar D,** Primhak, R, Kumar, A: Variable phenotype in Kaufman-McKusick syndrome: Report of Inbred Muslim Family and Review of Literature. Clinical Dysmorphology 1998;7:163-170.
29. **Kumar D:** A case of lateral facial clefts with Fallot's tetralogy, duodenal stenosis and intestinal malrotation- a new multiple congenital anomaly syndrome? Clinical Dysmorphology 1999; 8(1): 19-22.
30. William Reardon, Anne Smith, John W Honour, Peter Hindmarsh, Debipriya Das, GillRumsby, Isabelle Nelson, Sue Malcom, Lesley Ades, David Sillence, **Dhavendra Kumar**,Celia DeLozier-Blanchet, Shane McKee, Thaddeus Kelly, Wallace L McKeehan, Michael Baraitser, Robin M Winter: Evidence for digenic inheritance in some cases of Antley-Bixler syndrome? J Med Genet 2000, 37(1):26-32.
31. Bhola RM, Horne GV, Squirrell DM, Chan TK, **Kumar D**: Autosomal dominant congenital superior oblique palsy. Eye 2001, 15: 479-484
32. Slovtinek AM, Searby C, A;l-Gazali L, Hennekam RC, Schrander Stumpel C, Orcana-Losa M, Pardo-Reoyo S, Canani A, **Kumar D**, Capellini Q, Neri G, Zackai E, Biesecker LG: Mutation analysis of the MKKS gene in Mckusick-Kaufman syndrome and selected Bardet-Biedl syndrome patients. Human Genetics, 2002, 110(6):561-7.
33. Manir Ali, Lorna J Highet, Didier Lacombe, Cyril Goizet, Mary D King, Uta Tacke, Marjo S van der Knaap, Lieven Lagae, Chris Rittey, Han G Brunner, Hans von Bokhoven, Ben Hamel, Yvette A Oade, A Sanchis, I Desguerre, D Cau, N Mathieu, M L Moutard, Pierre Lebon, **D. Kumar**, Andrew P Jackson, and Yanick Joseph Crow. A second locus for Aicardi-Goutiéres syndrome at chromosome 13q14-21. J Med Genet (Published Online First: 20 May 2005.) 2006, 43(5):444-450.
34. Woods CG, Stricker S, Seemann P, Stern R, Cox J, Sherridan E, Roberts E, Springell K, Scott S, Karbani G, Sharif SM, Toomes C, Bond J, **Kumar D**, Al-Gazali L, Mundlos S. Mutations in WNT7A cause a range of limb malformations, including Fuhrmann syndrome and Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome. Am J Hum Genet. 2006 79(2):402-8.
35. **Dhavendra Kumar**. Genomic medicine: a new frontier of medicine in the twenty first century. Genomic Med. 2007; 1:3-7.
36. **Dhavendra Kumar**. Genome Mirror-2006: 1) The human variome project 2) The Nobel worthiness of RNA interference 3) Metabolomics and beyond. Genomic Med. 2007; 1:87-90.
37. **Dhavendra Kumar**. From evidence based medicine to genomic medicine. Genomic Med. Published on-line doi. 10.1007/s11568-007-9013-6; Genomic Med. 2007;1: 95-104; doi 10.1007/s11568-007-9013-6;

38. **Dhavendra Kumar**. Genome Mirror 2007: 1) The future of genomic medicine- satellite symposium at the American Society of Human Genetics, 22 October 2007, San Diego, USA; 2) Rapid commercialization of the personalized medicine- a slippery slope- commentary on mini-symposium 'Navigenics and the era of personalized medicine- the science, policy and ethics of personalized medicine'. Genomic Med. 2007; 1:147-148.
39. **Dhavendra Kumar**. Genome Mirror 2008: 1. Recent molecular advances in essential hypertension- Alcohol and risk for hypertension & a possible genome-based vaccine for hypertension; 2) Personalized medicine: the emerging paradigm of warfarin. Genomic Med. 2008; 2:51-53.
40. **Dhavendra Kumar**. The personalised medicine- a paradigm of evidence-based medicine. Annali dell'Instituto Superiore di Sanita 2011; 47(1): 31-40.
41. **Dhavendra Kumar**. Applied and translational genomics- what is new? Applied and Translational Genomics 2012; 1:1-2.
42. **Dhavendra Kumar** (2013)The molecular biology of chronic heart failure . Colloquium series on Genomic & Molecular Medicine, Morgan & Claypool Life Sciences, DOI:10.4199/C00071ED1V01Y201212GMM0 03, pp1-80.
43. Louis J. Muglia, Special Edition Editor* and **Dhavendra Kumar,** Editor-in-Chief. Introduction to evolutionary genomic approaches to human disease☆ Appl Transl Genom. 2013 Dec 1; 2: 41; Published online 2013 Oct 21. doi: 10.1016/j.atg.2013.10.003; PMCID: PMC5121262
44. **Dhavendra Kumar**. Genetic and genomic perspectives of obesity and diabetes mellitus:Implications for clinical medicine and public health. In 'Gains of Genomic Research in Biology and Medicine', Eds. N.Mehra & R.Jalali, Ranbaxy Science Foundation, New Delhi.2014. pp3-53.
45. **Dhavendra Kumar**. Harnessing genomics for the developing world. In 'Gains of Genomic Research in Biology and Medicine', Eds. N.Mehra & R. Jalali, Ranbaxy Science Foundation, New Delhi.2014. pp215-228.**;**
46. **Dhavendra Kumar**. 'GENOMIC MEDICINE'- Prospects, Promises and Expectations- Inaugural editorial. *CurrTrendGenomicMed* 2015;1:2.
47. **Dhavendra Kumar**. 'Applied and translational genetic and genomic practice of the cardiovascular medicine and surgery'- Inaugural Editorial. *CardiovascularGeneticsGenomics* 2015;1:1-3.
48. Jeremy F McRae,……..**Dhavendra Kumar,** …….. Matthew E Hurles: Prevalence, phenotype and architecture of developmental disorders caused by *de novo* mutation - The Deciphering Developmental Disorders Study . bioRxiv 049056; doi: https://doi.org/10.1101/049056
49. Fadil M. Hannan Sarah A. Howles **Dhavendra Kumar** …..Rajesh V. Thakker. Adaptor protein-2 sigma subunit mutations causing familial hypocalciuric hypercalcaemia type 3 (FHH3) demonstrate genotype–phenotype correlations, codon bias and

dominant-negative effects; *Human Molecular Genetics*, Volume 24, Issue 18, 15 September 2015, Pages 5079–5092; https://doi.org/10.1093/hmg/ddv226

50. Mark J Hamilton, Richard Caswell, Natalie Canham, ...**Dhavendra Kumar**, ...The Deciphering Developmental Disorders Study, Mohnish Suri

"Heterozygous mutations affecting the protein kinase domain of CDK13 cause a syndromic form of developmental delay and intellectual disability"(Journal of Medical Genetics http://creativecommons.org/licenses/by/4.0/ http://dx.doi.org/10.1136/jmedgenet-2017-104620

51. Prevalence and architecture of *de novo* mutations in developmental disorders; Deciphering Developmental Disorders Study : Jeremy F. McRae……., **Dhavendra Kumar** & Matthew E. Hurles; *Nature* volume542, pages433–438 (23 February 2017); doi:10.1038/nature21062

52. Prevalence, phenotype and architecture of developmental disorders caused by denovo mutation. JeremyF McRae et al. with **Dhavendra Kumar**, ……, Matthew E Hurles. doi: https://doi.org/10.1101/049056

53. Quantifying the contribution of recessive coding variation to developmental disorders. Hilary Martin et al. *bioRxiv* (2017) Key: citeulike:14481973

54. Histone Lysine Methylases and Demethylases in the Landscape of Human Developmental Disorders.

VíctorFaundes[12]DhavendraKumar[7]……..SiddharthBanka[13]https://doi.org/10.1016/j.ajhg.2017.11.013

55. Autosomal recessive coding variants explain only a small proportion of undiagnosed developmental disorders in the British Isles. HilaryC. Martin, WendyD. Jones et al, **Dhavendra Kumar**, withMatthewE. Hurles, JeffreyC. Barrett;

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56**. Kumar, D**. (2020) The genomic and precision medicine in clinical practice Current perspectives and future directions. The Physician vol 6; issue 3; epub 02.10.2020: DOI: 10.38192/1.6.3.1

57. Irbesartan in Marfan syndrome (AIMS): a double-blind,

placebo-controlled randomised trial. Mullen et al. Lancet 2019; 394: 2263–70

Published Online, December 10, 2019; https://doi.org/10.1016/

S0140-6736(19)32518-8; **Dhavendra Kumar**. Supplementary

58. Ensuring best practice in genomics education and evaluation: reporting item standards for education and its evaluation in genomics (RISE2 Genomics). Amy Nisselle[1],…… **Dhavendra Kumar[19]**, Helen Jordan[38] and Clara Gaff. Genetics in Medicine. https://doi.org/10.1038/s41436-021-01140-x

59. **Dhavendra Kumar**, Edward J. Steele, N.Chandra Wickramsinghe (2020). The origin of life and astrobiology. *Cosmic Genetic Evolution; Advances in Genetics*, Volume 106: xv-xviii.

60. **Dhavendra Kumar**. Genomic and Molecular Cardiology (2021). *The cardiovascular*

genomic medicine- a global initiative. ***WWW.genomicmedicine.org***
61. **Dhavendra Kumar** & Madhukar Mittal**.** *India's Covid-10 emergency: overarching conclusions belie facts.* Lancet. 2021 26 June-2 July; 397(10293): 2465.
Published online 2021 Jun 24. doi: 10.1016/S0140-6736(21)01243-5
62. **Dhavendra Kumar**. The emergence of clinical genomics and genomic medicine across India: the role of the UK India Genomic Medicine Alliance. Genetic Clinics 2022;vol15:19-20.
63. **Dhavendra Kumar**. The genomic healthcare in modern medicine. Editorial. Apollo Medicine, Volume 20 (2), April-June 2023, 91.
64. **Dhavendra Kumar**. From the Double-Helix to the personal genomes. Review, Apollo Medicine, Volume 20(2); July 2023, pp115-128.
65. **Dhavendra Kumar**. 'Indigenous population genome databases for India and South Asia- an emerging need for health and social applications', Journal of Genetics, 2023, 102:45-50.
66. **Dhavendra Kumar**. ' Drug repurposing for rare (orphan) diseases- scope and limitations'. Review, Apollo Medicine. 2024; https://doi.org/10.1177/09760016241287308

X SELECTED PAPERS AND BOOK CHAPTERS

This section includes 'first page' showing Abstract or Introduction. Full copy of the publication available on request.

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J Med Genet 1990; 27: 122–126

Syndrome of the month

Edited by D Donnai and R Winter

Moebius syndrome

Dhavendra Kumar

Moebius syndrome consists of congenital complete or partial facial nerve palsy with or without paralysis of other cranial nerves (most commonly an abducens paralysis) and often associated with other malformations of the limbs and orofacial structures. The first description of congenital facial diplegia was given by von Graaefe in 1880[1] and this was soon followed by other reports. Moebius[2 3] drew attention to the association of congenital facial diplegia with other malformations. Alternative terms[4] used to describe the syndrome include congenital facial diplegia, nuclear agenesis, congenital nuclear hypoplasia, congenital oculofacial paralysis, and congenital abducens-facial paralysis. There is considerable overlap with the hypoglossia-hypodactyly syndrome, the glossopalatine-ankylosis syndrome, and Charlie-M syndrome.[4] The criteria for diagnosis are difficult to define; however, based on previous published reviews,[5–7] the following guidelines should assist in making a diagnosis of Moebius syndrome.

Criteria for diagnosis

(1) Complete or partial facial nerve paralysis is essential for the diagnosis of Moebius syndrome.
(2) Limb malformations (syndactyly, brachydactyly or absent digits, and talipes) are often present.
(3) The following additional clinical features in association with complete or partial facial nerve (VII) paralysis may also be present and should be helpful in making a clinical diagnosis of Moebius syndrome: bilateral or unilateral ocular nerve palsies (commonly of the abducens (VI) and less commonly of the oculomotor (III) and trochlear (IV) nerves); hypoplasia of the tongue owing to hypoglossal (XII) nerve paralysis; swallowing and speech difficulties owing to trigeminal (V), glossopharyngeal (IX), and vagus (X) nerve palsies; malformations of the orofacial structures (bifid uvula, micrognathia, and ear deformities); other anomalies of the musculoskeletal system, for example, Klippel-Feil anomaly, absence of the sternal head of the pectoralis major, rib defects, and brachial muscle defects.

Clinical findings

The condition can usually be diagnosed soon after birth and manifests with incomplete closure of the eyelids during sleep, drooling of saliva, and difficulties in sucking. Later, it is noted that the child does not smile or move its facial muscles on crying, the so called 'mask-like facies' (fig 1). The seventh

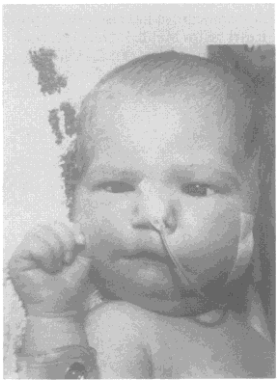

Figure 1 Seven day old female infant with Moebius syndrome. Note smooth, expressionless face, inner epicanthic folds, and convergent strabismus. This child also had talipes and small toes with syndactyly.

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Accepted for publication 27 June 1989.

American Journal of Medical Genetics 70:107–113 (1997)

Familial Aplasia/Hypoplasia of Pelvis, Femur, Fibula, and Ulna With Abnormal Digits in an Inbred Pakistani Muslim Family: A Possible New Autosomal Recessive Disorder With Overlapping Manifestations of the Syndromes of Fuhrmann, Al-Awadi, and Raas-Rothschild

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We describe four affected children belonging to a large, highly inbred Muslim family originating from the North West Frontier Province of Pakistan. All children have a similar pattern of skeletal abnormalities, including aplasia/hypoplasia of the ulnae, hypoplasia of the pelvis, aplasia/hypoplasia of the femora, fibular aplasia, and variable digital abnormalities and absent/dysplastic nails. The phenotype overlaps with the syndromes of Fuhrmann, Al-Awadi, and Raas-Rothschild. The present and previously reported families probably share the same geographic and racial origin, indicating a common genetic basis of the reported skeletal abnormalities in these limb-pelvis aplasia and hypoplasia syndromes. A possibility of a new autosomal recessive syndrome in the present family cannot be excluded. Further delineation and molecular studies are required to clarify the genetic cause and phenotypic variation in Fuhrmann, Al-Awadi, and Raas-Rothschild syndromes. Am. J. Med. Genet. 70:107–113, 1997.
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KEY WORDS: autosomal recessive; consanguinity; FFU complex; Fuhrmann syndrome; Al-Awadi syndrome; Raas-Rothschild syndrome; proximal focal femoral deficiency (PFFD)

INTRODUCTION

Congenital developmental defects of femur, fibula, ulna, fibular rays, and ulnar rays (FFU complex) are uncommon, and are probably causally heterogeneous. The term proximal focal femoral deficiency (PFFD), coined by Aitken [1969], can be part of the FFU complex [Lenz and Feldmann, 1977]. Autosomal recessive inheritance was suggested in the FFU complex [Zlotogora et al., 1983], although most cases are sporadic [Kühne et al., 1967; Lenz and Feldmann, 1977]. A subsequent case report [Fuhrmann et al., 1980] described an association of poly-, syn-, and oligodactyly with aplasia and hypoplasia of femur and fibula, but without developmental abnormalities of the ulna and ulnar rays. Familial occurrence of similar combinations of developmental skeletal abnormalities was described with thoracic "dystrophy" (the Al-Awadi syndrome) [Al-Awadi et al., 1985], and pelvis hypoplasia (the Raas-Rothschild syndrome) [Raas-Rothschild et al., 1988].

We report on a large, consanguineous Muslim family, originating from the North West Frontier Province of Pakistan, in which four children were born with malformations of the forearms, hands, fingers, pelvis, and lower limbs. All shared a variable degree of aplasia/hypoplasia of the femur, fibula, and ulna associated with digital abnormalities, including brachydactyly of the fourth and fifth fingers and toes bilaterally with hypoplasia of fingernails. Complex and multiple consanguinity in this family strongly supports autosomal recessive inheritance. The clinical findings in this family are discussed in the context of previous reports.

CLINICAL REPORTS

The family (Fig. 1) came to our attention following the birth of the proposita, V-7. Two other related children (V-3 and V-5) were then ascertained, born with similar developmental defects of the limbs. II-2 and

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Received 7 March 1995; Accepted 18 September 1996

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REPORT

Mutations in *WNT7A* Cause a Range of Limb Malformations, Including Fuhrmann Syndrome and Al-Awadi/Raas-Rothschild/ Schinzel Phocomelia Syndrome

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Fuhrmann syndrome and the Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome are considered to be distinct limb-malformation disorders characterized by various degrees of limb aplasia/hypoplasia and joint dysplasia in humans. In families with these syndromes, we found homozygous missense mutations in the dorsoventral-patterning gene *WNT7A* and confirmed their functional significance in retroviral-mediated transfection of chicken mesenchyme cell cultures and developing limbs. The results suggest that a partial loss of WNT7A function causes Fuhrmann syndrome (and a phenotype similar to mouse *Wnt7a* knockout), whereas the more-severe limb truncation phenotypes observed in Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome result from null mutations (and cause a phenotype similar to mouse *Shh* knockout). These findings illustrate the specific and conserved importance of WNT7A in multiple aspects of vertebrate limb development.

The tetrapod limb develops as an outgrowth of mesenchymal cells, from the lateral plate mesoderm, that are covered by a layer of ectoderm. Over time, the limb bud grows and lengthens, giving rise to the various components of the limb: skeleton, muscles, tendons, and nerves. The limb skeleton is laid down progressively, starting with the most proximal part—that is, humerus/femur—and finishing with the most distal, the tips of finger and toes. This complex patterning process is determined by a three-dimensional signaling system that defines a proximodistal axis (from shoulder to finger tip), an anteroposterior axis (from radius/thumb to the ulna/little finger), and a dorsoventral axis (from the dorsum of the hand to the palm).

Recent studies have unraveled the major molecular components that coordinate limb outgrowth along these three axes.[1] The proximodistal axis is under the control of fibroblast growth factors (FGFs) from the apical ectodermal ridge (AER). The anteroposterior axis is under the control of sonic hedgehog (*SHH*) from the posterior mesenchyme (zone of polarizing activity [ZPA]), whereas the dorsoventral axis is controlled by bone morphogenetic proteins (BMPs) and engrailed (EN1) from the ventral ectoderm and by Wnt7a from the dorsal ectoderm. Traditionally, these signals are regarded as independent entities, but their activities cannot be separated, because they are mutually dependent. For example, AER and ZPA signals each induce expression of the other and the removal of one equally results in down-regulation of the other.[2,3] Likewise, removal of the dorsal ectoderm or its signal Wnt7a results in a severe reduction of *SHH* expression,[4,5] indicating that maintenance of *SHH* expression requires both the dorsal ectoderm and the AER.

Alterations in the composition of this system—either by targeted gene inactivation in the mouse, by overexpression of certain genes in chick embryos, or by deleterious gene mutations in humans—result in specific and characteristic phenotypes.[6,7] Inactivation of Wnt7a in mouse, for example, results in a loss of dorsal structures of the distal limb that manifests as biventral autopods with footpads on both sides.[4] Wnt7a defines the dorsoventral axis by inducing the expression of the transcription factor *Lmx1* in the dorsal mesenchyme of the developing limb.[8] Mutations in *Lmx1*, in turn, result in nail-patella syndrome, a human condition characterized by loss of dorsal features, with nail dysplasia, hypoplastic patellae, and other skeletal changes.[9] The expression of *Wnt7a* is restricted to the dorsal ectoderm because it is repressed by *EN1* in the ventral ectoderm. Inactivation of *EN1* results in double-dorsal limbs, probably because of the successive misexpression of *WNT7A* in the ventral ectoderm.[10] We describe here the developmental defects of the human limb caused by malfunction of *WNT7A,* which were unexpectedly more severe than the mouse mutant phenotype.

Clinical findings.—We investigated two families with an autosomal recessive disorder that caused significant limb shortening with marked fibular and ulnar hypoplasia (fig.

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Received March 29, 2006; accepted for publication May 30, 2006; electronically published June 23, 2006.

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Am. J. Hum. Genet. 2006;79:402–408. © 2006 by The American Society of Human Genetics. All rights reserved. 0002-9297/2006/7902-0025$15.00

Hum Genet (1990) 85:525–526

Human Genetics

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Amplification of the COL2A1 3′ variable region used for segregation analysis in a family with the Stickler syndrome

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Summary. Amplification of a variable region 3′ to the human type II collagen gene (COL2A1) has permitted segregation analysis in a three generation Stickler syndrome pedigree. This family had previously proved uninformative for the known restriction fragment length dimorphisms. Amplification of the variable region revealed five distinguishable alleles, of which three were segregating in this family. The lod score in favour of linkage was 2.86 at zero recombination.

Introduction

Type II collagen is the major structural protein in cartilage and its encoding locus, COL2A1 (12q1.23–3.21), has been a favourite for analysis as a candidate gene in a range of heritable chondrodysplasias. Fortunately, the locus is quite rich in useful dimorphic restriction sites and several have been described (Sykes 1983; Sykes et al. 1985a; Wordsworth et al. 1988). Nonetheless, some analyses have been frustrated by the limited heterozygosity imposed by two-allele marker systems. An example of this is a three-generation Stickler syndrome pedigree with 11 meioses of which only two proved to be informative. This family had been referred to us in 1986 during a broad linkage survey of several chondrodysplasias, the results of which have been published (Wordsworth et al. 1988).

The Stickler syndrome is a dominantly inherited progressive arthro-ophthalmopathy first described in 1965. It is characterised by premature osteoarthritis, mild spondyloepiphyseal dysplasia, ocular degeneration, hearing loss and the Pierre-Robin sequence (Temple 1989). Francomano and her colleagues first reported concordance between COL2A1 and the Stickler syndrome in a large pedigree with a Lod score of 3.28 at $\theta = 0.00$ (Francomano et al. 1987). This was followed up by reports of other families, some of which supported and some of which disputed the original linkage (Francomano et al. 1988; Weaver et al. 1989; Knowlton et al. 1989). The uncertainty prompted us to look again at our three generation Stickler family.

Offprint requests to: B. Sykes

We were aware that there is a length polymorphism just beyond the 3′ end of the gene in a segment of tandemly arranged imperfect repeats of 31–34 bp (Sykes et al. 1985b; Stoker et al. 1985). Alleles differ in the overall length of the segment with a range of 300–600 bp. The variation in this region was first detected in *Eco*RI digests of DNA from Asians on Southern blots. Unfortunately the range of allele sizes in Caucasians seems to be much more restricted. It has proved to be technically difficult to distinguish the common alleles by blotting of restriction fragments mainly because the variable region is very AT-rich and gives a poor hybridisation signal. Choice of larger restriction fragments, so as to include sufficient flanking sequence to improve the hybridisation signal, further reduced the resolution between alleles. We therefore turned to polymerase chain amplification of the region.

Methods

Primers (Enzymatix, Cambridge, UK) were selected from sequences flanking the variable region. 5′-CAACTGATAAAACAGAGAGC (residues 1246–1265 of the 3′ untranslated region of COL2A1, sequenced from the cosmid clone CosHcol1 (Stoker et al. 1985)) was used as the forward primer and 5′-CTCCTTTGTCATGAACTAGC (residues 1964–1945) as the reverse. One μg of the genomic DNA was amplified with one unit of *Taq* polymerase (Amplitaq, Cetus) in a 50 μl reaction mix made up according to the suppliers instructions except that bovine serum albumin was added to a final concentration of 20 ng ml^{-1}. Thirty cycles of amplification (65C × 1 min, 72C × 1 min and 93C × 30 sec) were performed in a cycling water bath (Dale, Oxford, UK). The results were first checked on a 1.5% agarose gel, and then 25 μl of the reaction was run on a 5% polyacrylamide gel in TBE for 8 h at 140 volts. Bands were stained with ethidium bromide.

Results

Amplification distinguished five alleles in 64 unrelated caucasian chromosomes which were assigned letters A–E in decreasing length order. Preferential amplification of the shorter allele, particularly in samples which had previously given poor restriction digests, was a consistent feature but its extent varied between amplifications. The commonest allele (D) was approximately the same size as the amplified product of CosHcol1, itself a cauca-

26 *J Med Genet* 2000;**37**:26–32

Original articles

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Revised version received 19 August 1999
Accepted for publication 27 August 1999

Evidence for digenic inheritance in some cases of Antley-Bixler syndrome?

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Abstract
The Antley-Bixler syndrome has been thought to be caused by an autosomal recessive gene. However, patients with this phenotype have been reported with a new dominant mutation at the *FGFR2* locus as well as in the offspring of mothers taking the antifungal agent fluconazole during early pregnancy. In addition to the craniosynostosis and joint ankylosis which are the clinical hallmarks of the condition, many patients, especially females, have genital abnormalities. We now report abnormalities of steroid biogenesis in seven of 16 patients with an Antley-Bixler phenotype. Additionally, we identify *FGFR2* mutations in seven of these 16 patients, including one patient with abnormal steroidogenesis. These findings, suggesting that some cases of Antley-Bixler syndrome are the outcome of two distinct genetic events, allow a hypothesis to be formulated under which we may explain all the differing and seemingly contradictory circumstances in which the Antley-Bixler phenotype has been recognised.
(*J Med Genet* 2000;**37**:26–32)

Keywords: Antley-Bixler syndrome; *FGFR*; congenital adrenal hyperplasia; CYP21 deficiency

In 1975 Antley and Bixler[1] reported a patient with craniosynostosis, radiohumeral synostosis, and femoral bowing. A further 24 cases have since been added, showing that humero-ulnar synostosis and straight femora may also be consistent with the condition,[2] although the exact nosology can be controversial on occasion.[3–5] An intriguing aspect of these reports is the frequency of genital abnormalities among affected subjects, 14 of whom were noted to have this feature. Of these 14 cases, 10 were females with clitoromegaly, fusion of the labia minora, and hypoplasia of the labia majora.[2 6] Against this, eight females have been described in whom the genitalia were normal, or not thought worthy of comment by the authors.

The Antley-Bixler syndrome represents the severe end of the spectrum of syndromic craniosynostosis. Many such patients have choanal atresia and severe respiratory distress, often resulting in early death. In contrast with most clinically similar forms of syndromic craniosynostosis, which are transmitted in an autosomal dominant manner, Antley-Bixler syndrome has been thought to be an autosomal recessive disorder.[7] This is based upon three reports of affected sibs[8–10] and the birth of affected subjects to consanguineous parents.[9 11 12] It should be noted that joint ankylosis in the context of craniosynostosis is not exclusive to Antley-Bixler syndrome and is also seen in some cases of Pfeiffer syndrome, many of which arise as new autosomal dominant mutations.[13–15] However, unlike Antley-Bixler syndrome, genital malformations are not characteristic of Pfeiffer syndrome. Similarly, femoral bowing with craniosynostosis can be seen in some cases of thanatophoric dysplasia, again without accompanying genital anomalies. An important observation common to all three sibships with recurrence of Antley-Bixler syndrome is the concordance of genital abnormalities in all six cases.[8–10]

Mutation of members of the fibroblast growth factor receptor gene family (*FGFR*) has been established as the basis of several autosomal dominant forms of craniosynostosis.[16–18] Other mutations of this gene family have been established as the cause of several variants of skeletal dysplasia, including thanatophoric dysplasia.[19–21] As the effects of *FGFR* mutation on receptor function have become clearer, it has been suggested that these mutant forms are viable only in the heterozygous state and that homozygosity for *FGFR* mutation would be lethal.[18]

New dominant mutations at the *FGFR2* locus have been observed in patients with a phenotype very similar to that of Antley-Bixler syndrome,[15 22–24] although the genitalia in these reports, which included three females, did not show evidence of clitoromegaly. Genital abnormalities are not characteristic of syndromes arising as a result of *FGFR* mutation and the high prevalence of such anomalies, especially among female infants, is an unexplained aspect

American Journal of Medical Genetics 75:508–515 (1998)

Recognizable Inherited Syndrome of Progressive Central Nervous System Degeneration and Generalized Intracranial Calcification With Overlapping Phenotype of the Syndrome of Aicardi and Goutières

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Five boys and two girls from a large consanguineous British Muslim family of Pakistani origin are described. All presented from infancy to early childhood with progressive moderate to severe developmental delay, postnatal microcephaly, spastic quadriplegia, refractory seizures, and visual handicap. Cerebrospinal fluid (CSF) pleocytosis was present in three children. Neuroimaging with computerized tomography on three boys and a girl showed generalized cortical atrophy, dilatation of the lateral, third, and fourth ventricles, widening of the surface CSF spaces, hypoplasia of the posterior fossa structures, and multiple and solitary calcifications in the cerebral cortex and punctate calcifications involving basal ganglia, cerebellum, and the Sylvian fissure. Histopathological examination of the brain from three boys and one girl confirmed generalized cortical and cerebellar atrophy with widespread calcifications within the cortical grey and white matter, the basal ganglia, the cerebellum, and in some areas along the capillaries. Investigations excluded a possible nongenetic cause. Parental consanguinity favor autosomal recessive inheritance. This appears to be a recognizable syndrome overlapping the syndrome of Aicardi and Goutières (MIM 225750). Am. J. Med. Genet. 75:508–515, 1998.

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KEY WORDS: **intracranial calcification; cerebral calcinosis, familial encephalopathy, autosomal recessive; post-natal microcephaly, spastic paraparesis; seizures, basal ganglia calcification; cerebrospinal fluid (CSF) pleocytosis; interferon-alpha (IFN-α)**

INTRODUCTION

Progressive central nervous system (CNS) disorders with intracranial calcifications recognizable at birth or with early onset in infancy and childhood are uncommon. Both nongenetic and genetic causes are described. Several inherited syndromes with CNS involvement may manifest with intracranial calcifications [Baraitser, 1995; McKusick, 1995]. The natural history and spectrum of the neurological deficit might be similar to a progressive CNS degenerative disorder [Bundey, 1995]. Not uncommonly, these cases are investigated to exclude an intrauterine infection.

Apart from an intrauterine infection, other causes of congenital or early onset intracranial calcifications include cerebral abscesses, intracortical hemorrhages, metabolic problems related to acquired parathyroid disease, chronic renal disease, and nutritional problems. Focal or generalized cerebral calcinosis is a known manifestation in some recognizable genetic disorders, such as tuberous sclerosis, basal cell nevus syndrome, Sturge-Weber syndrome, and Cockayne dwarfism [Bundey, 1995]. Intracranial calcifications in adults could be an incidental finding on neuroimaging, often associated with a mild disorder of parathyroid function, probably unrelated to Albright pseudo or pseudo-pseudo hypoparathyroidism [Nicholls et al., 1961].

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Received 14 April 1997; Accepted 28 July 1997

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Downloaded from http://jmg.bmj.com/ on March 30, 2015 - Published by group.bmj.com

SHORT REPORT

A second locus for Aicardi-Goutières syndrome at chromosome 13q14–21

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J Med Genet 2006;**43**:444–450. doi: 10.1136/jmg.2005.031880

Background: Aicardi-Goutières syndrome (AGS) is an autosomal recessive, early onset encephalopathy characterised by calcification of the basal ganglia, chronic cerebrospinal fluid lymphocytosis, and negative serological investigations for common prenatal infections. AGS may result from a perturbation of interferon α metabolism. The disorder is genetically heterogeneous with approximately 50% of families mapping to the first known locus at 3p21 (AGS1).
Methods: A genome-wide scan was performed in 10 families with a clinical diagnosis of AGS in whom linkage to AGS1 had been excluded. Higher density genotyping in regions of interest was also undertaken using the 10 mapping pedigrees and seven additional AGS families.
Results: Our results demonstrate significant linkage to a second AGS locus (AGS2) at chromosome 13q14–21 with a maximum multipoint heterogeneity logarithm of the odds (LOD) score of 5.75 at D13S768. The AGS2 locus lies within a 4.7 cM region as defined by a 1 LOD-unit support interval.
Conclusions: We have identified a second AGS disease locus and at least one further locus. As in a number of other conditions, genetic heterogeneity represents a significant obstacle to gene identification in AGS. The localisation of AGS2 represents an important step in this process.

Aicardi-Goutierès syndrome (AGS; MIM 225750) is an autosomal recessive encephalopathy characterised by cerebral atrophy, leukodystrophic changes, intracranial calcification, chronic cerebrospinal fluid (CSF) lymphocytosis, raised levels of interferon α (IFN-α) in the CSF, and negative serological investigations for common prenatal infections (MIM 225750).[1 2] Clinically, AGS can usefully be considered as a Mendelian mimic of congenital viral infection. Recognition of the condition is therefore important because of the possibility of misdiagnosis as a non-genetic disorder and counselling of a falsely low risk of recurrence.

The features of AGS may have a prenatal onset or develop over the first few months of life.[2 3] Typically, neurodegeneration is associated with microcephaly, spasticity, dystonic posturing, and psychomotor retardation. Death frequently occurs within the first decade. However, we are aware of several children in their teenage years with apparently non-progressive disease. Systemic abnormalities include fever, raised levels of immunoglobulins and autoantibodies, thrombocytopenia, abnormal liver function with hepatosplenomegaly, and chilblain-like cutaneous lesions.[2 4–7]

Levels of CSF IFN-α are consistently elevated in the early stages of AGS and significantly higher than those recorded systemically.[2 8] Such raised levels of CSF IFN-α are not always accompanied by CSF lymphocytosis.[9] IFN-α does not cross the blood-brain barrier, so when 100 IU/ml of IFN-α is experimentally released into the blood, <1 IU/ml is detected in the CSF.[10] It is likely then that in AGS, IFN-α is produced intrathecally, possibly by astrocytes or microglia.[11 12]

The pathological finding of wedge shaped infarctions together with patchy myelin loss and calcified deposits in the media, adventitia, and perivascular space of small blood vessels suggests that AGS may represent a genetic cerebral angiopathy.[13] IFN-α is known to have an inhibitory effect on angiogenesis and astrocyte specific chronic overproduction of IFN-α in transgenic mice recapitulates the neuropathological findings seen in AGS.[14–17] These observations raise the possibility that the AGS phenotype results from exposure of the developing brain to high levels of IFN-α. Identification of the causative genetic defect in AGS may, therefore, provide novel insights into IFN-α metabolism.

Previously, we identified linkage to an interval on 3p21 in 48% of AGS families tested.[18] Locus heterogeneity was considered the explanation for a failure to identify genetic linkage in a previous study.[19] Since then, we have refined the AGS1 critical interval to a 3.47 cM region by demonstrating that AGS and Cree encephalitis are allelic disorders.[9]

Given that half of the families in our cohort were unlinked to the AGS1 locus, we performed a genome-wide scan using 10 families incompatible with linkage to AGS1. Herein, we report the identification of a second AGS locus at chromosome 13q14–21 resulting from an analysis of this data set.

METHODS

Subjects

For inclusion in the study, affected individuals had to demonstrate a compatible neurological phenotype with intracranial calcification and CSF lymphocytosis (>5 cells/mm^3) and/or raised levels of IFN-α in the CSF (>2 IU/ml; measured with a biological assay) as well as negative investigations for common prenatal infections.[2]

Seventeen families (15 consanguineous and two non-consanguineous comprising three affected siblings) satisfied the inclusion criteria (tables 1 and 2). Blood samples were obtained with consent from affected children, their parents, and unaffected siblings where possible, for DNA extraction, genotyping, and subsequent linkage analysis. The study was approved by the Leeds Health Authority/United Teaching Hospitals NHS Trust Research Ethics Committee.

Abbreviations: AGS, Aicardi-Goutières syndrome; HLOD, heterogeneity LOD; IFN-α, interferon α; LOD, logarithm of the odds

Hum Genet (2002) 110 : 561–567
DOI 10.1007/s00439-002-0733-3

ORIGINAL INVESTIGATION

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Mutation analysis of the *MKKS* gene in McKusick-Kaufman syndrome and selected Bardet-Biedl syndrome patients

Received: 26 September 2001 / Accepted: 27 March 2002 / Published online: 9 May 2002
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Abstract McKusick-Kaufman syndrome comprises hydrometrocolpos, polydactyly, and congenital heart defects and overlaps with Bardet-Biedl syndrome, comprising retinitis pigmentosa, polydactyly, obesity, mental retardation, and renal and genital anomalies. Bardet-Biedl syndrome is genetically heterogeneous with three cloned genes (*BBS2*, *BBS4*, and *MKKS*) and at least three other known loci (*BBS1*, *BBS3*, and *BBS5*). Both McKusick-Kaufman syndrome and Bardet-Biedl syndrome are inherited in an autosomal recessive pattern, and both syndromes are caused by mutations in the *MKKS* gene. However, mutations in *MKKS* are found in only 4%–11% of unselected Bardet-Biedl syndrome patients. We hypothesized that an analysis of patients with atypical Bardet-Biedl syndrome and McKusick-Kaufman syndrome (Group I; 15 probands) and patients with Bardet-Biedl syndrome who had linkage results inconsistent with linkage to the other loci (Group II; 12 probands) could increase the *MKKS* mutation yield. Both mutant alleles were identified in only two families in Group II. Single (heterozygous) sequence variations were found in three Group I families and in two Group II families. Combining these results with previously published data showed that only one mutant allele was detected in nearly half of all patients screened to date, suggesting that unusual mutational mechanisms or patterns of inheritance may be involved. However, sequencing of the *BBS2* gene in these patients did not provide any evidence of digenic or "triallelic" inheritance. The frequency of detected mutations in *MKKS* in Group II patients was 24%, i.e., six times higher than the published rate for unselected BBS patients, suggesting that small-scale linkage analyses may be useful in suitable families.

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Introduction

McKusick-Kaufman syndrome (MKS) is a rare syndrome inherited in an autosomal recessive pattern with a phenotypic triad comprising hydrometrocolpos (HMC), post-axial polydactyly (PAP), and congenital cardiac disease (McKusick et al. 1964; Kaufman et al. 1972; Lurie and Wulfsberg 1994; Slavotinek and Biesecker 2000). Bardet-Biedl syndrome (BBS) is a genetically heterogeneous disorder inherited in an autosomal recessive pattern characterized by retinitis pigmentosa (RP), PAP, truncal obesity,

Clin Genet 1997: 52: 30–36
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CLINICAL GENETICS
ISSN 0009-9163

A new multiple malformation syndrome of Müllerian dysgenesis and conductive hearing loss with facial hypoplasia, bilateral forearm deformity,brachydactyly, spinal stenosis and scoliosis

Kumar D, Masel JP. A new multiple malformation syndrome of Müllerian dysgenesis and conductive hearing loss with facial hypoplasia, bilateral forearm deformity,brachydactyly, spinal stenosis and scoliosis. Clin Genet 1997: 52: 30–36. © Munksgaard, 1997

Multiple congenital malformations in a young girl with bilateral conductive hearing loss are described. Facial dysmorphic features include prominent supraorbital ridges, facial hypoplasia, facial asymmetry, downward-slanting palpebral fissures, high prominent nasal bridge with bifid nasal tip and a small lower jaw, and hypoplastic ear lobules with bilaterally narrow and oblique external auditory canals. Recognisable skeletal abnormalities include hypoplastic facial bones, hypoplastic clavicles, narrow and anteriorly sloping shoulders, bowing of both forearm bones, brachydactyly due to short metacarpals and hypoplastic terminal phalanges, thoracolumbar kyphoscoliosis, narrow transverse measurements of most vertebrae with prominent coccyx, spinal canal narrowing, hypoplasia of lower ilia, medially bowed femora, tibiae and fibulae and brachysyndactyly of the second, third and fourth toes bilaterally. Gynaecological evaluation revealed abnormalities of the Müllerian duct structures: urogenital sinus, a vestigial uterus, a posteriorly placed small but patent vagina and a septum at the vaginal introitus. The pattern of MCA probably refers to a new syndrome within the "community of syndromes" involving anomalies of the Müllerian duct structures, limbs, spine and external ears.

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Key words: brachydactyly – congenital malformation syndrome – deafness – facial dysmorphism – limb deformity – Müllerian dysgenesis – scoliosis – vertebral anomaly

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Received in revised version 1 April, accepted for publication 18 April 1997

Agenesis and maldevelopment of the Müllerian duct structures are known to occur singly (Rokitansky sequence), with renal and cervical spine abnormalities (Müllerian duct aplasia–renal and cervicothoracic somite dysplasia: MURCS association) and may also form part of the spectrum of multiple congenital anomalies (MCA) included in the VATER association (Jones 1996). Various combinations of abnormal Müllerian duct development are often referred to as Mayer-Rokitansky-Hauser [MRH] syndrome [MIM 277000] (McKusick 1994). Several syndromes involving the limb and ear anomalies are also described with anomalies of the Müllerian duct structures (Baraitser & Winter 1995). We report a girl who presented with facial asymmetry and other dysmorphic features, a number of unusual skeletal abnormalities of long bones and vertebrae and anomalies related to maldevelopment of the Müllerian duct structures. We believe the constellation of MCA described in this report is suggestive of a new syndrome or association of multiple developmental defects.

Case report

The proband was a 23-year-old woman. Her younger sister and mother approached their GP regarding the recurrence risks of similar developmental defects in the offspring of the proband's sisters. The GP referred the family for genetic counselling.

The proband is the youngest daughter of unrelated, white parents. The family has lived in South Yorkshire for several generations. Detailed ques-

Genomic Med. (2007) 1:95–104
DOI 10.1007/s11568-007-9013-6

REVIEW

From evidence-based medicine to genomic medicine

Dhavendra Kumar

Received: 19 November 2007 / Revised: 26 November 2007 / Accepted: 28 November 2007 / Published online: 18 December 2007
© Springer Science+Business Media B.V. 2007

Abstract The concept of 'evidence-based medicine' dates back to mid-19th century or even earlier. It remains pivotal in planning, funding and in delivering the health care. Clinicians, public health practitioners, health commissioners/purchasers, health planners, politicians and public seek formal 'evidence' in approving any form of health care provision. Essentially 'evidence-based medicine' aims at the conscientious, explicit and judicious use of the current best evidence in making decisions about the care of individual patients. It is in fact the 'personalised medicine' in practice. Since the completion of the human genome project and the rapid accumulation of huge amount of data, scientists and physicians alike are excited on the prospect of 'personalised health care' based on individual's genotype and phenotype. The first decade of the new millennium now witnesses the transition from 'evidence-based medicine' to the 'genomic medicine'. The practice of medicine, including health promotion and prevention of disease, stands now at a wide-open road as the scientific and medical community embraces itself with the rapidly expanding and revolutionising field of genomic medicine. This article reviews the rapid transformation of modern medicine from the 'evidence-based medicine' to 'genomic medicine'.

Keywords Genetics · Genomics · Evidence-based medicine · Genomic medicine · Personalised medicine · Pharmacogenetics · Pharmacogenomics · Nutrigenomics

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Introduction

The philosophy behind the practice of 'evidence-based medicine' (EBM) is not new. Its philosophical origins date back to the mid-19th century Paris or even earlier (British Medical Journal 1996). Since then it has been hotly debated by clinicians, public health practitioners, health planners and commissioners, politicians and the public. It has now established a central position in the medical practice. The recent upsurge and interest about EBM was triggered in 1991 at the McMaster University in Canada (Guyatt 1991) that led to the North American initiative for EBM (Evidence-Based Medicine Working Group 1992) and establishment of the British centres for evidence-based practice in Oxford and York with the Cochrane Collaboration (Grahame-Smith 1995; Lancet 1995). The importance of EBM was quickly appreciated leading to the launch of a dedicated journal—*Journal of Evidence Based Medicine* (Davidoff et al. 1995). The importance of the evidence-based practice and teaching is reflected in its incorporation in the policy planning and implementation in both undergraduate and postgraduate medical teaching and training (Evidence-Based Medicine Working Group 1992; British Medical Association 1995; SCOPME 1994; General Medical Council 1994). Since its early days the evidence-based practice has evolved as the widely acknowledged paradigm for the health care providers and consumers (Haynes 2002).

The British health community and the public became interested in 'evidence-based medicine' when several articles and official government policy on medical education and training were published (British Medical Association 1995; General Medical Council 1994; House of Commons Health Committee 1995). It was followed by several key articles (Grahame-Smith 1995; Weatherall

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The genomic and precision medicine in clinical practice- Current perspectives and future directions

Abstract

An important milestone in the history of medical science is the recent completion of the human genome sequence. The progress on identification of approximately 22,000 *homo sapiens* genes and their regulatory regions provides the framework for understanding the molecular basis of disease. This advance has also laid the foundation for a broad range of genomic tools that can be applied to medical science. These developments in the gene and gene product analysis across the whole genome have opened the way for targeted molecular genetic testing in a number of medical disorders. This is destined to change the practice of medicine.

The future clinical practice will be more focused, precise and individualized, often referred to as "precision and personalised medicine." However, despite these exciting advances, many practicing clinicians perceive the role of molecular genetics, in particular that of medical genomics, as confined to the research arena with limited clinical applications. Genomic medicine applies the knowledge and understanding of all genes and genetic variation in human disease. The basic ingredient of the contemporary practice of medicine is clinical molecular medicine that encompasses genetic, genomic, and molecular applications. This article introduces genomics-based advances in personalised disease-susceptibility screening, diagnosis, prognostication, stratified approach for genomics-led therapeutics, and prediction of treatment outcome in various areas of medicine.

Key words:
Human genome; genome sequencing; genome variant; genomic medicine; precision medicine; personalised medicine; evidence-based medicine; stratified medicine

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Cite as: Kumar, D. (2020) The genomic and precision medicine in clinical practice – Current perspectives and future directions. The Physician vol 6; issue 3; epub 02.10.2020 DOI: 10.38192/1.6.3.1

Article Information
Submitted 16.09.2020
Peer reviewed 28.09.2020
Published 02.10.2020
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Introduction

Recent innovations and new developments in molecular biology, biotechnology, genomics, and many other *OMIC* sciences have revolutionised the contemporary and future practice of clinical medicine. The diagnosis of most complicated and rare conditions is now possible with high degree of precision. The "gene-specific" and "genome-driven" diagnoses in many inherited and genetic disorders are now possible. The understanding of molecular mechanisms in a number of common and complex medical conditions has vastly improved. Progress in targeted genetic and molecular approach in pharmacotherapy has led many improvements from the current therapeutic regimens, which are designed for the "average model patient" and "one-size-fits-all" model approach. However, this has changed

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Dhavendra Kumar. The Physician. Vol. 6 No. 3 (2021). **The Genomic and Precision Medicine in Clinical Practice: Current perspectives and future directions**.
https://doi.org/10.38192/1.6.3.1

The cardiovascular genomic medicine- a global initiative

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Abstract

Strengths and weaknesses of any scientific development are judged by its translation and applications in real life. Applications in medicine and healthcare are prime examples and conveniently judged and appreciated by millions all over the World. Since the completion of the human genome sequencing, genomic advances in medicine and healthcare have moved ahead with jetting speed. The genomic medicine is no longer a hype but now a realty targeted at specific individual (personalized medicine), at specific molecular disease target (precision medicine), delivered in carefully stratified manner (stratified medicine), and based on the most up to date top class adequately validated evidence (evidence-based medicine).

The cardiovascular genomic medicine is by far one of the best examples of specialist genomic medicine. The field offers fresh opportunity to review and organize management and prevention of wide ranging inherited and familial cardiovascular conditions. By any conservative estimate based on the current incidence and prevalence data, the burden of these disorders is huge in any healthcare settings. In addition to highly sophisticated and specific diagnostic accuracy, applications of genomic and molecular laboratory technologies offer much needed insight into basic cellular and molecular pathology underpinning the rare and common cardiovascular conditions. There is urgent need to harmonize protocols and tools for systemic and globally acceptable definitions, criteria and algorithms utilizing the modern computational and bioinformatic software. The need for globally managed and accessible genomic database is not disputed for recording and annotating several hundred gene-specific variants and genomic variants.

The new emerging field of cardiovascular genomic medicine requires a concerted and coordinated effort involving the global cohort of like-minded clinical, health, nursing and scientific professionals. The global familial heart challenge (GFHC) is a global initiative aimed at achieving the ambitious globalized cardiovascular genomic medicine.

The GFHC is led by the Genomic Medicine Foundation (UK) and supported by the Global Variome. It has generated wide interest amongst the emerging developing countries including India, Asia Pacific, Middle East and Arab, Southern Africa, Europe and Latin America. The NIH funded ClinVar and ClinGen groups are associated with the powerful and undeniably essential cardiovascular genomic mutation and variants database. The globalization of cardiovascular genomic medicine is with us and needs serious collaboration and cooperation to make it useful to patients, families, and all professionals involved.

Irbesartan in Marfan syndrome (AIMS): a double-blind, placebo-controlled randomised trial

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Summary

Background Irbesartan, a long acting selective angiotensin-1 receptor inhibitor, in Marfan syndrome might reduce aortic dilatation, which is associated with dissection and rupture. We aimed to determine the effects of irbesartan on the rate of aortic dilatation in children and adults with Marfan syndrome.

Methods We did a placebo-controlled, double-blind randomised trial at 22 centres in the UK. Individuals aged 6–40 years with clinically confirmed Marfan syndrome were eligible for inclusion. Study participants were all given 75 mg open label irbesartan once daily, then randomly assigned to 150 mg of irbesartan (increased to 300 mg as tolerated) or matching placebo. Aortic diameter was measured by echocardiography at baseline and then annually. All images were analysed by a core laboratory blinded to treatment allocation. The primary endpoint was the rate of aortic root dilatation. This trial is registered with ISRCTN, number ISRCTN90011794.

Findings Between March 14, 2012, and May 1, 2015, 192 participants were recruited and randomly assigned to irbesartan (n=104) or placebo (n=88), and all were followed for up to 5 years. Median age at recruitment was 18 years (IQR 12–28), 99 (52%) were female, mean blood pressure was 110/65 mm Hg (SDs 16 and 12), and 108 (56%) were taking β blockers. Mean baseline aortic root diameter was 34·4 mm in the irbesartan group (SD 5·8) and placebo group (5·5). The mean rate of aortic root dilatation was 0·53 mm per year (95% CI 0·39 to 0·67) in the irbesartan group compared with 0·74 mm per year (0·60 to 0·89) in the placebo group, with a difference in means of –0·22 mm per year (–0·41 to –0·02, p=0·030). The rate of change in aortic Z score was also reduced by irbesartan (difference in means –0·10 per year, 95% CI –0·19 to –0·01, p=0·035). Irbesartan was well tolerated with no observed differences in rates of serious adverse events.

Interpretation Irbesartan is associated with a reduction in the rate of aortic dilatation in children and young adults with Marfan syndrome and could reduce the incidence of aortic complications.

Funding British Heart Foundation, the UK Marfan Trust, the UK Marfan Association.

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Lancet 2019; 394: 2263–70

Published Online December 10, 2019 https://doi.org/10.1016/S0140-6736(19)32518-8

See Comment page 2206

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Introduction

Marfan syndrome is a dominantly inherited disorder of connective tissue caused by mutations in the gene that encodes fibrillin-1.[1] Cardiovascular complications, including aortic root dilatation, dissection, and rupture, are the leading cause of morbidity and mortality.[2] β blockers have been advocated to reduce the rate of aortic root dilatation in people with Marfan syndrome.[3,4] Experimental models of Marfan syndrome suggest that angiotensin-II type 1 receptor blockers (ARBs) can alter biological pathways, including excessive TGF-β signalling, that might contribute to the pathogenesis of aortic complications,[5–8] a finding that is supported by observational data in clinical studies.[9] Randomised trials in Marfan syndrome have compared the effects of the ARB losartan with either β blockers or control (where standard medical therapy could include β blockers) on aortic dilatation[10–15] without clear evidence of benefit. Other ARBs, such as irbesartan, might have greater bioavailability and a longer half-life than losartan with more potent antihypertensive effects. We aimed to determine the effects of the ARB irbesartan on the rate of aortic dilatation in children and adults with Marfan syndrome.

Methods

Study design and participants

The design and methods for the Aortic Irbesartan Marfan Study (AIMS) study have previously been reported.[16] Briefly, AIMS was an investigator-led, placebo-controlled, double-blind randomised trial done at 22 centres with experience of managing Marfan Syndrome in the UK. The study protocol was approved by the UK National Research Ethics Committee, participating institutions, and relevant regulatory authorities. All participants, or their legal guardians in the case of children, provided written informed consent. The study complies with the principles of the Declaration of Helsinki.

Individuals were eligible for inclusion if they were aged between 6 and 40 years and had clinically confirmed

Human Molecular Genetics, 2015, Vol. 24, No. 18 5079–5092

doi: 10.1093/hmg/ddv226
Advance Access Publication Date: 16 June 2015
Original Article

ORIGINAL ARTICLE

Adaptor protein-2 sigma subunit mutations causing familial hypocalciuric hypercalcaemia type 3 (FHH3) demonstrate genotype–phenotype correlations, codon bias and dominant-negative effects

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Received: May 1, 2015. **Revised and Accepted:** June 12, 2015

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Ann Ist Super Sanità 2011 | Vol. 47, No. 1: 31-40
DOI: 10.4415/ANN_11_01_08

The personalised medicine. A paradigm of evidence-based medicine

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Summary. The practice of "evidence-based medicine" aims at the conscientious, explicit and judicious use of the current best evidence in making decisions about the individualised patient care. The clinical genetics evolved from translational genetics research and contributes to the clinical care of patients and families through evidence-based health care in managing inherited disorders through accurate diagnosis, molecular pathology and assessing phenotypic correlations. Translational genetics and genomics research has led to the development of powerful tools for clinical diagnosis, assessing individual's genomic profile for disease prediction/prevention, high-throughput genome-wide screening for predisposition and/or protection to complex medical conditions, and discovery and development of new drugs and vaccines. Gene mapping and deciphering pathogenic mutations have helped in unravelling the basic biological mechanisms leading to new drug discovery and development. Targeted pharmacotherapy is now possible for managing the highly penetrant multi-system dominantly inherited conditions. Notable examples include rapamycin (sirolimus) in suppressing the mTOR pathway associated hamartomas in dominantly inherited cancer family syndromes and angiotensin converting enzyme receptor blockers (ACE-RB) in preventing aortic dilatation in Marfan syndrome and related familial arteriopathies. The *translational genomic research* is the essential prerequisite for developing sound *evidence-based* diagnostic, therapeutic and prognostic clinical protocols for the practice of *personalised clinical medicine*.

Key words: evidence-based medicine, genomic medicine, translational research, personalized medicine, micro arrays, genetic testing, high-throughput genomic screening, pharmacogenomics, clinical trials.

Riassunto *(La medicina personalizzata: un paradigma della medicina basata sull'evidenza)*. La pratica della medicina basata sull'evidenza (*evidence-based medicine*, EBM) mira all'utilizzo coscienzioso, esplicito e prudente della migliore evidenza attuale nel prendere decisioni sulla cura individuale dei pazienti. La genetica clinica rappresenta un'evoluzione della ricerca genetica traslazionale e contribuisce alla cura dei pazienti attraverso la gestione delle malattie ereditarie tramite diagnosi accurate, un approccio molecolare alle patologie e la valutazione delle correlazioni fenotipiche. La ricerca traslazionale genetica e genomica ha portato allo sviluppo di potenti strumenti per la diagnosi clinica, in grado di valutare il profilo genomico individuale per la predizione/prevenzione delle malattie, di effettuare un *high-throughput screening* sul genoma per la predisposizione e/o la correzione di condizioni mediche complesse, e la scoperta e lo sviluppo di nuovi farmaci e vaccini. La mappatura genetica e la decifratura delle mutazioni patogenetiche hanno contribuito a chiarire i meccanismi biologici di base che portano alla scoperta e allo sviluppo di nuovi farmaci. La farmacoterapia mirata è ora possibile per la gestione delle condizioni ereditarie ad alta penetranza. Esempi rilevanti includono il rapamycin (sirolimus) per la soppressione della via mTOR associata all'amartoma nelle sindromi oncologiche ereditarie dominanti e gli ACE inibitori, per la prevenzione della dilatazione aortica nella sindrome di Marfan e nelle arteriopatie familiari correlate. La ricerca traslazionale genomica è il prerequisito essenziale per lo sviluppo di solidi protocolli *evidence-based*, terapeutici e di diagnosi clinica per la pratica della medicina personalizzata.

Parole chiave: medicina basata sull'evidenza, medicina genomica, ricerca traslazionale, medicina personalizzata, screening genetico ad alta resa, farmacogenomica, sperimentazione clinica.

INTRODUCTION

The philosophy behind the practice of "evidence-based medicine" (EBM) is not new. Its philosophical origins date back to the mid-19th century Paris or even earlier [1]. Since its re-emergence, EBM has been hotly debated by clinicians, public health practitioners, health planners and commissioners, politicians and the public. It has now established a central position in the medical practice. The recent upsurge and interest about EBM was triggered in 1991 at the

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OPEN ACCESS

ORIGINAL ARTICLE

Heterozygous mutations affecting the protein kinase domain of *CDK13* cause a syndromic form of developmental delay and intellectual disability

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► Additional material is published online only. To view please visit the journal (http://dx.doi.org/10.1136/jmedgenet-2017-104620).

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Received 23 February 2017
Revised 4 September 2017
Accepted 8 September 2017
Published Online First 11 October 2017

To cite: Hamilton MJ, Caswell RC, Canham N, *et al*. *J Med Genet* 2018;**55**:28–38.

ABSTRACT

Introduction Recent evidence has emerged linking mutations in *CDK13* to syndromic congenital heart disease. We present here genetic and phenotypic data pertaining to 16 individuals with *CDK13* mutations.
Methods Patients were investigated by exome sequencing, having presented with developmental delay and additional features suggestive of a syndromic cause.
Results Our cohort comprised 16 individuals aged 4–16 years. All had developmental delay, including six with autism spectrum disorder. Common findings included feeding difficulties (15/16), structural cardiac anomalies (9/16), seizures (4/16) and abnormalities of the corpus callosum (4/11 patients who had undergone MRI). All had craniofacial dysmorphism, with common features including short, upslanting palpebral fissures, hypertelorism or telecanthus, medial epicanthic folds, low-set, posteriorly rotated ears and a small mouth with thin upper lip vermilion. Fifteen patients had predicted missense mutations, including five identical p.(Asn842Ser) substitutions and two p.(Gly717Arg) substitutions. One patient had a canonical splice acceptor site variant (c.2898−1G>A). All mutations were located within the protein kinase domain of CDK13. The affected amino acids are highly conserved, and in silico analyses including comparative protein modelling predict that they will interfere with protein function. The location of the missense mutations in a key catalytic domain suggests that they are likely to cause loss of catalytic activity but retention of cyclin K binding, resulting in a dominant negative mode of action. Although the splice-site mutation was predicted to produce a stable internally deleted protein, this was not supported by expression studies in lymphoblastoid cells. A loss of function contribution to the underlying pathological mechanism therefore cannot be excluded, and the clinical significance of this variant remains uncertain.
Conclusions These patients demonstrate that heterozygous, likely dominant negative mutations affecting the protein kinase domain of the *CDK13* gene result in a recognisable, syndromic form of intellectual disability, with or without congenital heart disease.

INTRODUCTION

The *CDK13* gene codes for a member of the cyclin-dependent serine/threonine protein kinase (STK) family, which phosphorylate targets in partnership with a cyclin co-factor; in this case, cyclin K. Recent work has shown that CDK13 plays a role in converting transcribing RNA polymerase II (Pol II) from an initiating to an elongating form, by phosphorylation of key residues in the C-terminal domain of Pol II. The genetic targets of *CDK13* activity, determined by knockdown of *CDK13* expression, appear to be largely involved in processes connected to extracellular and growth signalling.[1]

Mutations in *CDK13* had not previously been linked to human disease, until recent analysis of exome sequencing data arising from the Deciphering Developmental Disorders (DDD) study.[2] In subanalysis of 398 trios affected by syndromic congenital heart disease (S-CHD), in which the proband did not have a plausible de novo mutation in a known developmental disorder-associated or CHD-associated gene, a significant clustering of de novo mutations in *CDK13* was observed. This led to identification of seven individuals with S-CHD, all carrying predicted missense variants within the highly conserved protein kinase (PK) domain of *CDK13*, including four with identical c.2525A>G (p.Asn842Ser) mutations. All had a history of developmental delay and craniofacial dysmorphism, characterised by hypertelorism, upslanted palpebral fissures, wide nasal bridge and narrow mouth, with additional features including structural brain abnormalities, clinodactyly, joint hypermobility and skin changes.[3]

In this context, we present genetic and phenotypic data relating to 16 patients investigated for intellectual disability (ID) syndromes and found to carry de novo mutations in *CDK13*, including those described by Sifrim *et al*.[3] We have undertaken in silico analysis of the amino acid substitutions identified, including comparative protein modelling of selected variants based on the recently reported crystal structure for the kinase domain of CDK13 to predict their effect on ligand binding and thus catalytic activity. Key clinical data pertaining to the affected individuals are also presented, highlighting recognisable features that serve as pointers to this diagnosis.

J Med Genet: first published as 10.1136/jmedgenet-2017-104620 on 11 October 2017. Downloaded from http://jmg.bmj.com/ on December 6, 2023 by guest. Protected by copyright.

REPORT

Histone Lysine Methylases and Demethylases in the Landscape of Human Developmental Disorders

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Histone lysine methyltransferases (KMTs) and demethylases (KDMs) underpin gene regulation. Here we demonstrate that variants causing haploinsufficiency of KMTs and KDMs are frequently encountered in individuals with developmental disorders. Using a combination of human variation databases and existing animal models, we determine 22 KMTs and KDMs as additional candidates for dominantly inherited developmental disorders. We show that KMTs and KDMs that are associated with, or are candidates for, dominant developmental disorders tend to have a higher level of transcription, longer canonical transcripts, more interactors, and a higher number and more types of post-translational modifications than other KMT and KDMs. We provide evidence to firmly associate *KMT2C*, *ASH1L*, and *KMT5B* haploinsufficiency with dominant developmental disorders. Whereas *KMT2C* or *ASH1L* haploinsufficiency results in a predominantly neurodevelopmental phenotype with occasional physical anomalies, *KMT5B* mutations cause an overgrowth syndrome with intellectual disability. We further expand the phenotypic spectrum of *KMT2B*-related disorders and show that some individuals can have severe developmental delay without dystonia at least until mid-childhood. Additionally, we describe a recessive histone lysine-methylation defect caused by homozygous or compound heterozygous *KDM5B* variants and resulting in a recognizable syndrome with developmental delay, facial dysmorphism, and camptodactyly. Collectively, these results emphasize the significance of histone lysine methylation in normal human development and the importance of this process in human developmental disorders. Our results demonstrate that systematic clinically oriented pathway-based analysis of genomic data can accelerate the discovery of rare genetic disorders.

Post-translational methylation and demethylation of lysine residues on histone tails is a key dynamic chromatin modification that is mediated by specific methyltransferases (KMTs) and demethylases (KDMs) and underpins gene regulation and several cellular processes.[1,2] Twenty-seven KMT- and 24 KDM-encoding genes, classified into eight groups each, are known (Table S1).[3] Of these, heterozygous variants in seven KMT and four KDM genes are associated with autosomal and X-linked dominant inherited human developmental disorders (DDs) in the Online Mendelian Inheritance in Man database (OMIM) (Table S1).[4–18]

We reviewed published disease-causing variants in KMTs and KDMs in the Human Gene Mutation Database[19] and deduced that ~75% of these were predicted to be heterozygous protein-truncating variants (PTVs), suggesting that haploinsufficiency is the predominant mechanism for the associated diseases (Figure 1A) (Table S2). This is consistent with previous studies that have shown a high prevalence of *de novo* (DN) PTVs in dominant DDs.[20–22] We reviewed phenotypes of the available mouse models for KMT and KDM orthologs (Table S1)[23] and found that heterozygous mouse models for six of the 11 known dominant DD-associated KMTs and KDMs and 12 of the 40 of remaining KMTs and KDMs demonstrate anomalies. We reviewed phenotypes of the available zebrafish knockdown (KD) models for KMT and KDM orthologs (Table S1).[24] Anomalies were observed in KD of seven of the 11 known dominant DD-associated KMTs and KDMs and 18 of the 40 of remaining KMTs and KDMs. The human mutational landscape of KMTs and KDMs and the information from animal models led us to hypothesize that germline

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https://doi.org/10.1016/j.ajhg.2017.11.013.
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***Science*. Author manuscript; available in PMC 2019 September 04.**

Published in final edited form as:
Science. 2018 December 07; 362(6419): 1161–1164. doi:10.1126/science.aar6731.

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Quantifying the contribution of recessive coding variation to developmental disorders

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Competing interests: M.E.H. is a co-founder of, consultant to, and holds shares in, Congenica Ltd, a genetics diagnostic compan y.

Data and materials availability: Exome sequencing and phenotype data are accessible via the European Genome-phenome Archi ve (EGA) (Datafreeze 2016-10-03) (https://www.ebi.ac.uk/ega/studies/EGAS00001000775).

ARTICLE

doi:10.1038/nature21062

Prevalence and architecture of *de novo* mutations in developmental disorders

Deciphering Developmental Disorders Study*

The genomes of individuals with severe, undiagnosed developmental disorders are enriched in damaging *de novo* mutations (DNMs) in developmentally important genes. Here we have sequenced the exomes of 4,293 families containing individuals with developmental disorders, and meta-analysed these data with data from another 3,287 individuals with similar disorders. We show that the most important factors influencing the diagnostic yield of DNMs are the sex of the affected individual, the relatedness of their parents, whether close relatives are affected and the parental ages. We identified 94 genes enriched in damaging DNMs, including 14 that previously lacked compelling evidence of involvement in developmental disorders. We have also characterized the phenotypic diversity among these disorders. We estimate that 42% of our cohort carry pathogenic DNMs in coding sequences; approximately half of these DNMs disrupt gene function and the remainder result in altered protein function. We estimate that developmental disorders caused by DNMs have an average prevalence of 1 in 213 to 1 in 448 births, depending on parental age. Given current global demographics, this equates to almost 400,000 children born per year.

Approximately 2–5% of children are born with major congenital malformations and/or manifest severe neurodevelopmental disorders during childhood[1,2]. Although diverse factors, including gestational infection and maternal alcohol consumption, can cause such developmental disorders (DDs), damaging genetic variation in developmentally important genes makes a major contribution. Several recent studies have identified a substantial causal role for DNMs that are not present in either parent[3–16]. Despite the identification of many DDs caused by DNMs, it is generally accepted that many more disorders have not yet been discovered[15], and the overall contribution of DNMs to DDs is not known. Moreover, some pathogenic DNMs completely ablate the encoded protein, whereas others instead alter the function of the encoded protein[17]; the relative contributions of these two mechanistic classes are also not known.

We recruited 4,293 individuals to the Deciphering Developmental Disorders (DDD) study[15] via the genetics services of the UK National Health Service and the Republic of Ireland. Each of these individuals was referred with a severe undiagnosed DD and most were the only affected family member. Most individuals (81%) had been screened for large pathogenic deletions and duplications. We systematically phenotyped these individuals and sequenced the exomes of the affected individuals and their parents. Growth measurements, family history and developmental milestones were recorded, and detailed clinical phenotypes were captured using Human Phenotype Ontology (HPO) terms. Analyses of 1,133 of these individuals have been described previously[15,18]. We generated a high-sensitivity set of 8,361 candidate DNMs in the coding or splicing sequence (mean = 1.95 DNMs per proband), while removing systematic erroneous calls (Supplementary Table 1). This rate of candidate DNMs per proband is higher than those found in other studies[3–15], because we wanted to maintain high sensitivity and we could address the lower specificity through subsequent validation. We found that 1,624 genes contained two or more DNMs in unrelated individuals.

Twenty-three per cent of individuals had protein-truncating or missense DNMs that were probably pathogenic within the clinically curated set of genes robustly associated with dominant DDs[18]. We investigated factors associated with whether an individual had a probably pathogenic DNM in these curated genes (Fig. 1a, b and Extended Data Table 1). Males had a lower chance of carrying a probably pathogenic DNM ($P = 1.6 \times 10^{-4}$; odds ratio (OR) = 0.75; 95% confidence interval (CI) = 0.65–0.87), as has also been observed for autism[19]. We also observed that a greater extent of speech delay was correlated with an increased likelihood of having a pathogenic DNM ($P = 0.00115$), but no other indicators of severity relative to the rest of the cohort showed significant correlations. Individuals with other affected family members were less likely to have pathogenic DNMs (affected siblings: $P = 7.3 \times 10^{-18}$, affected parents: $P = 5.7 \times 10^{-9}$), as were individuals who were from self-declared consanguineous unions ($P = 8.0 \times 10^{-11}$). Furthermore, the total genomic extent of autozygosity (owing to parental relatedness) was negatively correlated with the likelihood of having a pathogenic DNM ($P = 1.7 \times 10^{-7}$). For every $\log_{10}$ increase in autozygous length, the probability of having a pathogenic DNM dropped by 7.5%, probably owing to increasing burden of recessive causation (Fig. 1c). Nonetheless, 6% of individuals with autozygosity equivalent to a first cousin union or closer had a plausibly pathogenic DNM, underscoring the importance of considering *de novo* causation in all families.

Paternal age has been shown to be the primary factor influencing the number of DNMs in a child[20,21], and is therefore expected to be a risk factor for pathogenic DNMs. Paternal age was only weakly associated with the probability of having a pathogenic DNM ($P = 0.016$). However, focusing on the minority of DNMs that were truncating and missense variants in known DD-associated genes limits our power to detect such an effect. Analysis of all 8,409 high-confidence exonic and intronic autosomal DNMs confirmed a strong effect of paternal age ($P = 1.4 \times 10^{-10}$, 1.53 DNMs per year, 95% CI = 1.07–2.01), and a weaker, independent, effect of maternal age ($P = 0.0019$, 0.86 DNMs per year, 95% CI = 0.32–1.40; Fig. 1d, e), as has recently been described using whole-genome analyses[22]. These genome-wide estimates were based on exome-based estimates, with a paternal effect of 0.0306 DNMs per year and a maternal effect of 0.0172 DNMs per year.

We identified genes that were significantly enriched for damaging DNMs by comparing the observed gene-wise DNM count to the expected count under a null-mutation model[23], as described

*Lists of participants and their affiliations appear in the online version of the paper.

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***Nature*. Author manuscript; available in PMC 2018 June 25.**

Published in final edited form as:
Nature. 2017 February 23; 542(7642): 433–438. doi:10.1038/nature21062.

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Prevalence and architecture of de novo mutations in developmental disorders

The Deciphering Developmental Disorders Study

Summary

Individuals with severe, undiagnosed developmental disorders (DDs) are enriched for damaging de novo mutations (DNMs) in developmentally important genes. We exome sequenced 4,293 families with individuals with DDs, and meta-analysed these data with another 3,287 individuals with similar disorders. We show that the most significant factors influencing the diagnostic yield of DNMs are the sex of the affected individual, the relatedness of their parents, whether close

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Code availability
Source code for filtering candidate DNMs, testing DNM enrichment, DNM clustering and phenotypic similarity can be found here: https://github.com/jeremymcrae/denovoFilter, https://github.com/jeremymcrae/mupit, https://github.com/jeremymcrae/denovonear, https://github.com/jeremymcrae/hpo_similarity

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Exome sequencing data are accessible via the European Genome-phenome Archive (EGA) under accession EGAS00001000775. Details of DD-associated genes are available at www.ebi.ac.uk/gene2phenotype. M.E.H. is a co-founder of, and holds shares in, Congenica Ltd, a genetics diagnostic company.

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EDUCATION REPORT

Ensuring best practice in genomics education and evaluation: reporting item standards for education and its evaluation in genomics (*RISE2 Genomics*)

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PURPOSE: Widespread, quality genomics education for health professionals is required to create a competent genomic workforce. A lack of standards for reporting genomics education and evaluation limits the evidence base for replication and comparison. We therefore undertook a consensus process to develop a recommended minimum set of information to support consistent reporting of design, development, delivery, and evaluation of genomics education interventions.

METHODS: Draft standards were derived from literature (25 items from 21 publications). Thirty-six international experts were purposively recruited for three rounds of a modified Delphi process to reach consensus on relevance, clarity, comprehensiveness, utility, and design.

RESULTS: The final standards include 18 items relating to development and delivery of genomics education interventions, 12 relating to evaluation, and 1 on stakeholder engagement.

CONCLUSION: These Reporting Item Standards for Education and its Evaluation in Genomics (RISE2 Genomics) are intended to be widely applicable across settings and health professions. Their use by those involved in reporting genomics education interventions and evaluation, as well as adoption by journals and policy makers as the expected standard, will support greater transparency, consistency, and comprehensiveness of reporting. Consequently, the genomics education evidence base will be more robust, enabling high-quality education and evaluation across diverse settings.

Genetics in Medicine (2021) 23:1356–1365; https://doi.org/10.1038/s41436-021-01140-x

INTRODUCTION

Genomic medicine as an emerging field has the promise of delivering greater diagnostic accuracy, targeted treatment options, and ultimately, improved patient outcomes. However, these achievements depend on skilled health professionals. Quality, evidence-based education that demonstrably improves health professionals' competence in genomics is essential to ensure that genomics is used appropriately in patient care and, ultimately, that the promise of genomic medicine does translate to improved patient outcomes.[1–5]

Genetics/genomics education initiatives—including programs, learning activities, and resources, collectively referred to as

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BOOK REVIEW

AMERICAN JOURNAL OF medical genetics PART A

GENOMICS AND HEALTH IN THE DEVELOPING WORLD. Edited by Prof. Dhavendra Kumar. ISBN13: 9780195374759, ISBN10: 0195374754.

How to Cite this Article:
Zahir FR. 2013. Book Review.
Am J Med Genet Part A 161A:1203–1206.

INTENTION AND SCOPE

This impressive compilation is the first of its kind in terms of scope and breadth. Edited by Prof. Dhavendra Kumar and published as part of the Oxford Monographs on Medical Genetics series, it provides a much needed overview of the state of genomics in the so called "developing world." Dr. Kumar, who has dedicated this work "*to millions of people in the developing world who live with poverty, hunger and disease,*" has certainly manifested a valiant effort to serve this demographic, which constitutes the majority of the world population (82%, 2009 UN estimates). Genomics is a relatively young branch of science that is currently undergoing rapid advance and transformation. From being a cutting edge science affordable only to high income countries and amenable to use by a few highly trained individuals, the rapid fall in cost of several genomics technologies (notably sequencing) coupled to an increase in training is making genomics services increasingly available to low and middle income (LMIC) countries. This has led to initiatives incorporating genomics and genetics services in both health and populations studies during the past decade in many LMIC countries. However, current publication trends tend to disfavor dissemination of scientific and medical epidemiological data from LMIC countries at most top ranked journals. Dr. Kumar's work steps in as a focused platform to highlight important reports from LMIC countries in this regard, not just in research but also in documenting trends in implementation of genomics, especially in the health care sector. Having said that, the text also collects several relevant studies from LMIC countries that have been published in world class journals, thereby it succeeds in portraying a truly rounded picture.

STRUCTURE AND CONTRIBUTORS

The book is organized as two main parts; part 1 gives a general overview of genomics and medicine in health, but with a distinct developing world flavor. Part 2 is a collection of chapters that discuss more specific genomics and health issues that are organized according to the following regions, Africa, Arab and Middle East, Asia-Pacific, Chinese Subcontinent, Indian Subcontinent, Latin America and the Caribbean and finally Russia, central Asia and Europe. This organization scheme is a definite strength as it aptly indicates the rich compendium of information contained therein. The reader is at once drawn to the chapter titles under each global region and the number of these as well as the breadth of information covered by them gives an initial taste of the current regional situation. However, what is also apparent is that there is an over-representation from some countries in a given region over others, which may be an indicator of the country-wise distribution and availability of genomics services rather than non-inclusion in this text. For example, of the 18 chapters included under "Africa," 1/3rd are specifically focused on South Africa, and apart from a single other chapter on Tunisia (chapter "Genetic neurological diseases in Tunisia"), the others discuss areas that encompass more than one, often several African countries. If this is indeed the case, it is surprising that there are relatively few chapters from the Chinese subcontinent (6) compared to the Indian subcontinent (26), as one would expect more genomics applications currently in China. The Indian subcontinent includes several more countries than the Chinese subcontinent and this may be a reason to explain the imbalance, or conversely the over-representation of information from India may indeed indicate the recent move by the Indian government to focus on science and technology research (http://articles.timesofindia.indiatimes.com/2012-08-11/india/33152919_1_private-sector-health-sector-12th-plan). While some comment on these issues by the editor would have been useful in the foreword, the massive effort in collating and organizing all this information is nothing but praise worthy. The availability of selected color figures as a series of color plates located in the middle of the book is welcome as in some cases the color is essential to understand the figure (Figs. 4 and 5, population admixture principal component analysis plots), though the placement of them ex situ is cumbersome. The index is a very useful addition that feels adequate for this edition, however not all topics are completely referenced. The list of contributors is impressive, truly a snapshot of experts in genomics in the developing world. While the designation of each contributor is listed at the beginning of the book, a little more information explaining the role of

Grant sponsor: Canadian Institutes of Health Research; Grant sponsor: NeuroDevNet Canadian National Center of Excellence; Grant sponsor: University of British Columbia Bluma Tischler Award.
Article first published online in Wiley Online Library (wileyonlinelibrary.com): 5 March 2013
DOI 10.1002/ajmg.a.35750

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GeNeFocus

The Emergence of Clinical Genomics and Genomic Medicine Across India: The Role of the UK-India Genomic Medicine Alliance

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Abstract

Genomic applications in precision medicine and healthcare are now globally recognised with huge public and private investments. The United Kingdom (UK)-India Genomic Medicine Alliance **(UKIGMA)** offers a unique opportunity for clinicians and scientists from UK and India, to work together and develop comprehensive genomic medicine and healthcare programmes through a series of genomic education and training courses, raising awareness on genomic applications for health and supporting the necessary infrastructure build-up for the benefit of the vastly heterogeneous people of India and South Asia.

Introduction

Genetic and genomic applications in healthcare are now globally acknowledged and considered as one of the most powerful and pertinent developments in the history of medicine. The practice of medicine is now for the first time, truly personalized, precise and evidence-based. India has made significant progress in this field and is one of the established leaders in South Asia. Education and training in all formats are the key for successful implementation. The successful movement for genetics-led medical education steered by the ***Indo-UK Genetic Education Forum,*** has generated much needed enthusiasm and direction across India and neighbouring regions. This forum has set its vision for genomic education and training aimed at medical and healthcare practitioners.

There are several unknown and undiagnosed rare diseases prevalent across India that are awaiting genomics input for precision diagnosis, novel therapeutic inventions, and precision prevention. It is extremely important that India takes the lead and develops a coordinated and comprehensive genomic medicine and healthcare programme.The Genomic Medicine Foundation (UK), offers a unique opportunity for the UK and Indian clinicians and scientists to work together and develop the genomic medicine and healthcare programme through a series of genomic education and training courses, raising awareness on genomic applications for health and supporting the necessary infrastructure build up for the benefit of vastly heterogeneous peoples of India. This is appropriately named the **'UK-India Genomic Medicine Alliance'** referred to as **'UKIGMA'.**

Aim of the UKIGMA

"To organise and lead a professional group of like-minded clinicians and healthcare professionals for promoting and supporting the genomic applications and translations in medicine and healthcare in India and across the Indian subcontinent"

Objectives of the UKIGMA

- Identify and enrol organisations andinstitutions engaged in scientific and applied research in genomics relevant to medicine and healthcare
- Encourage collaboration with individual genetic/ genomic clinicians andscientists, and other professionals in anthropology, population genetics, bioethics, social sciences and bio-economics
- Develop a programme for training and skills development through series of structured courses, workshops, and webinars in the key areas of applied and translational genomic medicine
- Plan and carry out specific audit on the outcomes of investments in institutions and laboratories as part of the current strategy for capital and infrastructure scientific developments for genomic medicine and healthcare
- Develop and steer through individual or group research projects related to utilization and the delivery of genomics-led medical and healthcare, specifically in laboratory genomics, functional

World Health Organization

WHO Science Council Workshop Series
Accelerating Access to Genomics Technologies for Global Health

Workshop 2: Technical and Financial Considerations
1330-1730h CET Thursday, November 18, 2021

WHO Science Council Workshop- Recommendations

Dhavendra Kumar, William Harvey Research Institute, Queen Mary University of London & The Genomic Medicine Foundation, UK

The World Health Organization's Science Council held a series of three workshops in November and December 2021 to gather information about the benefits and feasibility of accelerating access to genomics technologies, especially in low- and middle-income countries (LMICs). The Workshop #2 deals with the 'Technical and Financial' aspects relevant to the WHO goal of improving access to genomic technologies for global health in LMICs. The following summary and pertinent points are reiterated for inclusion with the recommendations to the WHO Director-General:

1. Member nations, particularly LMICs, need to prioritise genomic skills and competencies of scientific, healthcare providers and related professionals in the key areas of genome technology including bioinformatics, medical and health applications as per local needs, genomics for socio-economic development and legal or regulatory safeguards for ethical and socio-cultural issues. In this respect, the work promoted and carried out by the Global Consortium for Genomic Education (GC4GE; www.genomicmedicine.org) is likely to be helpful. The recent publication of the multi-author book includes comprehensive account on all aspects of the global genomic education and training.[Ref. 1].

2. The model of the Indo-UK Genetic Education Forum, encompassed within the UK-India Genomic Medicine Alliance (UKIGMA) is recommended for consideration, particularly in the LMICs. The forum has promoted genomic applications in South Asia and organised series of seminars, workshops and conferences targeted at specialists workforce, post-graduate courses, undergraduate curriculum development and the adult/public health education. This programme is one of the key areas of UKIGMA and has the potential to be adapted and replicated in LMICs. [Ref. 2]

3. The global genomic consortium, led by the Human Genome Organization (HUGO; www.hugo-international.org), is committed to genomic education and training as one of the priority sectors. The newly constituted HUGO Education Committee has set out the agenda, specifically targeted at LMICs. The main items of the agenda include- i) Explore and liaise with current global genomic educational / training activities and programs; ii) Emphasis on empowering and enhancing skills and competencies required for specific sectors including laboratory genomics, computational genomics, clinical genomics, specialist genomics, genetic/ genomic counselling; iii) community/ population genomics; Incorporate and enhance the skills and competencies across the worldwide diagnostic genomic laboratories; and iv) Designing and implementing genomic education teaching and training programs for students, trainees, non-genetic physicians and healthcare professionals, general public and continued adult education.

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1.

GENES, GENETICS, AND HUMAN GENOMICS

Dhavendra Kumar

INTRODUCTION

In the nineteenth and twentieth centuries, major discoveries and scientific advances in physical and biological sciences led to the Industrial Revolution and the massive transformation of the global landscape and standards of living. Towards the end of the last millennium, tremendous growth in the sophistication of the biological sciences was harnessed in medicine, the food industry, and related industries. This was aided by major applications and translations of physical sciences, particularly in the fields of computing and information technology.

New discoveries and innovations in biological sciences during the five decades preceding the twenty-first century have centered on genetics and genomics. It took just over 50 years following the unraveling of the structure of the molecule of nucleic acids, the key unit of the biological life, for scientists to embark on sequencing of major organisms' entire genetic constitution or genome. The word *genome* includes *gene* and *ome,* implying complete knowledge of all genes and related elements in any single organism. Inevitably, this led to enthusiastic expansion of the whole science and thence to the emergence of *genomics*.[1] The suffix *-omics,* derived from the ancient Greek, refers to in-depth knowledge. Not surprisingly, genomics was followed by a plethora of related *-omics*; for example, proteomics, metabolomics, transcriptomics, and so on.[2] Currently, we have over 30 such disciplines with the *-omics* suffix.

The ultimate goal of any scientific discipline is its translation for the benefit of all humans, crossing all possible barriers and boundaries. Major advances in medicine and health were only possible through understanding basic principles and mechanisms underlying disease processes. This was facilitated by rapid applications of physical and chemical sciences in medicine and health; for example, X-ray diagnostics, ultrasound diagnosis, microbiology diagnosis, immune-histochemical diagnosis, and finally, molecular diagnosis. Developments and advances in genetics have led to a better understanding of the principles governing heredity and the familial transmission of physical characteristics and diseases, better understanding of the pathophysiology of diseases, the development of new methods of clinical and laboratory diagnosis, and innovative approaches to making early diagnoses (e.g., prenatal diagnoses and newborn screening) and offering reproductive choices, including pre-implantation genetic diagnoses. All these developments are now accepted within the broad fields of human genetics, medical genetics, clinical genetics, and (lately) genetic medicine. Not surprisingly, the field remains wide open, encompassing the massive field of human genomics appropriately named *genomic medicine*.[3]

This chapter leads the section titled "Principles of Genomic Medicine." It is anticipated that the reader, probably less informed than the specialists herein (or even uninformed), might find this helpful in grasping the concepts of heredity, genes, genetics, and genomics. It is expected that the reader will proceed to further chapters in this section and the second section, "Practice of Genomic Medicine," better equipped with the introduction to genetic/genome sciences, genetic diseases, genetics and genomics in medicine, applications in public health, and specific issues related to society, ethics, and law. The reader will find a major change in the organization and presentation of material in this book from that of the previous edition.[4]

THE HEREDITY

The concept of *heredity* dates back several hundreds and even thousands of years. It is evident in all forms of biological life and evolution. Evolutionary scientists, philosophers, and biologists have used "heredity" to put forward their views on procreation, development, adaptation, and the transmission of species-specific traits. The popular Darwinian theory of natural selection rests on the core concept of the *transmission of hereditary factors.*[5] For several

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5.

GENES, GENOME, AND DEVELOPMENTAL MALFORMATIONS

Dhavendra Kumar

Disorders that affect tissue differentiation, organogenesis, and morphogenesis constitute a significant proportion of human genetic disease. These disorders may result from any of the known genetic mechanisms and may occur singly, in combination with other malformations, or as part of the multisystem complex phenotype. Clinical and laboratory analyses of these disorders have led to the emergence of clinical dysmorphology as a distinct discipline, now an integral part of medical genetics and clinical genomics. All practicing pediatricians, clinical geneticists, and genetic counselors are required to have the basic skills in order to deal with patients who present with a developmental malformation that may occur either singly or as part of a recognizable dysmorphic syndrome (Jones and Smith, 2006).

During the past two decades, clinical dysmorphologists (specialist clinicians dealing with clinical management of malformations) have delineated a large number of malformation syndromes that comprise multiple malformations affecting unrelated organs and tissues. Researchers and clinicians continue to generate more information, and the number of related syndromes continues to increase. Dedicated dysmorphology databases (London Medical Databases, www.lmdatabases.com [London Dysmorphology, LDDB and London Ophthalmic Genetics, GeneEye], Pictures of Standardized Syndromes and Undiagnosed Malformations [www.POSSUM.net.au]) are now available to help clinical geneticists and other clinicians for carrying out comprehensive database searches. Although considerable progress has been made in understanding the developmental pathology and possible causes of some of these malformation syndromes, there remains a huge gap in our understanding of the abnormal human development and clinical challenges.

Recent advances in genetics and genomics have made it possible to understand the molecular basis of developmental malformations. These fall into two broad groups. The first group, which includes advances in gene mapping, cloning, and identification of genes, has received a tremendous boost from the Human Genome Project (HGP) (see Chapter 1). Advances in genome sequencing, particularly exome genome sequencing, following the successes of HGP and other projects, have helped in identifying mutations and polymorphisms in specific human genes associated with particular syndromes. The HGP has also permitted comparisons between the human genome and the genomes of other organisms such as mouse and *Drosophila*, which has helped in the identification of new genes, deciphering evolutionary conserved genes and genomic regions, and the subsequent study of their role in abnormal development. The second group includes a number of highly interactive molecular pathways that govern the developmental process. These molecular pathways include several specific genes and polymorphisms belonging to a particular molecular family; for example, *RAS/MAPK, NOTCH* signaling, and many more. These advances have made it possible to develop a better understanding of development and morphogenesis and to work out a plausible genotype–phenotype correlation.

This chapter reviews some of the basic concepts in developmental biology, which are intricately related to genes and genomes. This chapter is not intended to provide the reader with a comprehensive account of normal and abnormal human development, as this field is enormous and beyond the scope of this review. The interested reader may refer to excellent texts available on this subject (see "Further Reading"). The main aim of this chapter is to introduce the subject from the perspective of genomics. It is anticipated that the reader may find the contents of this chapter helpful in understanding aspects of advances in genomic-related science and technology that are relevant to understanding developmental malformations, which may in turn influence their clinical practice.

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19.

GENETIC AND GENOMIC APPROACHES TO CLINICAL MEDICINE

Dhavendra Kumar

Ancient civilizationsin India, China, Greece,and Egypt recognized that heredity played an important part in human health. Writings, paintings, and sculptures belonging to people from these regions, and dating back several thousand years, provide evidence that they knew of a close association between heredity and health. Hippocrates in his medical texts noted that "heredity affects health."It is likely that this concept and its practical applications were recognized by other societies but lacked documentary evidence. But there are some concrete examples of this awareness, such as the reference in ancient Jewish texts to a young boy given exemption from circumcision because he had a male relative who died from bleeding following ritual circumcision. This reflects the practice of heredity medicine. However, scientific support for heredity and its biological relevance was not clearly understood until the mid–nineteenth century, when the "evolution of species" theory proposed by Charles Darwin, and Gregor Mendel's seminal observations on cross-breeding various forms of green pea plants, laid the foundations of the science of genetics. Darwin's theory elucidated the biological importance of genetic variation, and Mendel put in place the fundamental principles of heredity based on individual hereditary factors that were eventually to be identified as genes. Unfortunately, the medical applications of these major discoveries remained unrecognized for almost half a century.

Archibald Garrod, one of the pioneers of "genetics in medicine" first began applying this knowledge to human health at the start of the twentieth century. In his Harveian Oration of 1924, he quoted from a letter written by William Harvey, the Founder of Modern Medicine:

> Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows traces of her workings apart from the beaten path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of Nature, by careful investigation of cases of rarer forms of disease. For it has been found, in almost all things, that when they contain of useful or applicable is hardly perceived unless we are deprived of them, or they become deranged in some way.

Garrod, in his seminal paper on the patient with "alkaptonuria," provided the necessary evidence to support the "one gene—one enzyme" theory. This laid the foundation for molecular medicine, and showed the way forward for genetic medicine. Surprisingly, all this happened well before the elucidation of the chromosomal and nucleic acid basis of inheritance. However, it was widely agreed that the individual genetic complement was locked in the nucleus.

The science of human genetics probably began with the discovery of the full chromosomal complement of man by Tjio and Evans in 1956 (see Chapters 1and 2).[1] This led to the rapid expansion of the whole field of human genetics, and its divergence into various specialist fields such as medical and clinical genetics. Developments in medical genetics and subsequent applications in clinical practice provided a strong base for wider applications of genetics in medicine. Genetic medicine gained wide recognition over a period of 40 years and led to the historical decision of 1996 to sequence the whole human genome.[2] This mammoth task, called "The Human Genome Project," was immediately acknowledged as similar to, or even larger than, the Manhattan Project to build the atomic bomb, or the Apollo Mission for the trip to the Moon and back.[3] Some enthusiasts regard this as the "genomic period," followed by the "post-genomic" phase. This is probably incorrect. The genomic era has only just begun. The first glimpse of the human genome was made possible with the publication of the full sequence of the human mitochondrial genome.[4]

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Introduction to Genes, Genome and Inheritance

1

Dhavendra Kumar

Abstract

The introductory chapter introduces genes, genome, genetics and genomics in simplified manner that, irrespective of any specialty, any clinician or healthcare professional should know. In addition to core basic information on nucleic acids, structure of the gene and organisation of the whole genome, the text includes clinical examples relevant to cardiovascular medicine and surgery. Selected examples might be of interest to medical and healthcare professionals predominantly engaged with cardiovascular conditions. Emphasis is given on developing reasonable grasp of genetic or genomic factors, heritable, incidental or somatic, that is either etiologically relevant or capable of influencing the natural course of any cardiovascular disease, acting alone or in combination with environmental (infection and toxins etc.) or life style factors (nutrition and occupation etc.). The text is supported with generous illustrations, tables and boxes with key learning points.

Keywords

Nucleic acids • DNA • RNA • Gene • Genome • Genomic variation • Single nucleotide polymorphism • Copy number variation • Mendelian inheritance Complex disease • Genomic medicine

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© Springer International Publishing AG 2018

D. Kumar, P. Elliott (eds.), *Cardiovascular Genetics and Genomics*,
https://doi.org/10.1007/978-3-319-66114-8_1

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CHAPTER

1

The human genome and molecular medicine

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1.1 Introduction

Toward the end of the last millennium, tremendous growth in the sophistication of the biological sciences was harnessed in medicine, the food industry, and related bioindustries. New discoveries and innovations in biological sciences during the five decades prior to the 21st century have centered on genetics and genomics. It took just over 50 years following the unraveling of the structure of the molecule of nucleic acids, the key unit of the biological life, for scientists to embark on sequencing of major organisms' entire genetic constitution or genome. The word *genome* includes *gene* and *ome*, implying complete knowledge of all genes and related elements in any single organism. Inevitably, this led to enthusiastic expansion of the whole science and thence to the emergence of *genomics* [1]. The suffix *-omics*, derived from the ancient Greek, refers to in-depth knowledge. Not surprisingly, genomics was followed by a plethora of related *-omics*, for example, proteomics, metabolomics, and transcriptomics [2]. Currently, we have over 30 such disciplines with the *-omics* suffix.

The ultimate goal of any scientific discipline is its translation for the benefit of all humans, crossing all possible barriers and boundaries. Major advances in medicine and health were only possible through understanding basic principles and mechanisms underlying disease processes. This was facilitated by rapid applications of physical and chemical sciences in medicine and health, for example, X-ray diagnostics, ultrasound diagnosis, microbiology diagnosis, immunohistochemical diagnosis, and finally, molecular diagnosis. Developments and advances in genetics have led to a better understanding of the principles governing heredity and the familial transmission of physical characteristics and diseases, better understanding of the pathophysiology of diseases, the development of new methods of clinical and laboratory diagnosis, and innovative approaches to making early diagnoses (e.g., prenatal diagnoses and newborn screening) and offering reproductive choices, including preimplantation genetic diagnoses. All these developments are now accepted within the broad fields of human genetics, medical genetics, clinical genetics, genetic medicine, and new emerging field of genomic medicine. Not surprisingly, the field remains wide open, encompassing the massive field of human genomics broadly focusing on medical and health genomics [3].

This chapter leads the book providing the basic factual information for grasping the concepts of heredity, genes, genetics, and genomics. It is expected that the reader will proceed to subsequent chapters better equipped with the introduction to genetic/genome sciences, genetic diseases, genetics and genomics in medicine, applications in public health, and specific issues related to society, ethics, and law [4].

1.2 Hereditary factors: genes, genetics, and genomics

The concept of *heredity* and *hereditary factors* dates back to several hundreds and probably even thousands of years. The popular Darwinian theory of natural selection rests on the core concept of the *transmission of hereditary*

Clinical Molecular Medicine.
DOI: https://doi.org/10.1016/B978-0-12-809356-6.00001-0

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CHAPTER

15

Molecular medicine of diabetes mellitus

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15.1 Introduction

Diabetes mellitus (DM) is a multisystem metabolic disorder of relative insulin deficiency, resistance or both leading to persistent and irreversible chronic hyperglycemia. It is commonly discussed in the context of overweight or obesity. However, in a small proportion of cases, there is no correlation with obesity. The International Diabetes Federation estimated that 382 million people (8.3% of the global population) had diabetes in 2013 and estimates an increase to 592 million (10.1%) in 2035 [1]. There is alarming rise of prevalence in new emerging developing nations in South Asia (India), Far East (China), and Asia-Pacific (Papua New Guinea and Polynesian islands) [2]. India alone is estimated to have around 70 million overt cases and probably similar number of covert diabetics [3].

Diabetes is generally irreversible, and, although patients can lead a reasonably normal lifestyle, its late complications result in reduced life expectancy and major health costs. Associated overweight and obesity complicated long-term morbidity. Major chronic complications include micro/macrovascular disease, leading to an increased prevalence of coronary artery disease, peripheral vascular disease and stroke, and microvascular damage causing diabetic retinopathy and nephropathy. Sensory and autonomic neuropathy is another major complication [4].

This chapter describes the current understanding of the syndrome of DM in the context of molecular biology of glucose homeostasis, role of insulin secretion and resistance, genetic/genomic and molecular pathology, relationship with overweight and obesity, the spectrum of clinical manifestations, pharmacotherapy, and supportive treatment strategies for the management of DM.

15.2 Molecular basis of glycemic homeostasis

Understanding molecular arrangements governing the glycemic homeostasis are essential for the diagnosis and management of DM. In normal physiological conditions the blood glucose levels are closely regulated and maintained in the range of 3.5–8.0 mmol/L (63–144 mg/dL), irrespective of food intake, fasting or physical activity. The principal organ of glucose homeostasis is the liver, which absorbs and stores glucose as glycogen in the postabsorptive state and releases it into the circulation between meals to match the rate of glucose utilization by peripheral tissues (Fig. 15.1). The liver also combines three—carbon molecules derived from the breakdown of fat (glycerol), muscle glycogen (lactate), and protein (e.g., alanine) into the six-carbon glucose molecule by the process of gluconeogenesis. On average, approximately each day 200 g of glucose is produced and consumed. The liver contributes around 90% of the glucose predominantly derived from liver glycogen and hepatic gluconeogenesis. A small proportion is also produced from renal gluconeogenesis.

Clinical Molecular Medicine.
DOI: https://doi.org/10.1016/B978-0-12-809356-6.00015-0

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CHAPTER

22

Molecular biology of acute and chronic inflammation

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22.1 Introduction

Inflammation is a natural response of tissues and organs following acute or chronic trauma, acute infection, or acute immune-mediated tissue damage. It is spontaneous and often positive and beneficial in response to acute injury or invading pathogen.

New advances in molecular medicine have enhanced understanding of inflammatory response to injury and shock at the molecular level. Several mechanisms are under consideration for the development of acute inflammation following acute trauma or sepsis. Among these main molecular mechanisms include the macrophage theory, the gut hypothesis, the two-hit theory, and the microvascular environmental theory (Fig. 22.1) [1,2].

Lately, the neutrophil-mediated tissue-injury theory has gained much acceptance. It suggests adherence of activated neutrophils to the endothelium resulting in creation of local intercellular microenvironment, isolated from circulating oxidant scavengers and antiproteinases. This mechanism results in very high concentrations of toxic metabolites resulting in unopposed endothelial injury. A number of molecular markers are now available, which can predict severity of endothelial injury and offer opportunity for targeted therapeutic intervention and may

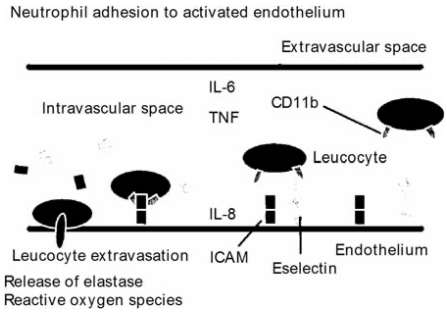

FIGURE 22.1 Molecular display of the microvascular environment theory [1]. Source: *Adapted with permission from Giannoudis PV, Hildebrand F, Pape HC. Inflammatory serum markers in patients with multiple trauma—can they predict outcome? J Bone Joint Surgery (Bri) 2004;86-B (3):313–23.*

Clinical Molecular Medicine.
DOI: https://doi.org/10.1016/B978-0-12-809356-6.00022-8

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CHAPTER

30

Gene, genome, and molecular therapeutics

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30.1 Introduction

Apart from understanding cellular and molecular mechanisms, the strength of molecular medicine is largely appreciated by diagnostic precision and exploiting molecular pathology for specific therapeutic interventions. In the previous chapters, information and discussion are confined to genetic and genomic basis of drug metabolism and drug response. In the current chapter, recombinant drugs and new therapeutic avenues targeting at specific genes, molecules, and cellular structures are discussed. There are many such approaches largely confined to biomedical research. However, few are now approved for clinical use, and the list is fast expanding. The chapter includes separate sections on stem-cell therapy, gene therapy, antisense oligonucleotides (AS ONs), ribozymes, RNA interference (RNAi), aptamers, and CRISPR/Cas9 gene/genome editing. In keeping with the size and scope of the book, scientific and experimental details are avoided. Emphasis is given to potential clinical applications. There are key references cited at the end of chapter to assist interested reader and student for further reading.

30.2 Recombinant protein drugs and vaccines

The invention and large-scale use of recombinant protein drugs are by far the best example of targeted molecular therapeutics. Insulin was the first recombinant protein drug that was approved by the United States Food and Drug Agency (https://www.fda.gov/) in 1982, followed by around 250 drugs produced by heterologous expression. This area is perhaps the biggest revenue earner for the pharmaceutical industry estimated to be approximately $150 billion. A number of diseases including cancer, diabetes mellitus, cardiovascular disease, inflammatory disease, and microbial and genetic diseases are now successfully managed by different classes of recombinant drugs. Some of these agents have revolutionized the treatment for a number of rare diseases, commonly referred to orphan drugs. Most importantly, some of these new classes of drugs are used for common diseases, such as diabetes mellitus [1].

30.2.1 Recombinant pharmacotherapy

In early 1980s the development of recombinant DNA technologies provided a path for the production of protein drugs in expression organisms, notably *Escherichia coli*. This procedure allowed large-scale production of markedly pure and safe proteins that were isolated from animal or human sources. In addition, the pharmacological properties of these proteins can be altered by the introduction of mutations or posttranslational modifications, for example, the attachment of covalent polyethylene glycol (PEG). Following the human genome sequencing, novel human proteins that were previously not available can now be designed and synthesized. Large-scale protein production is possible using *E. coli* cultivated in huge quantity in bioreactor microorganisms.

Clinical Molecular Medicine.
DOI: https://doi.org/10.1016/B978-0-12-809356-6.00030-7

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CHAPTER

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Integrated genomic and molecular medicine

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32.1 Introduction

Recent innovations and new developments in molecular biology, biotechnology, genomics, and many other omic sciences have revolutionized the contemporary and future practice of medicine. The diagnosis of most complicated and rare conditions is now possible with high degree of precision. The "gene-specific" and "genome-driven" diagnoses in many inherited and genetic disorders are now possible. The understanding of molecular mechanisms in a number of common and complex medical conditions has vastly improved. Progress in targeted genetic and molecular approach in pharmacotherapy has led many improvements from the current therapeutic regimens, which are designed for the "average model patient" and "one-size-fits-all" model approach. However, this has changed dramatically with rapid advances made in *evidence-based precision and personalized medicine* [1]. The whole process involves a stepwise approach in building the holistic picture referred to as stratified medicine with the ultimate aim of individualized or personalized therapeutic interventions [2]. The scope and limitations in the new exciting field of stratified and personalized medicine are reviewed in this chapter.

During the last decade, new genomic diagnostic tools and molecular innovations have led to the emergence of *precision medicine*, an innovative approach to disease prevention and treatment, which takes into account individual differences in people's genes, environments, and lifestyles. The precision medicine is central to stratified and personalized medicine. It provides the clinician with tools to better understand the complex molecular mechanisms underlying a patient's health, disease, or condition, and to better predict which treatments will be most effective. Advances in precision medicine have already led to powerful new discoveries and several new treatments, which are tailored to specific characteristics of individuals, such as a person's genetic makeup, or the genetic profile of an individual's tumor. This is leading to a transformation in the way we can treat diseases such as cancer. Patients with breast, lung, and colorectal cancers, as well as melanomas and leukemia, for instance, routinely undergo molecular testing as part of patient care, enabling physicians to select treatments that improve chances of survival and reduce exposure to adverse effects [3]. The potential for precision medicine to improve care and speed up the development of new treatments has only just begun to be exploited. Translating initial successes to a larger scale will require a coordinated and sustained global effort. Through collaborative public and private partnerships, the stratified and precision medicine initiatives will harness advances in genomics and biotechnology for accelerating biomedical discoveries [4].

32.2 Genetic, genomic, and molecular revolutions in medicine

Following the phenomenal discovery of the structure of the nucleic acids (DNA and RNA) and subsequent sequencing of the human genome, rapid progress is continually being made in understanding the genetic and molecular bases of human disease. In early stages the focus was largely on the peptide molecular basis, for

Clinical Molecular Medicine.
DOI: https://doi.org/10.1016/B978-0-12-809156-6.00032-0

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CHAPTER

7

Global perspectives of genomic education and training

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1 Introduction

Scientific and technical education combined with research and development are the main drivers for globalization of any branch of science and technology. Among the biological and life sciences, genetics and contemporary genomics hold a significant status. Several universities and academic institutions are actively engaged in delivering and enhancing the status of genetic or genomic education at all levels. Core and advanced elements of genetic and genomic sciences feature in most curricula and syllabuses of secondary education, graduate courses, postgraduate diploma and master's courses, and several adult and continued education courses. These can be conveniently searched and catalogued through Google Scholar (www.scholar.google.com) and several other online sources.

While the momentum and quality of global genetic and genomic education have continually expanded in the developed nations, several countries in the underdeveloped and developing nations are unable to invest and offer even basic levels of life sciences education, particularly related to genetics and genomics. Inevitably, huge gap exists in both quantitative and qualitative parameters. However, to some extent, this gap is gradually narrowed down with the help of international charitable organizations, notably the Wellcome Trust (www.wellcome.ac.uk), the Rockefeller Foundation (www.rockfellerfoundation.org), and the Gates Foundation (www.gatesfoundation.org). In addition, there are several United Nations educational programs harnessed by many less developed nations. The United Nations Educational, Scientific and Cultural Organization (www.UNESCO.org) supports and collaborates with many global projects that include genetic and genomic education, such as the Human Variome Project discussed later in this chapter (www.humanvariome-project.org). Similarly, several streams of scholarships and training fellowship exist funded by the Commonwealth (www.commonwealtheducationtrust.org), the International development projects of the United Kingdom government (www.gov.uk), and the British Council

Genomic Medicine Skills and Competencies
https://doi.org/10.1016/B978-0-323-98383-9.00007-2

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Journal of Genetics (2023)102:46
https://doi.org/10.1007/s12041-023-01444-8

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PERSPECTIVES

Indigenous population genome databases for India and South Asia: emerging need for health and social applications

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Received 6 March 2023; revised 27 July 2023; accepted 27 July 2023

Abstract. With increased technological sophistication and rapidly reducing costs, currently, a huge amount of personal and population-level human genomic data and information is generated globally. There is an urgent need for an adequately curated and annotated human genome variant database for successful and large-scale application and translation in biomedical research, medical (healthcare) applications, socio-economic benefits and many other applications. The bulk of the available genomic data is generated from peoples of European descent. The genome data, particularly the human genome variant data is skewed with minimal content from other populations, particularly the minority or diverse populations. It has further contributed to global health inequality, which is visible in inefficiency, lack of effectiveness and disparity in clinical diagnosis, and precision-personalized medicine and preventive healthcare. Inevitably, this gap is widened with ensuing socio-economic implications. This problem is now faced by medical practitioners and healthcare providers in India, South Asia and other low and middle-income countries (LMICs). The current review provides views and critical appraisal of the current status of genomic research, clinical utility and genome variant databases in India and South Asia. A few observations and recommendations are made to ensure harmonization that requires further structured audit and appraisal by the indigenous populations' consortium. Emphasis is made on the urgent need for statutory regulation of genome data generation, storage, and retrieval systems in research and diagnostic genomic laboratories.

Keywords. clinical genomics; genomic medicine; precision medicine and healthcare; genome variants; genome database; population variation; genomics and society.

Introduction

The success of any scientific and technological development is judged by its wide applications, efficacy, efficiency and positive socio-economic impact on the people and society. Perhaps the best example would be the global use of mobile phones and digital devices. These are affordable and accessible to most in low and middle-income countries (LMICs). The key to this major success is universal coordination and regulation of online service providers. Individual nations and consortia of nations have set up regulatory and governance mechanisms to safeguard data storage and retrieval, accessibility, and applications within the agreed legal and ethical parameters. However, these are not adequate and require continuous review, audit and amendments (Comfort *et al.* 2018).

Lessons learnt from the global digital revolution are applied to many other services, particularly digital education and healthcare (Barnett *et al.* 2019). Digital healthcare offers several benefits to the consumer, however, requires sophisticated computational systems, organizational and regulatory mechanisms for effective and efficient delivery in keeping with ethical standards. An important and essential component of any digital healthcare provision is a centrally managed robust database system. It would be the State's responsibility to ensure funding and governance in collaboration with private healthcare providers. Necessary statutory instruments might be required. International organizations, such as the World Health Organization, would be expected to offer guidance and set standards through the International Health Regulatory strategic guidelines.

Since the completion of the human genome project and rapid advances in number of genomic and omics

Published online: 08 September 2023

Editorial

The Genomic Health Care in Modern Medicine

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The current special issue of the *Apollo Medicine* celebrates the progress made by genetics, particularly human genetics in modern medicine and health care. Among several key discoveries and innovations, the deciphering of the double helix structure of the deoxyribonucleic acid (DNA) by James Watson and Francis Crick in 1953 unquestionably remains the most significant milestone. This special issue is dedicated to this landmark discovery that conceptually revolutionized the cell and molecular biology with far-reaching implications. It offered the much-needed physical evidence for heredity and its correlation with physical and many other traits. We are now cherished with its applications and positive impact in managing the human disease and prospects of optimal human health.

The concept of heredity in living creatures dates back to the ancient times. Interpretations of hymns and inscriptions in the *Vedas*, particularly the *Rigveda,* refer to heredity. Scientists and the Vedic scholars have revisited the evidence collected from the Indus Valley Civilization consistent with the genetic evolution and recombination. It is claimed that some of the hymns when decoded relate to the complex processes such as the synthesis of chromosome, DNA replication, protein translation, and nucleotide pairing for nuclear reaction (https://www.dnaindia.com/bangalore/report-rig-veda-a-treasure-trove-of-transgenics-1506241). The team in the Council of Scientific and Industrial Research-Institute of Genomics and Integrative Biology is actively pursuing the role of the ancient Vedas in the context of modern genomic technologies (https://www.igib.res.in/?q = ayurgenomics/).

There are many anecdotes from the ancient Greek literature and mythology that relate to human heredity and health implications. Most of these are related to the times of Hippocrates around 380–350 BC. There is reference to "mothers who bear sons dying of bleeding when wounded in the war." Many acknowledge this as a clear reference to the classic X-linked hemophilia A. Perhaps the most pertinent evidence comes from the Aristotle's "Generation of Animals" book, in which the *heritable factors* are argued with the laws of inheritance, mainly during the act of reproduction (*Devin Henry, 2006. Aristotle on the mechanism of inheritance. Journal of the history of biology; doi 10.1007/s10739-005-3058-y.).*

There is an ongoing argument whether Aristotle's Greek philosophy favored natural selection theory for the biological evolution, later put forward by Charles Darwin? Despite the differing views on Charles Darwin's theory of evolution governed by the natural selection, many agreed with the concept of hereditary factors put forward in the Darwin's famous book "On the origin of species." Several years later, the evidence for dominant and recessive hereditary factors was provided by Gregor Mendel in his elegantly illustrated mathematical experiments on garden pea plants with different physical traits. However, this work was not appreciated for almost 60 years; when in the early 1900s, biologists became serious about the Mendel's laws of inheritance and the science of heredity. This generated tremendous interest on the mysteries of heredity material, possibly located in the nucleus of the cell.

During the early part of the 20th century, a large amount of data was generated on physical traits like height, and functional traits like intelligence, in the context of positive or negative heredity. The term "*eugenics*" was coined by Francis Galton, the great grandson of Charles Darwin. Whist this movement was full of good intentions, sections of the society started using this as the divisive and discriminatory tool both in the USA and UK, including the parts of the Europe. Later, the eugenic ideas and logic became the central theme of the Nazi Germany as evident from the doctrine of the *Race Hygiene* clearly targeted at Jews, Gypsies, and a few other minority sections, including people with physical and learning disabilities.

Despite the negative impact of the World War II and the eugenics movement, the progress in genetics and heredity continued. The period between 1950 and 1960, described as the *golden decade of genetics,* is decorated with discoveries and innovations in genetics, notably the Watson-Crick's double helix model of the DNA, Tjio-Levan's 46 chromosomes in the human cell, and Hargobind Khorana's triple nucleotide genetic code governing the assembly of amino acids for the peptide molecule synthesis. Since then the progress in genetics, later expanded to genomics, led to many more discoveries to the successful completion of the Human Genome Project in early parts of the new millennium. In 2003, advances in molecular technology allowed nearly 98% sequence of the human genome. The remainder 2% of the genome, comprising the repetitive DNA in telomeres (the terminal ends of the chromosomes) was eventually sequenced in 2022.

Although the practice of genetics in medicine became established in the early 1970s, it remained miniscule restricted to a few chromosomal disorders, selected multiple malformation rare dysmorphic syndromes, and common monogenic (single-gene Mendelian) diseases. The concept of polygenic multifactorial diseases was appreciated with the mathematical models of heritability and linkage disequilibrium. The practice of genetic counseling found its firm base with the development of genetics in medicine. This period witnessed

Review Article

From the Double Helix to the Personal Genomes

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Abstract

In 1954, the seminal short paper in the *Nature* from James Watson and Francis Crick proposed the double helix model of deoxyribose nucleic acid. This amateur-looking concept changed the way molecular biology is now perceived. We are now celebrating the 70 years of the phenomenon discovery of the modern science that has revolutionized life sciences with a huge impact on many other related scientific disciplines. Fifty years later, the Human Genome Project offered the nearly complete draft sequence of the human genome that is now fully sequenced in the 70th year of the double helix. Technological advances have led to a rapid reduction in the cost of whole genome sequencing. It is now possible for anyone to get the personal genome sequenced for <US$500! The investigative field of human genetics has evolved into promising field of clinical genomics and genomic medicine. By far the major impact of human genome sequencing is evident from precision medicine and healthcare. Most common and rare disorders of unknown etiology can now be diagnosed and deciphered with precision using one of the next-generation genome sequencing techniques. Wide-ranging precision genome diagnostic opportunities now exist along with precision and personalized therapeutic options. In addition, precise personalized preventive healthcare is now possible for healthy people with a family history of monogenic/Mendelian disease or common complex medical conditions. The technology permits us to have the whole genome sequenced in a new born baby or anyone else of any age to assist with long-term preventive health and life style planning and necessary precautions.

Keywords: Clinical genomics, deoxyribose nucleic acid, double helix, ethical, genome sequencing, genomic healthcare, genomic medicine, human genome project, human genomics, legal and social issues (ELSI), molecular biology, personal genomics, personalized medicine, precision medicine, preventive genomics

Introduction

Charles Darwin, the famous biologist of generations, referred to *hereditary factors* in his seminal book "*On the Origin of Species*." However, it took several years before biologists and others working on different aspects of life sciences could properly conceptualize the shape and location of these so-called *hereditary factors*. Gregor Mendel's seminal simple garden pea cross-over experiments and wealth of observations probably offered the first physical evidence for Darwin's theory. Following a series of deliberations and research, most scientists agreed on the nucleus as the possible location of the heredity. Biological chemists were convinced that nucleic acids should have the key role in heredity. As soon as the term "*gene*" became the common reference for hereditary factors, intense work began on the precise location, structure, and function of genes. The focus was largely on nucleic acids-the ribose nucleic acid (RNA) and the deoxyribose nucleic acid (DNA). Historical archives describe several models of structure and function that were proposed, investigated, and eventually discarded.

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	DOI: 10.4103/am.am_65_23

This article provides an overview of the genes, genetics, and present-day genomics, all fundamentally linked to the structure of DNA. The focus is largely on its impact on clinical and healthcare applications with particular reference to personal genomics.

The Watson-Crick Deoxyribose Nucleic Acid Model

In the early stages of research and development, the preferred model for the DNA was considered to be the triple helical

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Submitted: 08-Mar-2023 **Accepted:** 14-Mar-2023
Published: ***
How to cite this article: Kumar D. From the double helix to the personal genomes. Apollo Med 2023;XX:XX-XX.

Review Article

Drug Repurposing for Rare (Orphan) Diseases—Scope and Limitations

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Abstract

Effective and affordable treatment for rare diseases remains a huge challenge. Only a few drugs have made inroads into the therapeutic arena for rare diseases. The current focus is shifted to different uses for expensive new drugs, referred to as drug repurposing. It is also called drug repositioning or reprofiling, refers to the identification of new therapeutic applications of existing or investigational drugs. This concept and novel approaches have promising role in the treatment of many potentially incurable diseases, particularly certain forms of cancer, neurodegenerative conditions, immunological disorders and uncommon infectious diseases. There are huge expectations filled with optimism that the drug repurposing would offer fresh opportunities for the treatment and management of rare diseases. This is undoubtedly more relevant for low and middle income countries.

Keywords: Rare diseases, precision diagnosis, next-generation genome diagnosis, multi-OMICS, drug discovery, drug development, pharmaceutical industry

Introduction

With increasing successes and sophistication in the genomic and multi-OMIC diagnosis of rare diseases, the focus is now on targeted and precision therapy. Tremendous success has been achieved in new drug discovery and drug development for rare or so-called neglected orphan diseases (Drugs for Neglected Diseases initiative; https://dndi.org/research-development/treatments-delivered/).[1] Some of these novel therapeutic avenues are approved by regulatory organisations, such as the Food and Drug Administration (https://www.fda.gov). However, most of these are far too expensive to be made available in less-resourced low and middle-income countries (LMICs). The focus has now shifted to searching for new indications of currently licensed novel drugs. Such approaches have opened the window of opportunities for specific therapy in cancer, autoimmune disorders (like rheumatoid arthritis), multiple sclerosis, HIV/AIDS, and a few rare (Orphan) diseases.[2] The emerging innovative field, justifiably called 'Drug Repurposing', is full of challenges for research and development.[3] This movement has gained high momentum in just a few years and is often referred to as drug repositioning, drug reprofiling and drug rescue.[4] At present, there are diverse innovative techniques and pharmacological targets for drug repurposing or drug repositioning. These illuminate various experimental and computational models used in the search for expanded and alternative uses of drugs and experimental molecules, including natural products, within the broad domain of 'Drug Repurposing'.

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Apollo Medicine
1–7, 2024
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DOI: 10.1177/09760016241287308
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Submitted: 12-Jun-2024 **Revised:** 02-Sep-2024
Accepted: 02-Sep-2024 **Published:** XXX
How to cite this article: Kumar D. Drug repurposing for rare (orphan) diseases—scope and limitations. Apollo Med 2024; XX:XX-XX.

1

From the double helix to the personal genomes

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Introduction

Charles Darwin, the famous biologist of generations, referred to *hereditary factors* in his seminal book *On the Origin of Species*. However, it took several years before biologists and others working on different aspects of life sciences could properly conceptualize the shape and location of these so-called *hereditary factors*. Soon after the invention of the microscope, an initial description of the cell shape and structure became possible. Following a series of deliberations and research, most scientists agreed the nucleus as the possible location of the heredity. Biological chemists were convinced that nucleic acids should have a key role in heredity. As soon as the term *gene* became the common reference for hereditary factors, intense work began on the precise location, structure, and function of genes. The focus was largely on nucleic acids—the ribose nucleic acid (RNA) and the deoxyribose nucleic acid (DNA). Historical archives describe several models of structure and function that were proposed, investigated, and eventually discarded.

This article provides an overview of the genes, genetics, and present-day genomics, all fundamentally linked to the structure of nucleic acids, particularly the DNA. The focus is largely on its impact on clinical and healthcare applications with particular reference to personal genomics.

The Watson-Crick DNA model

In the early stages of research and development, the preferred model for the deoxyribose nucleic acid (DNA) was considered to be the triple helical molecule. This remained for almost 20 years. However, this concept and limited scientific evidence failed to convince many scientists. It was almost impossible to agree on the basic requirement of the gene splitting into two halves and then reuniting again at conception.

Molecular biology research inevitably suffered during the Second World War. The momentum in this field started rising again soon after the war. The team at the King's

Genomics, Populations, and Society. https://doi.org/10.1016/B978-0-323-91799-5.00006-5
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5

The genomic and precision medicine in clinical practice—Current perspectives and future directions

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Introduction

Recent innovations and new developments in molecular biology, biotechnology, genomics, and many other *OMIC* sciences have revolutionized the contemporary and future practice of clinical medicine. The diagnosis of the most complicated and rare conditions is now possible with a high degree of precision. The "gene-specific" and "genome-driven" diagnoses in many inherited and genetic disorders are now possible. The understanding of molecular mechanisms in a number of common and complex medical conditions has vastly improved. Progress in targeted genetic and molecular approaches in pharmacotherapy has led to many improvements from the current therapeutic regimens, which are designed for the "average model patient" and "one-size-fits-all" model approach. However, this has changed dramatically with rapid advances made in evidence-based precision and personalized medicine [1]. The whole process in the practice of genomic and precision medicine involves a stepwise approach in building the holistic picture referred to as stratified medicine with the ultimate aim of individualized or personalized therapeutic interventions [2]. The scope and limitations in the new exciting field of stratified and personalized medicine are reviewed in this article.

During the last decade, new genomic diagnostic tools and molecular innovations have led to the emergence of precision medicine, an innovative approach to disease prevention and treatment, which takes into account individual differences in people's genes, environments, and lifestyles. The precision medicine is central to stratified and personalized medicine. It provides the clinician with tools to better understand the complex molecular mechanisms underlying a patient's health, disease, or condition, and to better predict which treatments will be most effective. Advances in precision medicine have already led to powerful discoveries and several new treatments, which are tailored to specific characteristics of individuals, such as a person's genetic makeup, or the genetic profile of an individual's tumor. This is leading to a transformation in the way we can treat diseases

Genomics, Populations, and Society. https://doi.org/10.1016/B978-0-323-91799-5.00017-6
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Chapter 1

Introduction to genomic and molecular biology

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Introduction

Most medical practitioners and specialist physicians are oblivious of basic biological facts that govern the whole body and organ-specific structure and function. In this context, understanding genes, genome, genetics and other intricately related facts is most fundamental to structure and function of any form of life. Higher mammals, including humans, have evolved over several thousands of years through repetitive cycles of transmission of genetic traits under enormous environmental pressures. Thus, it is not surprising to find many unexplained and complex elements with the human genetic makeup or genome. The human biology is perhaps one of the most complex and intriguing life sciences. Major organs and arbitrarily set out body systems have specifically assigned parts of the genome as the common denominator of structure and life-long functioning. Nevertheless, system-wide approach is relevant to medicine. In this context, understanding the role of genes and related elements of the human genome is pertinent to any medical practitioner, whether general or system specialist, such as the cardiovascular physician [1,2].

The present chapter introduces genes, genome, genetics and genomics in simplified manner that any clinician or healthcare professional should know. The broad spectrum of genetics and genomics includes many aspects of the genome (Fig. 1.1). Cardiovascular genetics and genomics are broadly similar to any other body system. Selected examples might be of interest to medical and healthcare professionals predominantly engaged with cardiovascular conditions. Emphasis is given on developing reasonable grasp of genetic or genomic factors, heritable, incidental or somatic, that is either etiologically relevant or capable of influencing the natural course of any cardiovascular disease, acting alone or in combination with environmental (infection and toxins) or life style factors (nutrition and occupation) [3].The text is supported with generous illustrations, tables and boxes with key learning points. An interested reader or student might like to choose any book or resource listed under 'Further reading'.

Basic facts – Cell biology, nucleic acids, gene, genome

Human genome – Structure and functional organisation

Living organisms have two types of cells – nucleated, called *eukaryotes* and non-nucleated, called *prokaryotes*. Bacteria are essentially prokaryotes and all other multi-cellular organisms are basically eukaryotes. Both cell types share ancestral evolution characteristics and interchangeable [4,5]. The total genetic constitution in either cell is called genome. In eukaryotes, it is contained within the nucleus and hence referred to as *nuclear genome*. However, the cytoplasm of a eukaryote cell also contains another genome within the energy-rich intracellular organelle, mitochondria, referred to as the *mitochondrial genome*. Morbid changes in both genomes are associated with a number of human disorders. The cardiovascular system, by virtue of its diversity, complexity and high energy turnover, has many disorders caused by pathogenic changes in either the nuclear DNA (nDNA) or the mitochondrial DNA (mtDNA) [6].

Genetic information is transferred from one generation to the next by small sections of the nucleic acid, deoxyribonucleic acid (DNA), which is tightly packaged into subcellular structures called *chromosomes*. Prokaryotes usually have a single

Genomic and Molecular Cardiovascular Medicine. https://doi.org/10.1016/B978-0-12-822951-4.00016-3
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Chapter 20

Cardiovascular precision and personalised medicine

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Introduction

Conceptually, the precision medicine is closely related to the historic movement of the evidence-based medicine (EBM). It looks more appealing when combined with emphasis on personalised practice. There is no single definition of the practice of EBM. It is agreed that the practice includes integrating individual clinical expertise with the best available external clinical evidence from systematic research [1]. Montori et al. [2] set out the ground rules for EBM. The practice of EBM is a process of life-long, self-directed learning in which caring for our own patients creates the need for clinically important information about diagnosis, prognosis, therapy and other clinical and health care issues, and in which we (1) convert these information needs into answerable questions; (2) track down, with maximum efficiency, the best evidence with which to answer them (whether from the clinical examination, the diagnostic laboratory from research evidence, or other sources); (3) critically appraise that evidence for its validity (closeness to the truth) and usefulness (clinical applicability); (4) integrate this appraisal with our clinical expertise and apply it in practice and (5) evaluate our performance [2]. Thus core aims of personalised and precision medicine closely overlap with the EBM paradigm [3].

Rapid advances in molecular biology, medical biochemistry, immunology, microbiology and imaging technologies provided new and robust tools for evidence collection. This was supported by Archie Cochrane's classified statistical evidence collection methodology of carefully supervised and controlled double-blind randomised clinical trials.

Edwards and Moore [4] the key component was universally the Mendelian randomisation of both the clinical and control arms [5]. The level of evidence became much more refined and sensitive with advances in genomic technologies following the completion of the human genome project. The era of genomic medicine offered a fresh leap forward for the practice EBM [3]. Both conventional and next-generation genome technologies are now regarded as probably the most powerful source of evidence required for the practice of precision and personalised medicine [6,7]. In addition to the completion of the human genome project, there are many more scientific developments credited for the current shape and format of the precision medicine (Table 20.1) [7].

Whilst outcomes of the precision and personalised medicine are more attractive, other anticipated outcomes of EBM should include being predictive, preventive, pre-emptive and participatory, commonly referred to as the '6 P's of Modern Medicine' [6]. These highly ambitious goals require a robust integrated system of dynamic phenotyping, 'OMIC' data generation, annotation and curation, digital imaging data, microbiome data combined with external (exposomes) and environmental (ecosystems) factors (Fig. 20.1) [7].

The potential applications and outcomes of precision medicine approaches are evident in many branches of clinical medicine, notably in clinical oncology, microbiology and acute medicine. The cardiovascular medicine has enormous opportunities for precision medicine, particularly as it requires individualised integrated and comprehensive care including prevention both at individual and community levels. The genomic revolution is at the verge of new dimensions in clinical cardiology where precision diagnosis using specific gene and genomic variants offers best possible selection for precision therapy using new drugs and devices targeted at specific molecular points of the disease pathway, for example, in hypertrophic cardiomyopathy (HCM), amyloid heart disease, Fabry's disease, TGF-beta-related aortic and arterial diseases,

Genomic and Molecular Cardiovascular Medicine. https://doi.org/10.1016/B978-0-12-822951-4.00017-5
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Review Article

Drug Repurposing for Rare (Orphan) Diseases—Scope and Limitations

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Abstract

Effective and affordable treatment for rare diseases remains a huge challenge. Only a few drugs have made inroads into the therapeutic arena for rare diseases. The current focus is shifted to different uses for expensive new drugs, referred to as drug repurposing. It is also called drug repositioning or reprofiling, refers to the identification of new therapeutic applications of existing or investigational drugs. This concept and novel approaches have promising role in the treatment of many potentially incurable diseases, particularly certain forms of cancer, neurodegenerative conditions, immunological disorders and uncommon infectious diseases. There are huge expectations filled with optimism that the drug repurposing would offer fresh opportunities for the treatment and management of rare diseases. This is undoubtedly more relevant for low and middle income countries.

Keywords: Rare diseases, precision diagnosis, next-generation genome diagnosis, multi-OMICS, drug discovery, drug development, pharmaceutical industry

Introduction

With increasing successes and sophistication in the genomic and multi-OMIC diagnosis of rare diseases, the focus is now on targeted and precision therapy. Tremendous success has been achieved in new drug discovery and drug development for rare or so-called neglected orphan diseases (Drugs for Neglected Diseases initiative; https://dndi.org/research-development/treatments-delivered/).[1] Some of these novel therapeutic avenues are approved by regulatory organisations, such as the Food and Drug Administration (https://www.fda.gov). However, most of these are far too expensive to be made available in less-resourced low and middle-income countries (LMICs). The focus has now shifted to searching for new indications of currently licensed novel drugs. Such approaches have opened the window of opportunities for specific therapy in cancer, autoimmune disorders (like rheumatoid arthritis), multiple sclerosis, HIV/AIDS, and a few rare (Orphan) diseases.[2] The emerging innovative field, justifiably called 'Drug Repurposing', is full of challenges for research and development.[3] This movement has gained high momentum in just a few years and is often referred to as drug repositioning, drug reprofiling and drug rescue.[4] At present, there are diverse innovative techniques and pharmacological targets for drug repurposing or drug repositioning. These illuminate various experimental and computational models used in the search for expanded and alternative uses of drugs and experimental molecules, including natural products, within the broad domain of 'Drug Repurposing'.

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Apollo Medicine
1–7, 2024
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DOI: 10.1177/09760016241287308
journals.sagepub.com/home/aom
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Submitted: 12-Jun-2024 **Revised:** 02-Sep-2024
Accepted: 02-Sep-2024 **Published:** XXX
How to cite this article: Kumar D. Drug repurposing for rare (orphan) diseases—scope and limitations. Apollo Med 2024; XX:XX-XX.

XI BOOKS AND JOURNALS

Metrics:

Number of Books: Edited and Co-Authored= 32

Number of Books Commissioned and In progress= 3

Number of Books Under development= 4

Number of Chapters reviewed and edited= 606

Number of Contributors= 989

Total number of published pages= 11234

XI.1 Author/ Editor- New Books-

1. "**Genetic disorders of the Indian subcontinent", Springer-Kluwer, Dordrecht, 2004**

The population of the Indian subcontinent consists of an amalgamation of people. A significant proportion of health problem is linked to hereditary factors. This text includes an account of the social and cultural diversity, medical demography, genetic epidemiology, and common genetic disorders affecting people from the Indian subcontinent.

Written by a team of clinicians, geneticists and other health professionals from Indian subcontinent and other places with experience and understanding of different genetic disorders and related clinical, health and socio-cultural issues. Excellent reviews are published in Journal of Medical Genetics, Human Genetics, South African Medical Journal and Am J Medical Genetics.

FOREWORD

The Indian subcontinent is a vast land mass inhabited by over one billion people. Its rich and varied history is reflected by its numerous racial and ethnic groups and its distinct religious, cultural and social characteristics. Like many developing countries in Asia, it is passing through both demographic and epidemiological transitions whereby, at least in some parts, the diseases of severe poverty are being replaced by those of Westernisation; obesity, diabetes, and heart disease, for example. Indeed, as we move into the new millennium India has become a land of opposites; on the one hand there is still extensive poverty yet, on the other hand, some of the most remarkable developments in commerce and technology in Asia are taking place, notably in the fields of information technology and biotechnology.

India has always fascinated human geneticists and a considerable amount of work has been done towards tracing the origins of its different ethnic groups. In the current excitement generated by the human genome project and the molecular and genetic approach to the study of human disease, there is little doubt that this field will develop and flourish in India in the future.

Although so far there are limited data about genetic diseases in India, enough is known already to suggest that this will be an extremely fruitful area of research. This work will encompass studies of monogenic diseases, the genetic component of some of the major killers of later life including heart disease, diabetes and obesity, and, in particular, genetic variation in response to the serious infections which still plague the country, notably malaria and HIV/AIDS. There are many potentially productive areas for study. Why is the form of sickle cell disease, which is so common in some parts of India, different in its phenotypic expression to the same disease in Africa? Why is there a rapidly increasing epidemic of type II diabetes and obesity in India? How much of this has a genetic component compared with environmental factors such as low birth weight? Does the occurrence of disease in the widely different population groups in India offer clues about their cause? And so much more.

Dr. Dhavendra Kumar and the excellent team of writers that he has drawn together have done a major service in summarising what is known about human genetics and the different genetic disorders of the Indian subcontinent. This new work, which could not be more timely, will provide a valuable reference and starting point for the many studies which will undoubtedly be carried out towards an analysis of the genetic component of diseases in India over the coming years. The future health and well-being of the Indian population will depend on improved public health combined with advances in the understanding of some of its common diseases, which will undoubtedly arise from the new field of genomics, particularly as it relates to communicable disease and the major illnesses of middle and old age. These advances may not come quickly, but come they will. This book will be an excellent starting point for students and young research workers who wish to take advantage of what the modern biomedical sciences are offering them. I wish it all the success it deserves.

D.J. Weatherall
Oxford 2004

PREFACE

In the year 1953, the 25th April issue of the science journal *Nature* published three scientific papers, which revolutionised the science of biology[1]. All these papers put forward hypotheses on the structure of deoxyribose nucleic acid [DNA], the genetic material located in the nucleus of each eukaryotic cell. Among these, the paper by Watson and Crick attracted attention of biologists around the world. It led to discovery of the double helix molecular structure of the DNA. From that time onward the science of genetics has rapidly moved forward. Fifty years later, the whole human genome was sequenced and a new era has begun[2]. On this stunning feat, Dr. Francis Collins, director of the Human Genome Project [HGP], stated, " It is humbling and awe-inspiring to realize we have caught the first glimpse of our won instruction book, previously known only to God". Unsurprisingly, it has generated tremendous interest in genetics of the human race, the *Homo sapiens sapiens*[3].Mike Dexter, director of the Wellcome Trust described the HGP's significance as surpassing the invention of wheel. "The code will be used as long as humans exist," he said. The Wellcome foundation celebrated the 50th anniversary by launching an interactive web-site[4]

The science of human genetics has been on the horizon for almost 150 years from the time of Charles Darwin's famous 'origin of species and selection' theory. This was later complicated and challenged by the discovery of Mendel's laws of inheritance. For several years supporters of both hypotheses challenged each other. However, with the development of human genetics and deciphering and sequencing of the human genome, it became clear that both Charles Darwin and Gregor Mendel were correct in their approach in understanding the molecular origin of biological life and shaping of it in varied environments. This is reflected in wide variation in the human genome (genetic polymorphisms) and disorders resulting from changes (mutations) in about 30,000 genes distributed across 23 pair of chromosomes. A number of other discoveries and inventions have helped in understanding the normal and abnormal expression of changes in the DNA structure.

Numerous researchers in Human Genetics have concentrated on various major population groups to understand the genetic variation and specific patterns of disease. Examples include peoples of Jewish[5], African[6] and Arab[7] origin. There is tremendous socio-cultural and genetic diversity among these population groups. Some selected population groups are relatively homogeneous and are burdened with specific genetic disorders. For example, the Amish in the United States are well recognized with a number of genetic disorders[8]. Other heterogeneous population groups, such as those from the Chinese and Indian subcontinent, have received less attention. However, a number of Mendelian disorders have been documented from these populations groups [9]. Both population groups form one of the largest global population groups and possess distinct physical and social-cultural characteristics dating back to several thousand years.

The Indian subcontinent populations consist of a fine amalgamation of people from diverse tribal, cultural, religious and social backgrounds. Several countries constitute the Indian subcontinent- India, Pakistan, Bangladesh, Sri Lanka, Nepal,

Bhutan and the Maldives. Some of these countries are also designated as '*developing countries*', which could be a convenient term to indicate rapidly changing political and economic status. However, terms like '*underdeveloped countries*' and '*developing countries*' are inappropriate and do not provide any information on the diversity of origin, structure and socio-cultural characteristics of a major population group, such as that from the Indian subcontinent. Wherever possible these terms have been avoided in this book.

The people from the vast region of the Indian subcontinent are also referred to as '*South Asians*', '*South-West Asians*', or '*Asian Indians*'. These are often misleading and inaccurate. A *South-Asian* could be any person originating from the southern part of Asia. Similarly any person designated as a *South-West Asian* could belong to any country between the middle-east and south-east Asia! These arbitrary terms and designations were used during the World War II as part of the strategic planning, and have been retained for political and economic purposes. An *Asian Indian* refers to any person originating from the Indian subcontinent and living in the North America who can be distinguished from other people with an *Indian* suffix, such as Ameri-Indian, Brazilian-Indian, and Mexican-Indian etc. The initial name for this book was '*Genetic Diseases among the Asian Indians*', but this title would have been misleading. It was discarded for reasons as explained above. The present title has been chosen to include all peoples living and/or originating from the Indian subcontinent.

The major population of the Indian subcontinent comprise of Caucasians. The other major populations include Dravidians, Mongoloid and Australoid peoples. The genetic variation is abundant. In addition, there are a number of smaller isolated population groups, which are highly inbred providing ample biological opportunities for genetic admixture and genetic disorders. Mortality and morbidity from a vast number of medical and surgical conditions in the subcontinent is significant and well above compared to the developed countries. Consequently, it has maintained a constant drain on the human, economic and social resources. Although, a large component of the human health problem is related to infection, malnutrition and other environmental causes, a significant proportion is linked to hereditary factors manifesting in the form of chromosomal, single gene (Mendelian) and complex medical diseases of polygenic/multi-factorial origin. Unusual and unique monogenic disorders are not uncommon. A number of common complex medical conditions, such as ischaemic heart disease and diabetes mellitus are known to be relatively more prevalent among people belonging to the Indian subcontinent. In addition, genetic variation and specific genetic associations are recognised with susceptibility and/or protection to a number of infectious diseases, including the therapeutic outcome to anti-microbial treatment.

The true burden of the inherited disorders among these people is unknown, and probably underestimated. There is no collective data and/or information to provide useful resource for the benefit of the medical and health professionals. In view of this observation, the need for a reference text was recognised to present relevant data and information on genetic variation and disorders among the Indian subcontinent populations. The book is aimed at a wide audience including medical and scientific genetic research professionals, various categories of health professionals including primary care physicians, specialist clinicians, public health

professionals, medical sociologists/ demographers and hospital managers and health administrators.

The book includes contributions made by number of experts in human and medical genetics and as well as from allied disciplines. These contributors and co-authors are genetic and allied health professionals from various countries of the Indian subcontinent and abroad. It reflects widespread interest and experience in dealing with people from India, Pakistan, Sri Lanka and other countries of the Indian subcontinent. These people have settled down in various continents as a result of regular migration. Various sections of the book deal with specific issues related to the indigenous and migrant population groups. It is hoped that the book will generate an interest and initiate debate and discussion on the development of the infrastructure for the human genetics and its health application for the benefit of people from the Indian subcontinent.

The text is presented in a uniform format. However, the views and opinions expressed by individual contributor remain unchanged. An interested reader may approach the respective author or contributors for further information or clarification on a specific subject. The success of the book depends upon its acknowledgement as a useful reference resource.

And perhaps as a final comment, knowing that the people from the Indian subcontinent culturally have a strong belief in fate and astrology, the quote by the Nobel Laureate J.D.Watson, the co-discoverer of the DNA-double helix is probably relevant, *"We used to think our fate was in our stars. Now we know, in large measure, our fate is in our genes."*

Dhavendra Kumar

Oxford, 2004

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CHAPTER 1

THE INDIAN SUBCONTINENT AND HUMAN GENETICS: AN INTRODUCTION

DHAVENDRA KUMAR

1. THE GEOGRAPHY OF THE INDIAN SUBCONTINENT

The Indian subcontinent is a vast region inhabited by heterogeneous populations. Geographically it is often referred to as 'South-West Asia'. The people from this region are often collectively referred to as '*South Asians*'. However, inappropriate use of the term '*Asian*' can be misleading and damaging (Bhopal et al. 1991). For example '*South Asians*' may be confused with '*South-East Asians*', who are entirely different. The term *Asian Indian* is preferably used in North America in the socio-political context to refer to people originating from the Indian subcontinent (Fisher, 1996). It helps to differentiate them from other populations with '*Indian*' suffix, for example '*American Indian, Brazilian Indian*' etc. The Indian subcontinent is one of the largest geo-political regions of the Asian continent. The geographic and political boundaries include India, Pakistan, Bangladesh, Sri Lanka, Nepal, Bhutan and other small islands of the Indian Ocean. There is marked cultural and ethnic diversity with considerable overlap. The admixture of various populations is evident in neighbouring states stretching from Afghanistan in the North West and Burma in the North East. The last census of India (www.censusindia.net) recorded the population of India close to the one billion mark. The combined population of the whole region exceeds than that of the Chinese subcontinent.

The physical map of the Indian subcontinent [Fig.1-1] illustrates a large region from north to south and east to west. Within these horizons are a number of rivers, mountains, deserts, basins and areas prone to natural disasters. The vast and dense Himalayan range stretches from the Hindu Kush in the north-west to the Korakoram range in the North, which descends into the vast plateau of Tibet. The vast terrain of the Himalayas covers the northern sector and extends to the east providing a long border to the north of India, and includes the sovereign Himalayan
States of Nepal and Bhutan. The highest point of Mount Everest lies between Nepal and Tibet, which is now part of China.

Below the vast Himalayan range of mountains lie the Shiwalik range. The mainland is divided between the plains of the Indus River in the north-west and the large plain of the River Ganges in most of the northern and eastern part of the Indian subcontinent. The River Yamuna and other rivers in the surrounding region join the River Ganges. The River Brahmaputra serves the north-eastern mountainous region and the wooded plains of Bengal. The land served by these rivers is rich in natural resources and provides the livelihood of millions of people.

The central part of India includes the Great Indian Desert and a large densely-populated region. It is separated from the southern part of India, called 'Deccan', by the Vindhya mountain range stretching from east to west. Two other mountainous ranges stretch along the western coastal region (Western Ghats) and the eastern coast (Eastern Ghats). These two ranges include southern Indian states. Several rivers and their tributaries serve this vast area. The region is densely populated and has a rich culture.

Figure 1-1: The physical map of the Indian subcontinent
[With permission from: Oxford School Atlas, 30th edition, Oxford University Press, India, 2002, page 6]

The political map of the subcontinent has seen many changes over the last 1,000 years. The land was divided between several hundreds of small and large states or kingdoms. These were included in major Empires including that of the Ashoka, Maurya, Moghuls and lastly, the British Empire. The present political map [Figure 1-2] includes the sovereign nations of Afghanistan, Pakistan, India, Nepal, Bhutan, Bangladesh, Sri Lanka and The Maldives. Although the political boundaries are clearly laid out, there remains some controversy surrounding the northern states of Jammu and Kashmir between India and Pakistan. There is an ongoing border dispute between China and India over Ladakh on the north-eastern side of the border. This book has not addressed these differences, but has concentrated on population heterogeneity, social-cultural variation between peoples and genetic factors affecting health.

Figure 1-2: The political map of the Indian subcontinent
[With permission from: Oxford School Atlas, 30th edition, Oxford University Press, India, 2002, page 7]

The Hindu Kush is the gateway to the north-west frontier region of Pakistan and Afghanistan. Historically, it has been one of the major entry routes to the Indian mainland for foreign invaders. Numerous invasions, spanning over several hundreds of years, brought people from the Middle-East, Central Asia and Mongolia. These peoples, from various corners of Asia and Central and Eastern Europe, laid the foundation for a large heterogeneous population. The native people of the Indian subcontinent were gradually outnumbered and now remain confined to the deep-south or scattered throughout in small tribal populations. The Dravidians in South India are probably the oldest, authentic, distinct ethnic group of the Indian subcontinent.

2. THE PEOPLE OF THE INDIAN SUBCONTINENT

The name of the subcontinent is derived from the river 'Indus' or *Sindhu*. This river has attracted hundreds of historians and archaeologists. The Indus valley civilization is believed to have existed in this region about five thousand years ago (Nehru, 1946). Proof has been provided by the excavations of Harappa in the west Punjab (Pakistan) and Mohanjeo-daro in the Sind. The existence of a highly-organised and developed ancient civilization has been the subject of much interest and debate. Professor Childe (1943) writes, 'The Indus civilization represents a very perfect

adjustment of human life to a specific environment that can only have resulted from years of patient effort. And it has endured; it is already specifically Indian and forms the basis of modern Indian culture'. It is astonishing that any culture or civilization should have continued for five thousand years and more. There is evidence that during this period there was constant and intimate contact with people from other continents, including Persians (Iranians), Egyptians, Greeks, Chinese, Arabs, Central Asians, and peoples from the Mediterranean. This resulted in a multilateral population and cultural admixture reflected in physical and cultural heterogeneity (Nehru, 1946).

The Indus Valley civilization was highly-developed and must have taken thousand of years to evolve. It was a predominantly secular civilization and the religious element, though present, did not exert a strong influence. It was also clearly the precursor of later cultural periods. Among several important observations about the Indus civilization, comments of Childe (1943) provide evidence that the cities were governed by a well-planned and administrated system. This is reflected in well-planned streets and a regularly maintained magnificent system of drains. The municipal government had town-planning bye-laws, and a maintenance system for streets, lanes and properties rendered necessary by recurrent floods.

This civilization was probably not restricted to the north-western regions. There can be little doubt that many other cities and places lie buried together with the remains of a rich ancient cultural heritage. Evidence of this civilization has been found as far apart as Kathiawar in the western Indian state of Gujarat and the Ambala district of the state of Haryana in India. There is good reason to believe that it spread to the Gangetic valley. It is thus clear that the Indus Valley civilization evolved over many millenniums. This civilization is equally important to that of Persia, Mesopotamia and Egypt.

The people of the Indus Valley had much contact with the Sumerian civilization of that period, and there is some evidence for an Indian merchant colony in Akkad. Childe (1943) adds that produce from the Indus cities reached as far as the markets on the Tigris and Euphrates. Also, produce from these places reached the Indus Valley, as shown by the presence of Sumerian artefacts and Mesopotomian toilet sets. Trade was not confined to raw materials and luxury articles. Fish was regularly imported from the Arabian seacoasts, augmenting the food supplies of the Indus Valley cities.

Who were these people who inhabited the Indus Valley? This question has been debated by several eminent anthropologists and population geneticists. It is possible that the whole valley came to an abrupt end due to some natural catastrophe such as an earthquake or major floods. The Indus River is well known for catastrophic flooding which could easily have washed away cities and villages. It is postulated that the Indus Valley culture was an indigenous culture since its roots and offshoots may be found in southern India. Some scholars find an essential similarity between these people and the Dravidian races and culture of south India. It is likely that migrations may have taken place several thousand years before the development of the Indus Valley civilization. This is in accordance with the 'out of Africa' concept of man's migration across the Arabian Sea, or by land through the Middle East [Figure 1-3] and which is believed to have taken place about 50-60 thousand years ago.

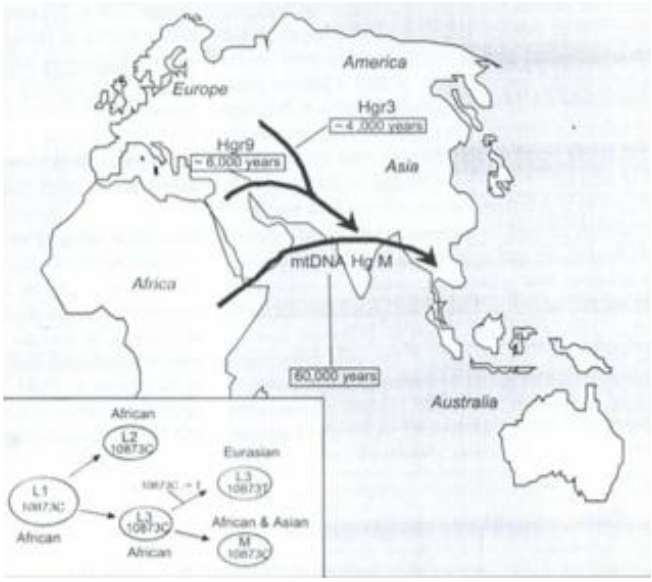


Figure 1-3: 'Out-of-Africa' migration of the man to the Indian subcontinent
[With kind permission from Dr. Ken McLreavey, Pasteur Institute, Paris, France]

The people inhabiting the region after the end of the Indus Valley civilization are referred to as Aryans. The word *Aryan* in ancient Sanskrit script means *Noble*. The Aryan migrations are believed to have taken place about a thousand years after the Indus Valley period. These people probably came from Central Asia and the European areas of the Baltic Sea, the Black Sea and the Caspian Sea. This race is also called 'Indo-European' and is recognised by its 'Indo-European' class of languages. It is now firmly believed that the first great cultural synthesis and fusion took place between the incoming Aryans and the Dravidians, who were probably the true and original representatives of the Indus Valley civilization.

Out of this synthesis and fusion grew the modern races and cultures of the Indian subcontinent, which have distinctive elements of both races. Over the following hundreds of years, a number of other races were assimilated into the Aryan-Dravidian race. These included Iranians, Greeks, Parthians, Bactrians, Scythians, Huns, Turks (before Islam), early Christians, Jews and Zoroastrians. They came, left their mark, and were absorbed like a drop of water in the ocean (Nehru, 1946). It is thus not surprising to find evidence of population heterogeneity in recent reports using mitochondrial DNA (mtDNA) polymorphisms and Y-chromosome linked genetic polymorphisms (McElreavey and Quintana-Murci, 2002).

Population geneticists are keen to establish the origin of the human populations inhabiting the Indian subcontinent. Population movements can be dated using inherited mutated alleles (Jobling and Tyler-Smith, 2000). Studies using mtDNA polymorphisms (Quintana-Murci et al., 1999) and Y-linked DNA polymorphisms (Quintana-Murci et al, 2001) provide evidence of the origin of various population groups thorugh maternal and paternal lineages. There is now data available in support of major population movements having taken place from east Africa to western and southern Asia around 60,000 '*years before present*' [YBP]. Migrations of populations to India from the Fertile Crescent in south-western Iran date back to 8,000 YBP, and of the Indo-European speakers from Central and West Asia to approximately 5,000 YBP.

The analysis of two Y chromosome variants, Hgr9 and Hgr3 provides interesting data (Quintan-Murci et al, 2001). Microsatellite variation of Hgr9 among Iranians, Pakistanis and Indians indicate an expansion of populations to around 9,000 YBP in Iran and then to 6,000 YBP in India. This migration originated in what was historically termed Elam in south-west Iran to the Indus valley, and may have been associated with the spread of Dravidian languages from south-west Iran (Quintana-Murci et al., 2001). The same study has shown the distribution of another haplogroup, termed Hgr3, among the central and eastern European populations. This marker is seen with decreasing frequency towards west Europe and East Asia.

The distribution of Hgr3 in Iran shows marked differences between the western Caspian province (3%) and the eastern provinces (31%), with a decreasing frequency cline towards India. This suggests a population movement from central Eurasia into modern Iran and, following an eastern route, into India [Figure 1-3]. The estimation of Hgr3 expansion times determined from populations at different geographical locations suggests that the migration occurred approximately 4,000 YBP, a date which coincides with the disappearance of the Harrapan culture in the Indus valley and the appearance of Indo-European languages in the Indian subcontinent (Quintan-Murci et al., 2001).

The diversity of the Indian subcontinent is tremendous, both in physical appearance and social-cultural practices. All these people are unique by way of their racial origin and traits. The Pathans of Afghanistan and Tamils of south India and Sri Lanka apparently have little in common; they differ in physical appearance, style of clothing, food habits and language, but even so, they share common strands. There is ample evidence of a Central Asian presence in the north-western province and in Kashmir. For several thousands of years, Afghanistan has had close links with the states and people of the Indian subcontinent, of which it geographically is a part. Historically, this part of the subcontinent enjoyed great popularity for its famous University of Taxila, which was an important place of learning about two thousand years ago.

The Pathan and Tamil are probably two extreme examples. Majority of the people are somewhere in between. All of them have their distinctive features. It is fascinating to see how the Pathans, the Sindhis, the Punjabis, the Kashmiris, the Rajputs, the Hindustani-speaking people of north and central India, the Bengalis, the Gujratis, the Tamils, the Andhras, the Oriyas, the Assamese, the Canarese, the Malyalis and the Tamils share, and have maintained, unique, distinct, similar characteristics for hundreds of years. These people share a common heritage. There

is something living and dynamic about this heritage, which is reflected in lifestyles and philosophical attitudes to life and its problems. Ancient India, like ancient China, was a world unto itself, with a culture, civilization and heritage shaped by numerous invasions and external influences.

3. SOME BASIC FACTS ABOUT GENETIC DISEASES

A detailed description of the basic principles of genetics and human genetic diseases is beyond the scope of this section. These facts are explained in various other texts on basic genetics and medical genetics (see 'further reading'). However, some basic principles and relevant information are outlined in this section to assist a reader without any genetics background.

3.1 What are genes and how do they function?

The living organisms are divided into two large classes- the eukaryotes and prokaryotes. The cells of the eukaryotes have a complex compartmentalized internal structure; these include algae, fungi, plants and animals. On the other hand prokaryotes are single-celled microorganisms, which include bacteria and other related micro-organisms. The other types of living organisms are viruses, which are intracellular parasites, living in both eukaryotes and prokaryotes.

Genetic information is transferred from one generation to the next by small sections of the nucleic acid, deoxyribnucelic acid [DNA], which is tightly packaged into subcellular structures called chromosomes. Prokaryotes usually have a single circular chromosome, while most eukaryotes have more than two and in some cases up to several hundred. In humans there are 46 chromosomes arranged in 23 pairs; one of the pair inherited from each parent [Figure 1-4]. Twenty two pairs are called autosomes and one pair is called sex chromosomes, designated as X and Y; females have two X chromosomes [46, XX] and males have an X and Y [46, XY].

A chromosome consists of a tightly coiled length of DNA, together with the proteins (e.g., chromatins) that help to define its structure and level of activity. DNA consists of two long strands of nucleotide bases wrapped round each other along a central spine made up of phosphate and sugar [Figure 1-5]. There are four bases: adenine [A], guanine [G] cytosine [C] and thymine [T]. There are strict rules of pairing of these bases: A always pairs with T and C with G. Two strands are therefore complementary to each other.

Genes are made up of specific lengths of DNA that encode the information to make a protein or ribonucleic acid [RNA] product. RNA differs from DNA in that the base thymine is replaced by uracil [U] and the sugar is ribose. It acts as a template to take the coded information across to ribosomes for final assembly of amino acids into the protein peptide chain [Figure 1-6]. The bases are arranged in sets of three referred to as *codons*. Each *codon* codes for a specific amino acid, so called the genetic code. Codons are located in *exons*, which contain the coding sequences. A gene may consist of several such coding DNA segments. Exons are separated from each other by non-coding sequences of DNA, called introns. Although, these are not known to be associated with any specific function, it is likely that some of these might be of evolutionary significance or associated with other fundamental biological functions? During the transcription of DNA, the

Reviews:

1.Lord Bhuki Parekh, London School of Economics, UK

"To the best of our knowledge, this is the only book written and compiled to focus on human genetics and genetic disorders in relation to people of the Indian subcontinent. It is hoped that the reader will have a good overview and background information on the key subjects ranging from social and cultural aspects to the application of the science of human genetics in the practice of modern clinical medicine." "This is excellent and long overdue" *(Professor Bhuki Parekh, London School of Economics, UK)*

2. 'Genetic Disorders of the Indian Subcontinent', edited by Dhavendra Kumar : Book review
Beighton, Peter
South African medical journal, 2006-01, Vol.96 (1), p.46

"In this excellent monograph, Dhavendra Kumar and forty expert contributors have provided a comprehensive overview of genetic conditions that have been identified in persons with origins of the Indian subcontinent. The first section of this 607-page book contains accounts of the historical, social and demographic factors that underlie the rich ethnic and cultural diversity of the population of India."

3.Y Yamada, Journal of Medical Genetics

288 *J Med Genet* 2006;**43**:288

PostScript

BOOK REVIEW

Genetic Disorders of the Indian Subcontinent

Edited by Dhavendra Kumar. Published by Kluwer Academic Publishers, the Netherlands: 2004, $231.00 (hardback), pp 626.

Genetic Disorders of the Indian Subcontinent is a unique book that reviews the human genetics and human genetic disorders of the Indian subcontinent. It is a multiauthor book for which experts were engaged to review the state of research in given fields, and it provides a valuable reference for future studies of the genetic component of various diseases that affect individuals of the Indian subcontinent.

The book consists of 28 chapters which are organised into three sections. The first six chapters (section A) introduce the human genetics of the Indian subcontinent. Selected genetic disorders are reviewed in the following 18 chapters (section B), while the last four chapters (section C) cover health care and genetic services in this region.

In section A, the first chapter provides a basic introduction to the geography and people of the Indian subcontinent as well as to genetics and genetic diseases. This chapter also gives a brief introduction to the regional burden of genetic diseases. Chapters 2 and 3 address the diversity of people in the Indian subcontinent with regard both to ethnic, cultural, and religious differences and to genetic differences as revealed by polymorphisms in nuclear and mitochondrial DNA. Chapter 4 is a brief review of the epidemiology of genetic diseases, and chapter 5 provides a detailed review of the role of immunogenetic variation in disease susceptibility, focusing on the relationship of molecular variation in the major histocompatibility complex to inflammatory and infectious diseases. The relationship of consanguinity to health and the risk of genetic diseases is addressed in chapter 6.

The 18 chapters of section B cover the genetics of various monogenic disorders and common multifactorial diseases in the Indian subcontinent. For example, in chapter 7, various congenital developmental anomalies, including abnormalities of the central nervous system; cleft lip and cleft palate; heart, gastrointestinal, genitourinary, and limb defects; and multiple anomaly syndromes, are reviewed. In chapters 8 and 9, malformation syndromes and Down syndrome in India are briefly summarised. Chapter 10 presents in detail various inherited metabolic diseases that affect south Asians in the United Kingdom, including disorders of intermediary metabolism (amino acid, fatty acid oxidation, and organic acid disorders), disorders of carbohydrate metabolism (glycogen storage diseases, fructose-1,6-bisphosphatase deficiency, and disorders of triglyceride metabolism), disorders of lysosomal storage (sphingolipidoses, GM1/GM2 gangliosidosis, metachromatic leukodystrophy, Krabbe disease, Niemann-Pick disease, and mucopolysaccharidoses), disorders of the mitochondrial respiratory chain, peroxisomal disorders (disorders caused by single or multiple enzyme deficiencies and Zellweger syndrome), and transport disorders. Chapter 11 covers diagnosis and management of these inherited metabolic diseases in India. The following eight chapters describe in great detail individual genetic disorders in India, including Indian childhood cirrhosis and other metabolic liver diseases, thalassemias and other haemoglobinopathies, disorders of haemostasis and thrombosis, glucose-6-phosphate dehydrogenase deficiency and other inherited red cell defects, genetic neurological and psychiatric diseases, inherited skeletal dysplasias and collagen diseases, deafness and related syndromes, and genetic diseases of the eye. In the next four chapters, the genetics of common complex diseases in the Indian subcontinent, including various cancers, diabetes mellitus and related disorders, coronary heart disease and related diseases, and renal diseases, are summarised with regard to their scientific, clinical, and epidemiological aspects. The final chapter of section B covers the relationship of genetic traits to resistance to malaria. This section of the book thus provides a rich source of information on the genetics of monogenic disorders and the population genetics of common complex diseases in the Indian subcontinent.

Chapter 25 in section C gives an overview of the epidemiology of genetic disorders, health care systems, and genetic services in India, while chapter 26 addresses ethnicity, religious affiliation, medical statistics, health care systems, and genetic services as well as the genetics of single-gene disorders and the population genetics of common complex diseases in Sri Lanka. The final two chapters of the book provide a review of genetic counselling for families and ethical issues in clinical genetics in the Indian subcontinent.

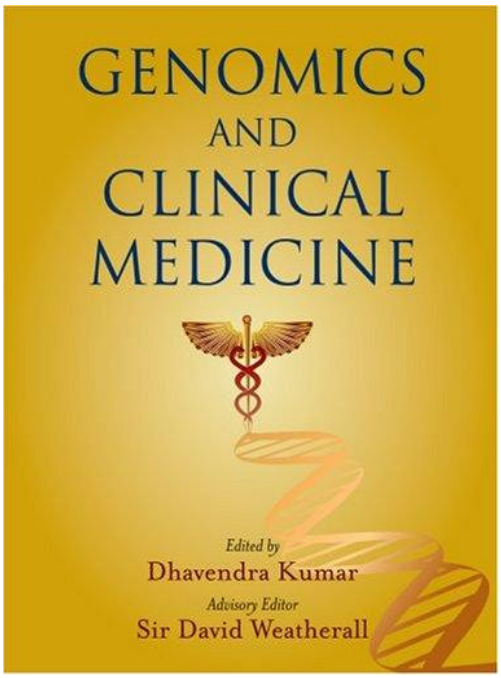
Genetic Disorders of the Indian Subcontinent thus provides a detailed and concise account of social and cultural diversity, medical demography, genetic epidemiology, and consanguinity in this important region as well as of monogenic disorders and common complex diseases that affect its people. It also comprehensively addresses specific issues relating to health care systems, genetic services, and ethical concerns in clinical genetics in this region. Overall, I wholeheartedly recommend this book not only to physicians, researchers, and students in the field of genetics but also to public health consultants, medical demographers, medical and social anthropologists, and health administrators who are interested in the Indian subcontinent. I think all such readers will find much to their benefit.

Y Yamada

4. Charulata Deshpande, Clinical Geneticist, Guy's Hospital, London & Centre for Genomic Medicine, Manchester, UK

"Genetic disorders of the Indian subcontinent is a comprehensive and timely book that addresses the burden of genetic disorders in the people of the Indian subcontinent. There is an admirable attempt to explain the complex interaction of age-old beliefs, social practices, cultural influences … . This book is an invaluable resource to all clinicians dealing with genetic disorders among this population not only in the subcontinent but even in other countries such as UK where there is a sizeable population from this region."
(Charulata Deshpande, Human Genetics, Vol. 120, 2006)

2. **"Genomics and Clinical Medicine", Oxford University Press, New York, 2008**



An important milestone in medicine has been the recent completion of the Human Genome Project. The identification of 30,000 genes and their regulatory proteins provides the framework for understanding the metabolic basis of disease. This advance has also laid the foundation for a broad range of genomic tools that have opened the way for targeted genetic testing in a number of medical disorders. This book is designed to be the first major text to discuss genomics-based advances in disease susceptibility, diagnosis, prognostication, and prediction of treatment outcomes in various areas of medicine. After building a strong underpinning in the basic concepts of genomics, the authors of this book, all leaders in the field, proceed to discuss a wide range of clinical areas and the applications now afforded by genomic analysis.

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41:The Regulation of Human Genomics Research

Glossary of selected terms and phrases
On-line resources and other useful contact addresses

Excellent reviews in New England Journal of Medicine, JAMA and European Journal of Human Genetics.

1. I can see it having a place in the libraries of hospitals and clinical departments alongside other classic textbooks. - *Human Genetics*
2. NEJM, October, 2008

The NEW ENGLAND JOURNAL of MEDICINE

BOOK REVIEWS

GENOMICS AND CLINICAL MEDICINE

(Oxford Monographs on Medical Genetics. 53.) Edited by Dhavendra Kumar and Sir David Weatherall. 651 pp., illustrated. New York, Oxford University Press, 2008. $175. ISBN 978-0-19-518813-4.

TRANSLATIONAL RESEARCH IN GENETICS AND GENOMICS

By Moyra Smith. 220 pp., illustrated. New York, Oxford University Press, 2008. $79.50. ISBN 978-0-19-531376-5.

THE DEATH IN JULY 2008 OF VICTOR A. McKusick marked the end of an era. McKusick, widely considered to be the founding father of medical genetics, gave both a name and an important identity to a new scientific discipline — genomics — when he and Frank Ruddle launched a new journal by that name 3 years before the 1990 launch of the Human Genome Project. When McKusick asked me to succeed him as the editor-in-chief of *Genomics* in 2003, the year in which the "finished" human genome sequence was published, I went back to his 1987 inaugural editorial to see how successful he had been at predicting the future of genome sciences. I found that he was remarkably prescient in identifying a number of concepts and themes that have stood the test of time throughout the Human Genome Project and into the current "genome era."

One of the fundamental methods and themes of genomics, identified by McKusick as "computational science," came to be known as "bioinformatics" in 1994. In 1995, the *Journal* published an article that I wrote on the subject, entitled "Hunting for Genes in Computer Data Bases," so I find it surprising that in 2008, the editor of a book called *Genomics and Clinical Medicine* describes bioinformatics as an "emerging field." This is also a quarter of a century after the founding of the National Institutes of Health's genetic sequence database, GenBank, and 20 years after the founding of the U.S. National Center for Biotechnology Information (NCBI). In a book that aims to "provide the reader [with] core information on the basic principles," the virtual absence of any coherent discussion of the principles, methods, and applications of biomedical informatics is a substantial flaw.

This criticism aside, *Genomics and Clinical Medicine* has much to offer. Part 1 consists of nine chapters on basic characteristics of the human genome, on genomic technologies, and on more specialized and derivative fields such as nutritional genomics and pharmacogenomics. The coverage of various genomic and proteomic forms of technology and their applications in part 1 is somewhat uneven and marred by redundancy. In one of the more thought-provoking chapters, entitled "Genetic and Genomic Approaches to Taxonomy of Human Disease," Dhavendra Kumar asserts that the use of genomics in medicine "has opened the way forward for a new taxonomy of human disease that will be free from limitations and bias in developing diagnostic criteria related to events that are often secondary and peripheral to its cause." However, after letting us peek through this door into the future, the editors fail to lead us through it.

The conventional organization of the topics in part 2, "Clinical Genomics," represents a missed opportunity. This section, the heart of the book, consists of 28 chapters that are organized by organ system or medical subspecialty. This conventional approach is only a way station to a time when genomics may unify some of the subspecialties and support a new grammar of drug discovery. Part 2 contains a number of outstanding chapters that are written by leaders in their fields, but I found myself wishing for more explicit coordination and cross-referencing.

Part 3, "Health Genomics," consists of four chapters on the subjects of global health; genetic testing; ethical, legal, and social issues; and the regulation of human subject research that involves genomics. These are important and interesting issues, but much of the material is presented in an impenetrable style and seems disconnected from the rest of the book.

Genomics and Clinical Medicine could be used during the first or second year of medical school to provide an underpinning of genomics as a unifying theme to the diverse array of topics that are typically taught at this time. Basic researchers and curious clinicians will also find a lot to learn and perhaps build on. But this is a transitional

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book that has appeared before a genomics mindset has been assimilated as a new way to teach and practice medicine.

In contrast, Moyra Smith, the author of *Translational Research in Genetics and Genomics*, takes for granted that we are already living in the genome era and proceeds to explain how various genomic mechanisms and phenomena are involved in the causes of disease and how this knowledge can lead to new treatments and means of diagnosis. The scope of this book is almost as broad as that of *Genomics and Clinical Medicine* but obviously less detailed, excluding historical topics and descriptions of technology and focusing instead on concepts and carefully selected examples of genomic pathophysiology and therapeutic approaches. The writing style is economical, resulting in a scant 178 pages of text that can be read in a single sitting. Most chapters begin with a short but effective introduction to essential definitions, concepts, and facts, and then quickly proceed to a number of specific diseases — illustrating the causal, diagnostic, or therapeutic relevance of the underlying genomics. Diseases are organized not according to traditional subspecialties but rather according to the underlying genetic or genomic mechanisms. This book is not for beginners but could profitably be read by a wide range of people, from advanced graduate students in the life sciences to heads of pharmaceutical research and development organizations. References for further exploration are carefully selected and are usually very recent publications.

In conclusion, these two books complement each other. However, readers most likely will still want some biomedical informatics tools, experience, and access to fully appreciate the potential power of genomic and translational medicine.

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MICROCOSM: *E. COLI* AND THE NEW SCIENCE OF LIFE

By Carl Zimmer. 243 pp. New York, Pantheon, 2008. $25.95.
ISBN 978-0-375-42430-4.

DID YOU KNOW THAT CORN ORIGINATED from weedy teosinte? Or that long before he became the first president of Israel, Chaim Weizmann worked as a biotechnologist in England, where he discovered bacteria that are capable of manufacturing acetone, an ingredient in explosives? Did you know that Jonathan Beckwith, a biologist at Harvard University, was the first person to isolate a gene? Or that cheese is traditionally made by spiking milk with rennet, an enzyme that is produced in the stomachs of cows? Or that the Industrial Revolution would probably never have happened if the threads of nuts and bolts had not been standardized in the mid-1800s? I didn't know these things. Nor did I know that the active ingredient in Roundup herbicide products is a glyphosate that was discovered by the Monsanto Company in the early 1970s, or that every year, an estimated 15 boulders from Mars crash into Earth. I learned all these things by reading Carl Zimmer's *Microcosm*, a treasure trove of such trivia.

Color-Enhanced Transmission Electron Micrograph of *Escherichia coli* O157:H7, Showing Flagella.

Courtesy of the Centers for Disease Control and Prevention/Elizabeth H. White, M.S.

Microcosm is also a biography of the bacterium *Escherichia coli* and an omnibus of anatomy, physiology, microbiology, molecular biology, epidemiology, therapeutics, evolution, astronomy, history, and biotechnology. It is a book of metaphors — those given to anthropomorphic characteriza-

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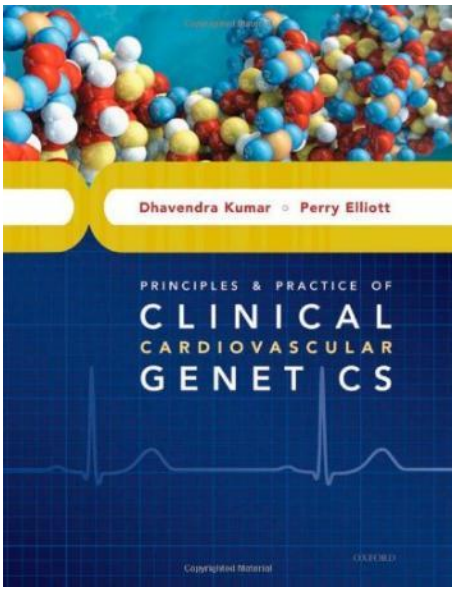
3. **"Principles and Practice of Clinical cardiovascular genetics", Oxford Univ. Press, New York, 2010**



Consisting of contributions from experts in all specialties of cardiovascular genetics and applied clinical cardiology, Principles and Practice of Clinical Cardiovascular Genetics serves as the comprehensive volume for any clinician or resident in cardiology and genetics. Each chapter provides a detailed and comprehensive account on the molecular genetics and clinical practice related to specific disorders or groups of disorders, including Marfan syndrome, thoracic and abdominal aortic aneurysms, hypertrophic, dilated and restrictive cardiomyopathies and arrhythmogenic right ventricular cardiomyopathy, and many other forms of inherited heart muscle disorders.

All sections comprehensively address cardiovascular genetic disorders, beginning with an introduction and including separate sections on the disease's basic biological aspects, specific genetic mechanisms or issues, clinical aspects, genetic management (e.g., genetic diagnosis, risk assessment, genetic counselling, genetic testing), and clinical management issues. The final section exclusively addresses the management of cardiovascular genetic disorders, specifically considering stem cell therapy, genetic counselling, pharmacogenomics and the social and ethical issues surrounding disease treatment.

Review:

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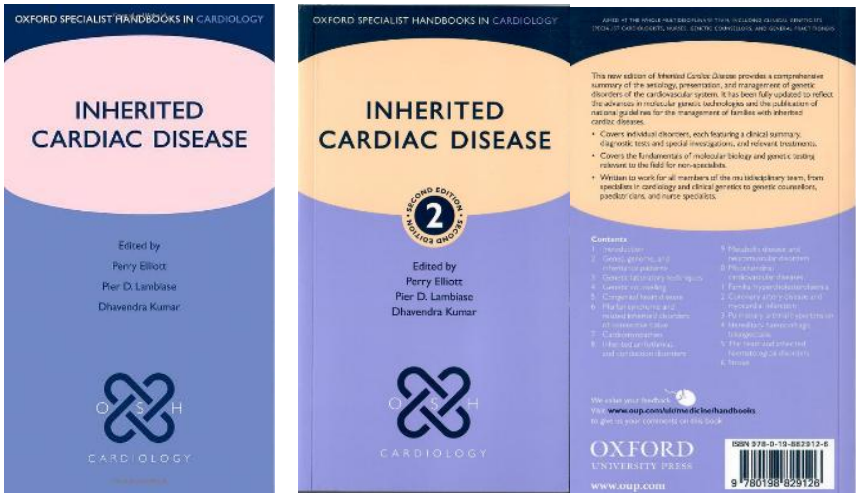
abdominal aortic aneurysms, hypertrophic, dilated and restrictive cardiomyopathies and Arrhythmogenic right ventricular cardiomyopathy, as well as many others. All sections comprehensively address cardiovasuclar genetic disorders, beginning with an introduction and including separate sections on the disease's basic biological aspects, specific genetic mechanisms or issues, clinical aspects, genetic management (e.g., genetic diagnosis, risk assessment, genetic counseling, genetic testing), and clinical management issues. The final section exclusively addresses the management of cardiovascular genetic disorders, specifically considering stem cell therapy, genetic counseling, pharmacogenomics and the social and ethical issues surrounding disease treatment.

Lehmans Media, Denmark

4. "Oxford Handbook of Inherited Cardiac Disease", Oxford Univ. Press, Oxford, 2011
2nd Ed. 2020



Containing summaries of inherited cardiovascular disorders with a focus on aetiology, presentation and management, this handbook covers the fundamentals of molecular biology and genetic testing, and the detailed clinical information relevant to patient management.

This handbook is widely popular among busy clinical cardiologists, cardiology and clinical genetics trainees, cardiac nurses and genetic counsellors. Recommended by the British Cardiovascular Society and Nominated for the Best BMA Medical Book Award for 2013.

The second edition (published November 2020) is fully revised with new text and illustrations.

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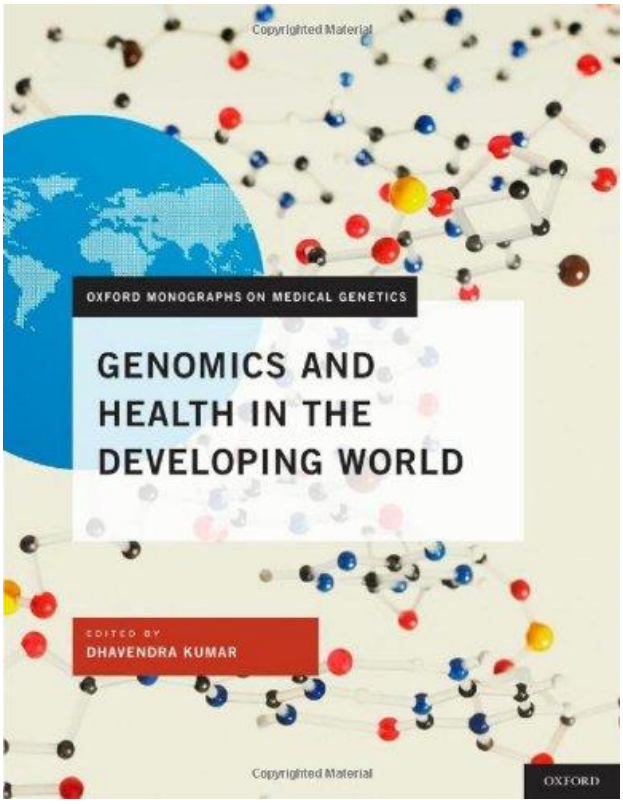

This large multi-author edited reference book provides detailed and comprehensive coverage of population structures, human genomics, and genome variation--with particular emphasis on medical and health issues in the emerging economies and countries of the developing world. With sections dedicated to fundamental aspects of genetics and genomics, epidemiology of human disease, biomarkers, comparative genomics, developments in translational genomic medicine, current and future health strategies related to genetic disease, and pertinent legislative and social factors, this volume highlights the importance of utilizing genetics/genomics knowledge to promote and achieve optimal health in the developing world.

Grouped by geographic region, the chapters in this volume address: - Inherited disorders in the developing world, including a thorough look at genetic disorders in minority groups of every continent - The progress of diagnostic laboratory genetic testing, prenatal screening, and genetic counselling worldwide - Rising ethical and legal concerns of medical genetics in the developing world - Social, cultural, and religious issues related to genetic diseases across continents. Both timely and vastly informative, this book is a unique and comprehensive resource for geneticists, clinicians, and public health professionals interested in the social, ethical, economic, and legal matters associated with medical genetics in the developing world.

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Reviews:

Genomics and Health in the Developing World provides detailed and comprehensive coverage of population structures, human genomics, and genome variation - with particular emphasis on medical and health issues - in the emerging economies and countries of the developing world. With sections dedicated to fundamentals of genetics and genomics, epidemiology of human disease, biomarkers, comparative genomics, developments in translational genomic medicine, current and future health strategies related to genetic disease, and pertinent legislative and social factors, this volume highlights the importance of utilizing genetics/genomics knowledge to promote and achieve optimal health in the developing world. Grouped by geographic region, the chapters in this volume address:
- Inherited disorders in the developing world, including a thorough look at genetic disorders in minority groups of every continent
- The progress of diagnostic laboratory genetic testing, prenatal screening, and genetic counseling worldwide
- Rising ethical and legal concerns of medical genetics in the developing world
- Social, cultural, and religious issues related to genetic diseases across continents
Both timely and vastly informative, this book is a unique and comprehensive resource for genetists, clinicians, and public health professionals interested in the social, ethical, economic, and legal matters associated with medical genetics in the developing world.

BOOK REVIEW

AMERICAN JOURNAL OF medical genetics PART A

GENOMICS AND HEALTH IN THE DEVELOPING WORLD. Edited by Prof. Dhavendra Kumar. ISBN13: 9780195374759, ISBN10: 0195374754.

How to Cite this Article:
Zahir FR. 2013. Book Review.
Am J Med Genet Part A 161A:1203–1206.

INTENTION AND SCOPE

This impressive compilation is the first of its kind in terms of scope and breadth. Edited by Prof. Dhavendra Kumar and published as part of the Oxford Monographs on Medical Genetics series, it provides a much needed overview of the state of genomics in the so called "developing world." Dr. Kumar, who has dedicated this work "*to millions of people in the developing world who live with poverty, hunger and disease,*" has certainly manifested a valiant effort to serve this demographic, which constitutes the majority of the world population (82%, 2009 UN estimates). Genomics is a relatively young branch of science that is currently undergoing rapid advance and transformation. From being a cutting edge science affordable only to high income countries and amenable to use by a few highly trained individuals, the rapid fall in cost of several genomics technologies (notably sequencing) coupled to an increase in training is making genomics services increasingly available to low and middle income (LMIC) countries. This has led to initiatives incorporating genomics and genetics services in both health and populations studies during the past decade in many LMIC countries. However, current publication trends tend to disfavor dissemination of scientific and medical epidemiological data from LMIC countries at most top ranked journals. Dr. Kumar's work steps in as a focused platform to highlight important reports from LMIC countries in this regard, not just in research but also in documenting trends in implementation of genomics, especially in the health care sector. Having said that, the text also collects several relevant studies from LMIC countries that have been published in world class journals, thereby it succeeds in portraying a truly rounded picture.

STRUCTURE AND CONTRIBUTORS

The book is organized as two main parts; part 1 gives a general overview of genomics and medicine in health, but with a distinct developing world flavor. Part 2 is a collection of chapters that discuss more specific genomics and health issues that are organized according to the following regions, Africa, Arab and Middle East, Asia-Pacific, Chinese Subcontinent, Indian Subcontinent, Latin America and the Caribbean and finally Russia, central Asia and Europe. This organization scheme is a definite strength as it aptly indicates the rich compendium of information contained therein. The reader is at once drawn to the chapter titles under each global region and the number of these as well as the breadth of information covered by them gives an initial taste of the current regional situation. However, what is also apparent is that there is an over-representation from some countries in a given region over others, which may be an indicator of the country-wise distribution and availability of genomics services rather than non-inclusion in this text. For example, of the 18 chapters included under "Africa," 1/3rd are specifically focused on South Africa, and apart from a single other chapter on Tunisia (chapter "Genetic neurological diseases in Tunisia"), the others discuss areas that encompass more than one, often several African countries. If this is indeed the case, it is surprising that there are relatively few chapters from the Chinese subcontinent (6) compared to the Indian subcontinent (26), as one would expect more genomics applications currently in China. The Indian subcontinent includes several more countries than the Chinese subcontinent and this may be a reason to explain the imbalance, or conversely the over-representation of information from India may indeed indicate the recent move by the Indian government to focus on science and technology research (http://articles.timesofindia.indiatimes.com/2012-08-11/india/33152919_1_private-sector-health-sector-12th-plan). While some comment on these issues by the editor would have been useful in the foreword, the massive effort in collating and organizing all this information is nothing but praise worthy. The availability of selected color figures as a series of color plates located in the middle of the book is welcome as in some cases the color is essential to understand the figure (Figs. 4 and 5, population admixture principal component analysis plots), though the placement of them ex situ is cumbersome. The index is a very useful addition that feels adequate for this edition, however not all topics are completely referenced. The list of contributors is impressive, truly a snapshot of experts in genomics in the developing world. While the designation of each contributor is listed at the beginning of the book, a little more information explaining the role of

Grant sponsor: Canadian Institutes of Health Research; Grant sponsor: NeuroDevNet Canadian National Center of Excellence; Grant sponsor: University of British Columbia Bluma Tischler Award.
Article first published online in Wiley Online Library (wileyonlinelibrary.com): 5 March 2013
DOI 10.1002/ajmg.a.35750

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the contributor in that country, especially if given as a footnote in the chapter itself, would be very useful to situate the reader.

THEMES

Two major themes are found in the book, both of them fascinating due to their LMIC perspective. They are; genomics in individual health (including ethical, legal, and social aspects as well as clinical), and population genetics (including ancestry, ethnic genetic make-up, and population admixture, as well as genetic epidemiology). The book contains a number of chapters that address specific areas of these foci singly or together. It raises various discussion points, some of which I will elaborate on below.

A significant number of chapters talk to the high level of consanguinity generally found in LMIC countries and then specifically discuss several medical genetics issues that arise due to this. Indeed, the reports on the extent of consanguinity to be found in the developing world are particularly noteworthy. The numbers presented are eye-openers that serve to establish in the reader's mind the high degree of prevalence for consanguinity in non-industrialized nations (*vide* chapter 80). This is important information as it directs a rethink of several standards (which are for the most part developed by industrialized nations) in clinical genetic practice as well as genomic study design and analyses when applying them to the developing world. The same is true for developed nations where there are large pockets of immigrant populations from LMIC countries. In this regard, noteworthy is the discussion of the results of several surveys assessing families understanding of the health implications of inter-marriage (*vide* chapters 121, 122, and 123) carried out among migrant communities in the UK in which there is a high degree of consanguinity. Approaches that must be incorporated in genetic counseling are discussed and a new sensitivity to the reasons for this wide-spread practice rather than an across the board condemnation are encouraged. Raising awareness of this issue and educating about the reasons behind the practice are especially a useful contribution with wide reaching impact.

A notable focus in the book, one that is closely tied to consanguinity (as consanguinity is widely practiced in Muslim countries), is the discussion of Muslim perspectives to modern genetic and genomic methods such as, for example, population genetic screening, pre-implantation genetic diagnosis, and therapeutic abortion. Following on her impactful publication a few years ago [Al Aqeel, 2007] Aida Aqeel provides a well-researched and detailed chapter on Muslim views on these issues (chapter 9). However others too, in particular contributors in countries with significant Muslim populations, comment on these areas. Most North African states as well as many in the Sub-Sahara region of Africa, several Central Asian, and South East Asian nations as well as many countries in South Asia have majority Muslim populations. India and China (which together include about 35% of the world population), both include large Muslim minorities which numerically dwarf populations of other whole countries. A recent poll by the Pew Research institute corroborates the indication that a significant proportion of the developing world follows some degree of Islamic belief or practice (http://www.pewforum.org/Muslim/the-worlds-muslims-unity-and-diversity-executive-summary.aspx). Given this, the focus on addressing genetics and genomics from the Muslim perspective is relevant. The frank discussion and depth of pertinent information shared in this regard is a particular strength of the book. However one encounters conflicting statements on Islamic religo-legal exegeses (loosely termed "shariah practices") that influence key genetic questions presented by different contributors; for example there is a difference of opinion on up to what stage of pregnancy it is Islamically permissible to abort (a complex issue with a sophisticated "shariah" handling) indicated in different chapters. A greater degree of academic rigour is called for when discussing such topics with adequate reference to religious scholarly opinions mandated or at least encouraged by the contributors. In this situation a poorly informed opinion may be as damaging as a non-informed opinion. This observation extends to other faith systems as well; for example in chapter 8, there is a discussion on the influence of religion on social practice in South Asia. This topic is an important one for the clinician encountering these populations, and its inclusion is lauded, however the discussion contains many generalizations without reference, a situation that could be quite misleading.

Another interesting area of information presented relates to nutrition practices in the developing world and traditional forms of medicine (which include diet as a significant medicinal component of health). In particular, reports on regional attempts to study traditional medical systems from a genomics angle, such as the "Ayurgenomics" (chapter 76) which uses genomics to understand Ayurvedic medicine, as well as similar efforts to better characterize Traditional Chinese medicinal practices, such as studies to understand "herb–drug" interactions that could possibly have adverse effects, are important. Information in these chapters will be useful in the developed world as well, which has witnessed a surge in popularity of ancient medical and nutritional systems in the past decade.

The second major theme-population genetics, is covered by many chapters offering a wealth of information. The Human Variome Project is discussed with specific reference to LMIC countries. Prof. Kumar's chapter (the genomic map of population diversity in Asia) in part 1 is remarkable for the extent of information it holds; especially interesting are details from the HUGO pan Asian SNP consortium's analyses on geophysical and linguistic categories of Asiatic peoples as well other expert opinion condensed in this chapter. Several chapters with country and sub-region specific population genetic information are found in part 2, especially with respect to epidemiological data. Some of these chapters include information particularly hard to normally locate, such as, for example, epidemiological information from the south Atlantic oceanic islands. Several chapters report studies on genetic population diversity. The majority of these are contributed by researchers in Latin America and Russia. While many of these chapters do reproduce published studies, the collection of them in one volume lends cumulative weight to furthering understanding of global population genetic trends and reading them together paints a fascinating picture in broad strokes of the human migratory picture. The present day developing

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world contains peoples who are descendants of the world's oldest recorded civilization, viz, the Indus valley civilization, the Yellow river civilization, those of the Lavant, Mesopotamia, etc. It is valuable to have a compendium of more detailed genetic studies of population diversity from these regions, over the current information generated by countries with relatively young populations, despite their best efforts to capture global population diversity by extension of their data. The extent of ethnic variation documented serves to emphasize the excessive population diversity present in the developing world, what may be another important "eye-opener" for most readers not familiar with the rich human diversity existing out of the "western" world. The many chapters dealing with genetic epidemiology and population diversity are complimentary and combine to offer a taste for the many ethno-specific genetic disease signatures that are, or may soon become apparent.

Apart from these main two themes, another area of notable focus is capacity building and development of genetics and genomics institutes at a national and region level. Both part 1 and part 2 contain several chapters discussing current LMIC countries' progress in this respect. These chapters are vital as a shared resource and will certainly be very beneficial to readers from LMIC countries. However this information is often buried within a chapter that broadly overviews the status of genomics within a country and requires a careful reading to unearth. Capacity building is often discussed with respect to offering newborn screening programs at the national level—a service gaining importance in the developing world as more is understood about region-specific disease burden. The shift towards a knowledge based economy by the oil-rich nations of the Middle East, in particular Saudi Arabia is interesting reading, on which note this reviewer must comment on the suitability of including Saudi Arabia among the LMIC nations. The discussion of challenges that LMIC countries face and are likely to face as they enter the genomics era by a few key contributors is an important addition. In addition to well-known experts in global genomic medicine based in the developed world, key contributions are made by experts who are based in LMIC nations addressing their home state. These latter chapters are perhaps more relevant as their voice can be considered more authentic. However again, they tend to be buried in large "state of the nation" chapters found in part 2 and are more difficult to locate.

POINTS FOR IMPROVEMENT

As with any work of such lofty aim there are several areas for improvement. One that is immediately obvious is the prohibitive size and weight of the volume. While no true seeker of knowledge should be fazed by how unwieldy the work is, the practical matter remains that it is not an easy tome to carry around. The contribution to the weight is not by any unnecessary formatting points such as large margins or empty pages, but by the simple fact of the many numbers of chapters and the lengths of each of these. A more thorough editing by the contributors themselves so that only pertinent information is succinctly summarized or by the editor to ensure no redundancy among different contributions may have reduced the size somewhat. Another solution might have been to include more material in the accompanying CD (although this avenue may give rise to significant copyright concerns given the nature of the work). Having said that, it is recognized this is a first compilation with a very broad scope and its size must be balanced by the wealth of information contained. The book is certainly an excellent library reference or useful addition to one's bookshelf. Another concern is the redundancy of some material, and sometimes conflicting data presented by different authors on the same issue as noted prior. The latter is a more serious issue and should be addressed by editorial remarks. However in relative terms this does not occur often but it is something to be aware of and the reader will need to make sure he or she reads all the chapters pertaining to a topic rather than only one, before forming an opinion on key issues. Finally the other significant limitation inherent in a work of this nature is the fact that it presents a static picture of a very dynamic field. This "developing world snapshot" as it were, may soon become outdated as the plummeting costs of genomics technologies is bringing about a very rapid transition of these technologies into the developing world. Several chapters that present a country-wide overview of genomics may soon need to be re-written. In this respect a more focused second volume that is smaller in size will certainly be appreciated and it is hoped the editors of the series have this in mind. A brief mention must be made on the appropriateness of the use of the term "developing world" as opposed to using "LMIC" which is gaining currency as being a more accurate and less demeaning descriptor in the title and throughout the text. While this reviewer prefers the latter she does not want to be pedantic, however does suggest some thought should be spent on terminology in future editions.

SUMMARY

In conclusion, this volume is certainly a first of its kind shining a much needed light on the developing world in this genomics era. While the volume can certainly be improved upon, in terms of sheer breadth and depth it is quite extraordinary. This work will be a "must have" reference for anyone interested in genomics beyond the industrialized world. It offers many pointers to tailor genetic counseling and other clinical genetic services to practitioners in the industrialized world as these countries now contain significant immigrant communities who have for the most part come from the developing world. Coupled to this, the high degree of consanguinity in the developing world means that there is a higher risk of genetic disease that will result in more and more referrals to medical genetics services. Therefore for the medical genetics professional in both the developed as well as the developing world, the book will serve as good background reading. The book will be essential reading for those engaged in teaching of genomics global applications. However at 250$ it may be out of the reach of many in the countries it sets out to serve. The fact that such a volume was conceived, edited, and published is laudatory. The main intention of the book is to provide an overview of genomics in the developing world, dealing with the "*issues and challenges for the emerging economies of the developing world in confronting the rapid advances*

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of genome science and technology." The work has accomplished what it set out to do to a large extent, a remarkable feat by itself but one that is all the more valuable as it serves to highlight the state of genomics that pertains to the vast majority of the world's population.

ACKNOWLEDGMENTS

F.R.Z. is supported by a CIHR (Canadian Institutes of Health Research) postdoctoral fellowship, a NeuroDevNet (a Canadian National Center of Excellence) award, and by the University of British Columbia Bluma Tischler award.

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Manuscript Received: 30 September 2012;
Manuscript Accepted: 11 October 2012

15:52:48 PM, 2015, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/ajmg.a.35?

6.'Genomic and Molecular Medicine', Morgan and Claypool, USA (2012-2018)

The '**Genomic and Molecular Medicine'** is the e-book series designed and edited by Professor Kumar. The Morgan and Claypool Life Sciences Publishers have published it as the Colloquium Lecture series. It includes several articles (monographs) on selected subjects written by top experts on the subject. The series is designed, developed and edited by the Author of the article 'The Molecular Biology of Chronic Heart Failure'. The other titles include Molecular Pathology of Stroke, Molecular heterogeneity in Neurofibromatosis Type1, Motor Neurone Disease, Genetic Perspectives of Sudden Cardiac Death in Sports and Osteogenesis Imperfecta. So far, the series includes nine monographs dealing with common genetic diseases encountered in clinical practice. Full series is published as the Colloquium Lecture Series.

6.1 Achondroplasia and Other FGFR3-related Short Limbed Dysplasia: Molecular Heterogeneity and Therapeutic Approaches
Sanjeeva G N, Meenakshi Bhat
2018; Abstract | PDF (14028 KB) | PDF Plus (1696 KB)

6.2 Clinical and Molecular Heterogeneity of Osteogenesis Imperfecta
Meena Balasubramanian
January 2017Abstract | PDF (2917 KB) | PDF Plus (1153 KB)

6.3 Molecular Genetics of Thalassemia Syndromes
Reena Das, Prashant Sharma
August 2016 Abstract | PDF (6210 KB) | PDF Plus (1593 KB)

6.4 Molecular Basis of Developmental Anomalies of the Human Gastrointestinal Tract
Charles Shaw-Smith
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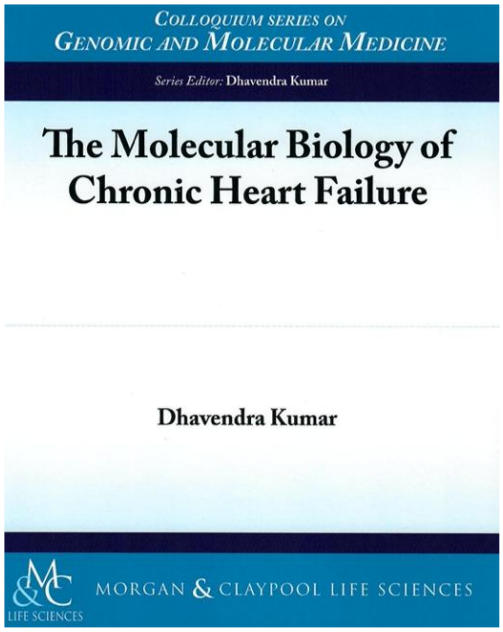
6.5 The Molecular Biology of Neurofibromatosis Type 1
Meena Upadhyaya
February 2014 Abstract | PDF (1886 KB) | PDF Plus (816 KB)

6.6 Clinical and Molecular Aspects of Motor Neuron Disease
Johnathan Cooper-Knock, Thomas Jenkins, Pamela J. Shaw
September 2013 Abstract | PDF (4370 KB) | PDF Plus (813 KB)

6.7 The Molecular Biology of Chronic Heart Failure
Dhavendra Kumar
February 2013 Abstract | PDF (5841 KB) | PDF Plus (1518 KB)



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CHAPTER 1

Introduction

Even before the idea for the Human Genome Project was conceived and debated, the concept of association of complex and heterogeneous phenotypes with many genes and related genetic variants had established its place in basic and applied biomedical science. Extensive data and information are now available on the public domain derived from a number of genetic studies on several common and uncommon phenotypes including chronic heart failure (CHF) (PubMed/OMIM). Following the completion of the Human Genome Project, rapid and continued advances in genomic profiling and basic molecular insights have led to a more complete and in-depth revelation of interactions between genes, genomic elements, environment, and affected tissues and organs (Morita, Seidman et al. 2005; Margulies, Bednarik et al. 2009). This has led to a comprehensive understanding of biological mechanisms underlying pathological changes within organs and tissues affected by complex and heterogeneous conditions like heart failure (HF). Two major themes have emerged from these studies—the patients' genetic endowment and the transcriptional changes within the target organ and tissue. Recent studies (MacRae 2010; Velagaleti RS 2010) provide new insights into the mechanisms contributing to the structural changes of the heart and the development of HF. New technological advances have enabled to characterize the patients' genotype and markers of gene expression in detail propelling to new diagnostic and therapeutic opportunities for HF patients (Braunwald 2008; Chaanine, Kalman et al. 2010). In this context, this review focuses on major genetic and genomic aspects of HF highlighting contemporary efforts to achieve greater personalization of prevention and treatment strategies to meet with the challenges of a growing HF epidemic.

6.8 Clinical and Genetic Aspects of Sudden Cardiac Death in the Practice of Sports Medicine

Lynne Millar, Nabeel Sheikh, Sanjay Sharma

June 2012 Abstract | PDF (30425 KB) | PDF Plus (4564 KB)

6.9 Molecular Genetics of Stroke

Yoshiji Yamada

March 2012 Abstract | PDF (5978 KB) | PDF Plus (1333 KB)

7. **"Genomic Medicine- Principles and Practice", Oxford Monographs on Medical Genetics, Oxford University Press, New York, USA, December 2014.**

The first edition of Genomics and Clinical Medicine provided an overview of genomics-based advances in disease susceptibility, diagnosis, and prediction of treatment outcomes in various areas of medicine. Since its publication, the science of genomics has made tremendous progress, and exciting new developments in biotechnology and bioinformatics have created possibilities that were inconceivable only a few years ago. This completely revised second edition of Genomic Medicine reflects the rapidly changing face of applied and translational genomics in the medical and health context and provides a comprehensive coverage of principles of genetics and genomics relevant to the practice of medicine. The first section lays foundation to the practice of genomic medicine. New chapters in this section include bioinformatics, proteomics, microbial genomics and genomic education. Detailed discussions of genetic/genomic testing and screening and the ethical, legal, and social issues (ELSI) crucially address genethics and genomethics in the practice of Genomic Medicine. The second section includes clinical practice oriented chapters highlighting genomic applications (array comparative genomic hybridization, exome genome sequencing and new generation generation sequencing) in clinical diagnosis of congenital developmental malformations, Mendelian genetic disorders, and complex cardiovascular, neuro-psychiatric, ophthalmic, dermatologic, inflammatory and paediatric disorders. Separate chapters discuss microbial genomics with emphasis on the role of genomics in targeted antimicrobial therapy and development of genomic class of new vaccines. New developments in gene/ cell-based somatic therapy, regenerative medicine and targeted molecular therapy are discussed in respective chapters. All chapters are thoroughly indexed and supported by a carefully compiled glossary relevant to genetic and genomic medicine.

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Review:

Hum Genet (2015) 134:927; DOI 10.1007/s00439-015-1569-y

BOOK REVIEW

Dhavendra Kumar and Charis Eng (eds): Genomic Medicine: Principles and Practice (Oxford Monographs on Medical Genetics) 2nd Edition

Hardcover, 24 October 2014, 852 Pages ISBN: 9780199896028, $195.00 John Christodoulou[1,2]

Published online: 26 May 2015
© Springer-Verlag Berlin Heidelberg 2015

Since the publication of the first edition of this book in 2008, much has progressed in the field of medical genom- ics. We have seen the cost of genomic sequencing plummet, with the prediction of the $1000 genome by 2018 being met well in advance of that target, and a doubling of the number of genes identified as the basis of inherited disor- ders. This edition has undergone extensive revisions, with the new content reflecting just how much genomic technol- ogies are now influencing all aspects of medical practice.

A stellar group of authors with deep practical experience in what the technology has to offer have been assembled to produce this volume, which is divided into two broad sec- tions. The first section covers the broad principles of genomic medicine, bringing the novice up to speed on the structure of the human genome and its anatomy, and giving general overviews relating to a number of the key components of the “omic” puzzle including proteomics, epigenomics and the mitochondrial genome. In addition, there is a synopsis of developmental biology, as well as topics relating to environ- mental contributors to human health and disease including microbial genomics and nutritional genomics, and chapters providing outlines of how genomic technologies have helped advance the development of new drugs, and how genomic variation impacts on responses to drug, critical knowledge in this era of personalized and precision medicine.

The second and larger section of this book, aptly entitled Clinical Genomics, focuses on how genomic technologies are impacting on complex disorders, offering a number of chapters that are each focused on individual organ or tissue systems, as well as covering the impact of clinical genom- ics on cancer, infectious diseases, pediatric medicine and critical care medicine.

This book is well written and practical, but given the wide-ranging scope of the topics covered, of necessity only a helicopter view of the current state of genomic sci- ence could be presented. It is well placed to be a general resource for medical students, and medical and science graduates who are not expert in the fields of medical genet- ics and genomics.

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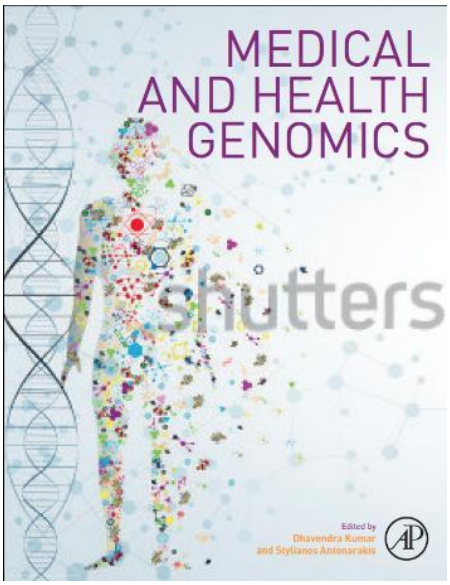
8. "**Medical and Health Genomics", Edited by Professors Dhavendra Kumar & Stylianos Antonarakis (Department of Medical Genetics, Univ. of Geneva, Swiss), Elsevier Publishers, The Netherlands; May 2016**



A multi-author edited textbook on wide ranging applications of genome sciences and technologies in contemporary and future practice of medicine and health. Major subjects covered in the book include 'Genomic technologies in medicine and health- past, present and future', Genomic databases and data mining- relevance to clinical medicine and public health, Genomics, Bioinformatics and Systems medicine, Epigenetics and Epigenomics, Pharmacogenomics, Metabolomics, Metagenomics/ Ecogenomics and Microbial genomics & Pathogenomics.

*Medical and Health Genomic*s provides concise and evidence-based technical and practical information on the applied and translational aspects of genome sciences and the technologies related to non-clinical medicine and public health. Coverage is based on evolving paradigms of genomic medicine—in particular, the relation to public and population health genomics now being rapidly incorporated in health management and administration, with further implications for clinical population and disease management.

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This book received the 'Highly Commended' certificate at the 'BMA Annual Medical Book Award 2017'

Book Review

Foreword

Although inherited diseases in man have been known since biblical times, and the first clear scientific descriptions of genetic disorders by Garrod and others date back to the early years of the 20th century, genetics was only introduced into regular medical practice with the advent of genetic counseling clinics in several countries, about 40 or 50 years ago. The discovery, in 1959, that Down syndrome was caused by a chromosome abnormality was an enormous step toward recognition that laboratory-based genetics had a role to play in medicine. In the early 1970s, few members of the public (or of the health professions) had heard of genetics and it was considered pretty irrelevant to healthcare practice.

The change since then has been astonishing. Genetics and genomics are now fully on the radar of most practicing physicians, researchers, and health managers, as well as journalists (who enjoy exaggerating the expected rate of progress) and politicians (who are commonly enthusiastic and sometimes surprisingly well informed). There can no longer be any doubt that the inherited components of disease are firmly embedded in medical practice and popular culture. When I say at parties that I am a medical geneticist, people more often look interested than mystified and bored.

Although it is true that much of this change has been driven by advancing technology, that is an oversimplification. The single biggest event was the sequencing of the human genome. That achievement and the decision of those involved to make their data freely available to all others, in academia and in industry, at an early stage of the research process, were transformative. Its echoes have completely changed not only medical research, but also anthropology, agriculture, and even historical research—witness the use of mitochondrial sequencing to confirm the identity of King Richard III several 100 years after his burial.

But the technology that we now enjoy was not there when the Human Genome Project started, and arguably would not be there today without that initiative. At the time, the genome project was an act of scientific imagination; a few people with extraordinary vision were able to see, long before most others and against a significant amount of scientific and public opposition, the immense value such sequence information would be. The technology was not confined to sequencing methodologies. The volume of data generated could not have been handled without commensurate improvements in computer hardware and software. Today it is arguable that the real block to understanding genetics and applying it clinically has more to do with our inability to understand and manage the vast amounts of data being generated, than to a need for better and cheaper sequencing.

Despite this meteoric progress, there is still actually rather little that modern genetics can do in the clinic, outside of defining the molecular basis of rare inherited disorders. But, particularly in cancer studies, that is changing rapidly. It is now very likely indeed that, despite all the previous overoptimistic statements that failed to materialize, genetics will pay big health dividends within a modest period of time. We can see it happening around us, eg, in new targeted cancer therapies. It is very exciting indeed.

Since the completion of the human genome sequence and rapid advances in genomic diagnostic methods, many avenues for diagnostic, therapeutic, and preventative intervention have emerged with promising medical and health applications. Those working in public and population health are considering many aspects of genomics for improving population health, particularly for the benefit of less developed or developing nations. Many national and international genetic and genomic communities and organizations are now actively engaged in furthering these objectives.

Against that background, this new book could not be better timed. It reviews many aspects of the field, and tries to help both professionals and interested observers to understand some of the core principles and complexities. Contributions from a distinguished group of authors, led by experienced and professional medical geneticists, provide an excellent resource of information. I am confident it will be of great value.

Martin Bobrow
Cambridge, England, August 2015

Preface

GENOMIC MEDICINE AND HEALTHCARE

In any sociocultural and geographic setting the provision of medical and healthcare are dependent upon several factors, including societal, financial, and political denominators. However, in the background of all these factors, the fact remains that peoples for whom any medical and healthcare system is aimed for are fundamentally different. The physical and psychological variation of the majority and minority population groups in any society or country determine the outcomes of medical and healthcare provision, however basic or sophisticated. Assessing human variation solely for the purposes of assessing the outcomes of medicine and healthcare practices would require many different approaches. Many such approaches include conventional anthropological and sociocultural variables. Since the discovery of the ABO, Rhesus, and other blood group systems in the early 20th century, the human variation has been assessed using a number of different biomarkers. However, despite many years' work and enormous data, a meaningful and scientific plausible correlation has not been possible. Following the Human Genome Project and the subsequent sequencing of thousands of individual human genomes, and the discovery of the extensive genomic variation and individuality, a major paradigm shift is taking place with considerable impact on the nature and pattern of medicine and healthcare. The people and the society at large have high expectations from the genomic-led contemporary and future medical and healthcare practices. There are huge expectations and hype surrounding the idea of genomic medicine (also known as *personalized/precision medicine*), which is based on the individual genomic variation. We are probably not fully prepared for this; there is a lot more to be learned and accomplished before the society and medical/health professions could offer genomic healthcare with robust scientific confidence while making this efficient and cost-effective.

Genetic and genomic variation among peoples and population groups are one of the many variables that influence the outcomes of any medical and healthcare practice. This needs to be linked with the specific "gene–molecule" systems that operate at the cell and tissue levels. Following the successes of clinical genetics, along with related genetic laboratory techniques, a number of specific genetic diseases (chromosomal, single gene, and rare genetic syndromes) are now causally linked to pathogenic changes in many genes and molecules that operate in conjunction with many other biological systems. Some of these rare conditions result from specific mutations or pathogenic sequence variation within one particular gene or loss of function of other genes that belong to a multigene family encoding many peptides with overlapping structural similarity and physiological functions. Examples include transcription factors, nuclear envelope genes, *RAS-MAPK* genes, *TBX* genes, genes for many inherited metabolic disorders, and a large number of gene–molecule families for sophisticated neuronal functions. Equipped with the knowledge from genetic and molecular advances in uncommon and extremely rare diseases, researchers and clinicians are now looking into solving the molecular complexities of common medical diseases with a considerable heritability. The scientific information from studying specific system and multisystem rare genetic disorders has given us insight to many fundamental molecular biological processes that are not only important for understanding the pathogenesis but also govern the outcomes of specific therapeutic interventions. Thus successful outcomes of genetic and genomic applications in medicine and healthcare practices would be dependent upon understanding the molecular biology of sequential diseases processes and their overall clinical impact governed by individual genomic variation. This is in essence the basis of *medical and health genomics*, rapidly emerging along with the practice of specific genetic and genomic medicine.

In keeping with the many dilemmas and predicaments surrounding the genetic and genomic applications in medicine and healthcare, this new book sets out to collate basic facts and information that could form the core of *genomic (personalized/precision) medicine* and *genomic healthcare*. A number of scientists, clinicians and healthcare professionals have contributed to this high profile work under the broad meaning title of *Medical and Health Genomics*.

The core concepts of human genomics are presented with emphasis on new emerging genomic technologies, burgeoning genomic databases with enormous amount classified and unclassified data, genomic applications, and translations in clinical medicine and public health, particularly the diagnostic genomics and clinical bioinformatics

contributing to deciphering many complex phenotypes, citing the specific example of the model of Victor McKusick's *Online Mendelian Inheritance in Man (OMIM)*.

Some additional areas of particular importance are highlighted, including epigenetics modifications in human health and disease; metabolomics with its many applications; introduction to metagenomics and ecogenomics; wide-ranging applications of microbial genomics in diagnosis, treatment, and prevention of microbial diseases; and the personalized pharmacotherapy based on the genetic variation of each individual (pharmacogenomics).

Medical and health aspects of genetics and genomics are discussed in detail with evidence on the relevance of genome variation in human health and disease. This is further supported by critical information on multidisciplinary medical management using examples of systemic rare genetic diseases, genetic and genomic testing and screening, and genomic perspectives of genetic counseling. The section on personalized and stratified medicine includes information on novel genomics-led drug discovery and development and discussion on novel genomics-led therapeutic approaches. The organization, availability, and harmonization of genetic and genomic healthcare are reviewed with emphasis on medical and health burden of rare genetic diseases, multidisciplinary genetics and genomics-led reproductive healthcare, and common and complex genetic cancer. This section includes a separate chapter on teaching and training genetics/genomics for medical and healthcare professionals. The detailed glossary lists a number of key phrases, definitions, abbreviations, and acronyms that the reader might find useful.

Editors and contributors hope that the book will convey the core concepts of medical and health genomics, highlighting the specialist genomic fields, emphasis on delivery of genetic/genomic medicine and healthcare, drawing attention to specific issues and requirements of human genomics in developing countries and emerging perspectives of human and medical genomics in the context of public and population health.

The society and many people have high hopes and expectations from many recent new developments and progress in human (medical) genomics in the diagnosis and management of both rare and common medical and health problems. These sentiments were echoed by Mr. Anthony Charles Lynton (Tony) Blair, the British Prime Minister, on the occasion of the White House announcement of the completion of the First Survey of the Entire Human Genome Project, broadcast (jointly with the United States President Bill Clinton) on the day of the publication of the first draft of the human genome, "Ever so often in the history of human endeavor, there comes a breakthrough that takes humankind across a frontier into a new era. ... today's announcement is such a breakthrough, a breakthrough that opens the way for massive advancement in the treatment of cancer and hereditary diseases. And that is only the beginning."

We are delighted to present this book at a critical historical phase of genome science, with the new global wave to incorporate strengths and unlimited potential of genomics for much needed advances in healthcare. This is reflected in President Obama's State of the Union address on 30 January, 2015, launching the new United States Precision Medicine initiative, "*To enable a new era of medicine through research, technology, and policies that empower patients, researchers, and providers to work together toward development of individualized treatments*."

Dhavendra Kumar, Cardiff, Wales, UK
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Editors
December 2015

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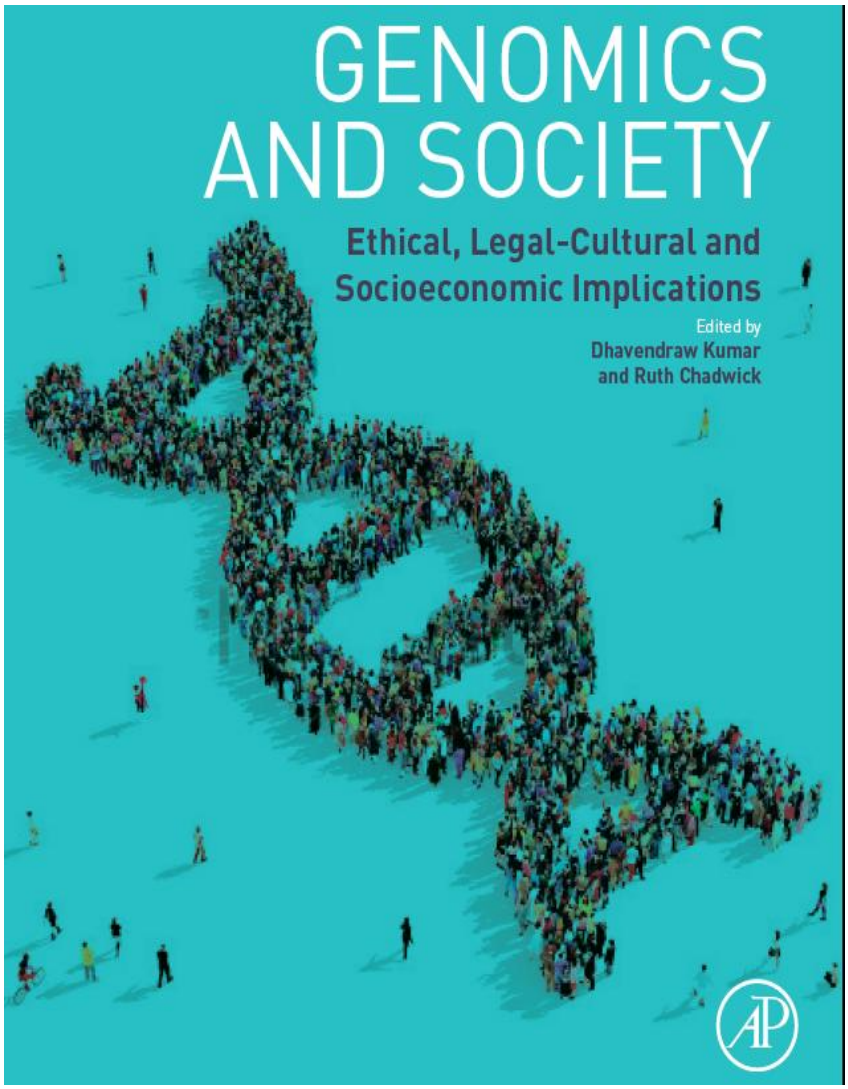
9. **"Genomics and Society", Edited by Professors Dhavendra Kumar & Ruth Chadwick (Department of Law and Bio-Ethics, University of Manchester, UK), Elsevier Publishers, The Netherlands; Published December 2015.**



A multi-author edited textbook on wide ranging applications and impact of genome sciences and technologies on the society and economic developments. Notable chapters include - Ethical issues in health and social genomics; Legal aspects of health applications of genomics; Forensic aspects of genetics and genomics and Human rights, patents and ownership issues related to genomics. Contributors to this new book include key world-class experts on many subjects that are closely related to genomics.

GENOMICS AND SOCIETY

Ethical, Legal, Cultural and Socioeconomic Implications

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Academic Press is an imprint of Elsevier

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PREFACE: INTRODUCTION TO SOCIAL AND ECONOMIC GENOMICS

Towards the end of the twentieth century, several major discoveries and applications in the science of genetics and genomics were achieved. This is evident from the impact of genetics and genomics in many areas notably in biotechnology, bioengineering, and healthcare. The beginning of the twenty-first century witnessed landmark achievements including the sequencing of the human genome and many other biological genomes. This truly led to the commencement of the genome era. Not surprisingly, several researchers and organizations committed themselves with huge resources to advance further basic, applied, and translational research in all areas of genetics and genomics. While the majority of the funded genetics and genomics research and other resources were assigned to molecular biology, biotechnology, and health, a limited number of projects were allocated to study the societal, economic, ethical, moral, and legal implications. Several leading experts and philosophers on economics, bioethics, and law continue to work and advise the genetics and genomics community, politicians, religious, and community workers. This book, conceptualized and led by a medical geneticist and a social and bioethical genetics researcher, reviews and consolidates the outcomes of genetics and genomics in the context of social and economic applications. Here, we briefly indicate the scope of topics covered in this volume.

The introductory chapter sets out how genetics and genomics might impact on the society and life in general with evidence and experience from the applications of electronics and computations sciences citing examples of automobiles, air travel, home appliances, computers, mobile phone, etc. on which all of us have become heavily dependent overcoming many fears and reservations put forward practically at every stage of many new discoveries and developments. In this context, the science of genetics and genomics would be no exception, and we are beginning to harness many benefits in medicine and health, food and agriculture, bioengineering, bioenergy, and ecology. Societal fears and obstacles are more likely to be overcome with rising awareness and acceptance of lay people and community leaders.

A number of ethical and moral concerns, for example, consent, confidentiality, rights to withhold information, etc., are encountered in medical genetic practice. A dedicated chapter examines these issues in the broader societal and health context. Several legal issues might be faced both by the family and health/social practitioner

when dealing with genetic/genomic information. A leading expert discusses existing laws that could be applicable in good genetic/genomic practice with reference to specific jurisdictions.

Forensic applications of genetics and genomics have dramatically changed the legal practice worldwide. The genetic and genomic information for personal identification (DNA finger printing and genomic signature) is routinely used in criminal and immigration matters. Other applications in this context include the use of new genetic tools in dealing with sudden unexplained death including sudden infant death and sudden cardiac death cases. In the wider context, major population level disasters (earthquakes, Tsunami, air crash, terrorist acts, etc.) have also seen benefits of genomic tools (genome sequencing and population-specific genomic databases) in rapid and accurate identification of the victims.

Other issues' reviews in this volume include those related to human rights violation, patents, individual or community ownership, and intellectual property rights of the genetic and genomic information at community and population levels. Like any other new technical and scientific field, adequate and appropriate teaching and training of genetics and genomics is vital for successful health and social applications. Information on several facets used in genetic/genomic teaching and training at various levels is included in this book. Lay people are major consumers of any service or product. A dedicated chapter reviews the various measures undertaken in information sharing, informing, and educating lay people about genetics and genomics.

Globally, several hundred rare diseases are encountered by medical practitioners. Most of these are either inherited or have a known genetic cause. There is a huge burden of these diseases in the context of scarce resources. The current state and efforts made in the multidisciplinary care of patients and family members is critically reviewed with evidence gathered from existing genetic healthcare.

Genomics is rapidly moving into biotechnology and bioeconomy applications with huge sociopolitical impact. The key areas of genomic bioeconomic applications include biosynthetic diesel, new drugs, efficient crop production, and livestock improvement are reviewed with evidence from healthcare, food and nutrition, bioenergy, and ecological balance and improvement.

Developing nations constitute around two-third of the growing global population. Among many hardships and hurdles faced by people in the developing world, health burden is huge. Diseases related to infection, malnutrition, and poverty are common, however, a small but collectively large proportion is due to genetic or inherited diseases. Progress and efforts made by few emerging economies (Brazil, Russia, India, China, and South Africa—BRICS nations) in adopting genomic applications are highlighted. Like any new science, the healthcare applications of genetics and

genomics are no exception facing challenges of traditional and customary health practices. There is data available on genetics and genomics in the context of traditional medical practices in China (traditional Chinese medicine, TCM), India (Ayurveda), and the Arab world (Arabic and Persian system of medicine). Projects like TCM Genomics and Ayurgenomics are funded by China and India, respectively. The evidence from specific areas where genetics/genomics could be applied in indigenous medical practices is presented, particularly on Ayurgenomics. These developments also have a socioethical dimension, in relation to the impact on traditional medical ethics in those areas: for example, implications for how new scientific understandings affect the healer–patient relationship, especially in the context of the expectations of evidence-based medicine.

Each society and cultural group is expected to have firm beliefs and taboos related to health matters, for example, children born with a physical abnormality like orofacial clefts. Examples and information derived from field genetic surveys carried out in tribal groups of China, India, South Africa are presented here. With the rapid advances and new developments in genetics and genomics, a number of leading international agencies have started looking at major issues of regulation, finance, and distribution of genomic applications. The dedicated chapter carries out in depth analysis on the current state of affairs at international level. There is increased awareness and interest on human genomics and global health. The global genomic alliance of major international agencies (Human Genome Organization, HUGO; UNESCO/WHO; Organisation for Economic Cooperation and Development, OECD; Wellcome Trust) and many others are convened aimed at genomic applications for global health, for example, "Global Alliance for Genomics and Health"—*GA4GH*. The charter for GA4GH includes ethical, legal, and social issues apart from setting out ground rules for genomic databases on specific disease conditions and many other genomic applications.

Finally, it is anticipated that the majority of genetic and genomic scientists, healthcare professionals, food and nutrition experts, and biotechnology workforce will remain committed to positive and ethically acceptable gains for the benefit of society and all population groups. However, regrettably there might be a minority who might exploit this science for developing dangerous mutated organisms, harmful plants and crops, and toxic biosynthetic chemicals for act of war, bioterrorism, and socioeconomic chaos. Mahatma Gandhi once said, "That atomic energy though harnessed by American scientists and army men for destructive purposes may be utilized by other scientists for humanitarian purposes is undoubtedly within the realm of possibility. . . . An incendiary uses fire for his destructive and nefarious purpose, a housewife makes daily use of it in preparing nourishing food for mankind." This seminal quote not only refers to the applications of the nuclear science for peaceful purposes, but also

has clear wide ranging implications on many other scientific discoveries and developments notably in genetics and genomics for global social and economic benefits irrespective of any society or nation.

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European Journal of Human Genetics (2016) 24, 1835
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BOOK REVIEW

Genomics for policy makers and for researchers

Genomics and society—Ethical, Legal, Cultural and Socioeconomic Implication
Edited by: Dhavendra Kumar and Ruth Chadwick
ISBN: 9780124201958
Published by: Academic Press. UK, 2016
Price: €48.71/£41.24/$67.46

European Journal of Human Genetics (2016) **24,** 1835; doi:10.1038/ejhg.2016.123; published online 21 September 2016

Genomics is a valuable tool for understanding biological development. It provides new technologies for use in medicine, animal breeding and food production. This book provides a remarkably broad overview of its implications in various sectors of the society, ranging from questions on how clinical genetics services may contribute to the empowerment of patients to questions about economic assessment of these genetic services and biotechnological applications. The challenges faced when genomics meet the local cultures and religious beliefs, for example, traditional Indian Ayurvedic and Chinese medicine, and sociocultural beliefs in South Africa are described with scholarly insight in a way that is not easily available in other contexts. As is common when scientists and scholars talk about the future, there is an element of speculation both regarding potential benefits and risks of harm. The contributors come from many different disciplines and it would sometimes have been helpful to include not only biologic terms in the glossary. I still do not understand what a 'sociotechnical expectation' is. Still, the editors manage to produce a comprehensive report that should be helpful for any policy maker interested to understand and assess genetic innovations in biotechnology, bioengineering and medicine.

I will not give an overview of all 19 chapters in this review. They are all worth reading. One chapter is in my view outstanding in scholarly insight and careful reasoning. Marion McAllister has examined the literature on how clinical genetic services may affect patients' wellbeing. May genetic testing, counselling and risk information be something good for the individual besides the medical benefit? She uses the concept of *empowerment* as an umbrella for various concepts (coping, perceived personal control, emotional regulation) used in instruments for investigation of the psychosocial aspects of genetic testing and discuss in detail how these concepts then relate to each other. She draws on the seminal work by Katherine Payne and others in Manchester who identified a high degree of discordance between different instruments for measuring patient-related outcomes. She then shows with good references how this field may move forward by applying strict criteria for the assessment of psychometric properties of health measurement scales, and try to bring the different measurements together under the construct 'patient empowerment'. This is done in a way that goes far beyond just using 'empowerment' as a new catchword, something that seems to be quite common among policy makers, social scientists and ethicists today. She concludes that genetic information can be empowering for people. For high-risk genetic conditions many of the benefits relate to feelings of personal control, emotional regulation and hope. More research is needed and several challenges are identified where research is underway or specific issues need to be addressed. There is a lot of interest in seeking out patient perspectives and preferences today. I highly recommend this chapter by McAllister to all researchers engaged in this field, and for policy makers who should not base their recommendations on sloppy research or on speculations about benefits and risks associated with genetic testing.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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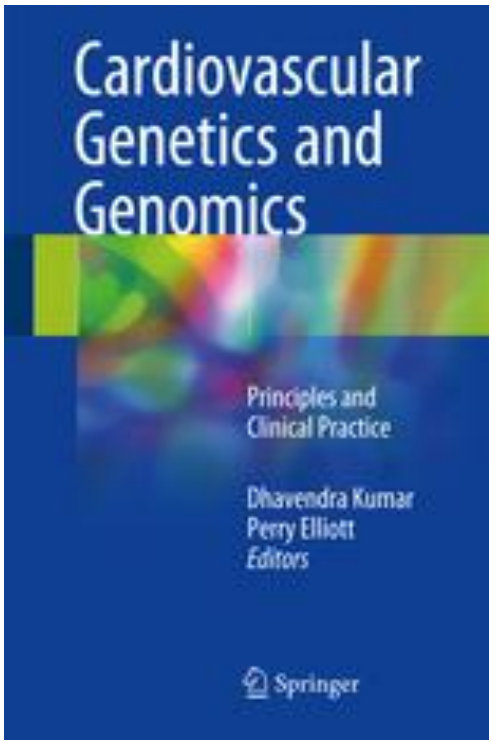
10. "Cardiovascular genetics & genomics – Principles & Clinical Practice", Edited by Professors Dhavendra Kumar and Perry Elliott (The Heart Hospital, University College Hospitals, London, UK), Springer-Nature, 2018



This book is the revised and practically rewritten version of the previous book by the above authors/editors- '***Cardiovascular Genetics & Genomics- Principles & Clinical Practice''***, published by the Oxford University Press (New York, 2010), in the Oxford Monographs on Medical Genetics series. Since the publication of the original textbook, there has been exponential growth in the knowledge and information on this subject with extensive clinical translation of the cardiovascular genetics and genomics in medical practice. The two co-editors and co-authors of the first edition propose this new version that is intended to be concise, clinically oriented and targeted at broad spectrum of clinicians who manage patients and families with a wide range of heterogeneous inherited cardiovascular conditions. The book shall be published in both electronic and print formats.

The e-format allows downloading the individual chapter to facilitate the reader and the subscribing institution. In addition, regular updates and reviews by the author and editors could also be possible at frequent intervals.

The book includes a concise and clear account on selected topics written by a team of leading world-class experts. Each chapter shall include key points for the clinician and where ever applicable relevant case histories to reflect the contemporary practice of clinical cardiovascular genetics and genomics. The book will include generous illustrations supported by set of data arranged in tables. The electronic format presents illustrations in the original format.

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1 Introduction to Genes, Genome and Inheritance
2 Spectrum and Classification of Inherited Cardiovascular Disease
3 Principles and Practice of Genetic Counselling for Inherited Cardiac Conditions
4 Genetic and Genomic Technologies: Next Generation Sequencing for Inherited Cardiovascular Conditions
5 Pharmacogenetics and Pharmacogenomics in Cardiovascular Medicine and Surgery
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Preface:

Where is the Life we have lost in living? Where is the wisdom we have lost in knowledge? Where is the knowledge we have lost in information?—T. S. Eliot

In 2010, we compiled, authored, and edited the first textbook on clinical cardio- vascular genetics—"*Principles and Practice of Clinical Cardiovascular Genetics"* (ISBN-10:0195368959 & ISBN-13:978-0195368956, Oxford University Press, NY, USA). It was an ambitious project given many unproven hypotheses, incom- plete evidence, loose fragmented scientific concepts, and controversial clinical applications. Nevertheless, the project was completed with the help of several experts from clinical cardiology, cardiovascular surgery, clinical genetics, genetic counseling, basic genetics and genomics, laboratory genetics, and many other health professionals. Fortunately, we were encouraged to receive largely welcome and positive feedback from medical, scientific, and allied health professionals.

Following the launch of the book, we were humbled to receive instructions and commission from Oxford University Press to produce a user-friendly specialist handbook for ready use and quick reference on factual clinically relevant informa- tion on inherited cardiovascular conditions. This Oxford specialist handbook further strengthened the new field of clinical cardiovascular genetics within the large field of clinical cardiovascular medicine. Subsequent years examined the purpose and applications of this new specialist field within the broad landscape of clinical medi- cine and clinical genetics.

The next five years witnessed exponential growth and enhanced genetic and genomic scientific applications and translations in many medical and health fields. The practice of cardiovascular medicine and surgery incorporates genetics and genomics that led to significant changes to the training curriculum and aspects of continued professional development necessary for enhancing the scientific basis of the clinical cardiology practice. This development is in line with other medical spe- cialist fields, such as clinical oncology, medical ophthalmology, clinical rheumatol- ogy, clinical neurology, and many more. Genomic medicine is now a reality, not just a hypothetical scenario. This is now the agreed basis for personalized, precision and preventive medicine.

With the rapidly increasing quantitative and qualitative growth in the genetic and genomic knowledge base and evidence in cardiovascular medicine, the peer demands and

expectations grew and persuaded us to revise and produce a new textbook. We debated and consulted many colleagues, trainees, and students on the likely format and title of the new book. It became clear that despite controversies surrounding the use of genetics and genomics, the new title would need to reflect these two intricately connected scientific fields. Further, we agreed to give the book much needed clinical focus moving away from the conventional scientific introduc- tion. We are convinced that the title and the format of the new textbook on inherited and genetic aspects of cardiovascular medicine and surgery clearly reflect the genetic and genomic basis of the clinical practice.

The book includes 31 chapters written and contributed by leading experts in specific scientific fields and recognizable inherited cardiovascular conditions. The first five chapters cover the basic aspects including one chapter on cardiovascular pharmacogenomics and pharmacogenetics. The format is largely clinically focused with examples reflecting patient and family stories managed by evidence-based clinical and genetics input. Wherever possible and applicable, the key practice points are highlighted in the box style. Concluding 3 chapters focus on interven- tional cardiology, the multidisciplinary care and public/population health. Readers will have the benefit of the detailed and carefully compiled glossary with most commonly used terms and phrases in the emerging new field of clinical cardiovas- cular genetics and genomics. Each section of the book is thoroughly indexed in the end to assist the reader fast and efficient access to any term or description to the respective page and paragraph.

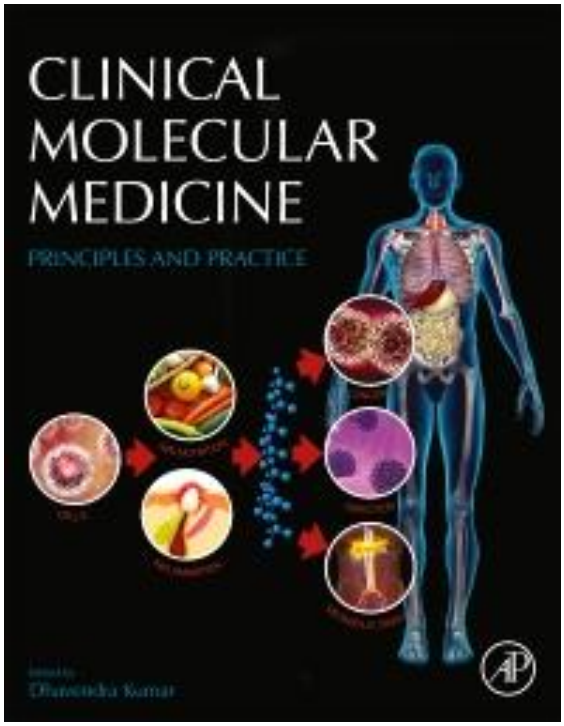
Finally, this book could not have been written and presented in the current format without sincere and painstaking efforts of all contributors and the publishing team. We remain greatly indebted for their kindness and generosity. We humbly submit this book to all students, trainees, and practitioners in clinical cardiovascular medi- cine and surgery, clinical genetics, genetic counseling, cardiac specialist nursing, public health practitioners and professionals, and other health professionals. The feedback and reflections on the book would be welcome in whatever quantitative or qualitative manner. We remain aware of possible errors and omissions and collec- tively take full responsibility.

Cardiff, UK London, UK September 2017

Dhavendra Kumar Perry Elliott

11. 'Clinical Molecular Medicine- Principles & Practice'

Authored and Edited text book; focuses on major molecular systems and clinical applications citing major disease examples irrespective of conventional anatomical and physiological body systems. Commissioned by the Academic Press of the Elsevier Publishers, Cambridge, MS, USA.



Clinical Molecular Medicine: Principles and Practice presents the latest scientific advances in molecular and cellular biology, including the development of new and effective drug and biological therapies and diagnostic methods. The book provides medical and biomedical students and researchers with a clear and clinically relevant understanding on the molecular basis of human disease. With an increased focus on new practice concepts, such as stratified, personalized and precision medicine, this book is a valuable and much-needed resource that unites the core principles of molecular biology with the latest and most promising genomic advances.

Key Features

- Illustrates the fundamental principles and therapeutic applications of molecular and cellular biology
- Offers a clinically focused account of molecular heterogeneity
- Includes comprehensive coverage of many different disorders, including growth and development, cardiovascular, metabolic, skin, blood, digestive, inflammatory, neuropsychiatric disorders, and many more

About the Author:

Professor Dhavendra Kumar is an accredited clinical geneticist (United States and United Kingdom) with special interests in clinical dysmorphology (congenital malforma- tion syndromes), clinical cardiovascular genetics (inherited conditions of heart and blood vessels), genomic and molecular medicine (precision and personalized medicine), and genomic applications in integrated health care.

He has coauthored/edited “Genetic disorders of the Indian Subcontinent,” 2004; “Genomics and Clinical Medicine,” Oxford, 2008; “Principles and Practice of Clinical Cardiovascular Genetics,” Oxford, 2010; “Oxford Specialist Handbook on Inherited Cardiac Disease,” Oxford, 2011; “Genomics and Health in the Developing World,” Oxford, 2012; “Genomic Medicine: Principles and Practice,” Oxford, 2014; “Genomics and Society,”Elsevier Cambridge (USA), 2015; “Medical Health Genomics,” Elsevier Cambridge (USA),2016; and “Cardiovascular Genetics and Genomics: Principles and Clinical Practice,” Springer Nature, 2018. In addition, he founded and served as the Serial Editor for “Genomic and Molecular Medicine” monographs series, Morgan Claypool, 2011!18, and currently leads the multivolume series “Clinical Genomic and Precision Medicine” of Springer Nature. He is the founding Editor-in-Chief for the new genomics biomedical publications— Genomic Medicine (Springer-Kluwer), Applied and Translational Genomics (Elsevier), Current Trends in Genomic Medicine (Genomic Medicine Foundation, UK), and Genomic and Molecular Cardiology (Genomic Medicine Foundation, UK).

He founded and leads the “Genomic Medicine Foundation UK” for promoting fellowship and scholarship in genomic medicine and health care. The key initiatives of the foundation include the “Global Familial Heart Challenge (GFHC),” “Global Consortium for Genomic Education (GC4GE),” the “UK India Genomic Medicine Alliance (UKIGMA),” and the Indo-UK Genetic Education Forum.

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Preface:

Historically, biomedical sciences have gone through many phases that followed major discoveries and inventions. Inevitably, peoples, communities, and nations around that time had demanded to embrace these new advances and developments in all aspects of life, particularly in medicine and healthcare. The molecular medicine is one of the most dynamic fields of all the life sciences that encompass many disciplines of biology, biochemistry, human biology, and human genetic. The main impact of molecular medicine is evident from many advances and applications in clinical pharmacology. Undoubtedly, the knowl- edge of the molecular basis of human disease has led to development of novel diagnostic and therapeutic strategies to manage a number of inherited and acquired diseases. This rel- atively young field of molecular medicine has made a huge impact on medical education and training of general and specialist doctors and healthcare providers.

The current phase of the explosion of public interest in the human genome and related scientific developments is no exception. This is the “genome era,” and understandably, globally peoples have high hopes from eventual medical and healthcare implications, the genomic medicine with its many other names such as stratified medicine, personalized, and precision medicine. However, fundamental to all these new promising avenues of clinical medicine is the molecular basis of human disease and its many applications.

Alongside this extraordinary scientific development, the revolution in information technology and widespread use of digital communication tools have created a public that is increasingly demanding that the present-day and future generation of doctors and healthcare professionals are experts in the diagnostic, therapeutic, and preven- tive implications of applied genomic and molecular medicine. Arguably there is a considerable conceptual over- lap and physical evidence that genomic and molecular medicine is not distinct but merely two ends of the spectrum. This is true as the genome provides the very basic components such as specific functional nucleic acid (DNA and RNA) sequences, promoting and regulating parts of the coding regions, evolutionary conserved wide- spread genomic polymorphisms and copy number variations, and hitherto unknown functional impact of the noncoding regions of the genome. Collectively, all cloned regions of the genome are molecules and then the gene product, the peptide chain, is in itself a molecule. However, in everyday practice of clinical medicine a number of molecular investigations are routinely carried, such as hemoglobin, clotting factors, immunoglobulins, lipopro- teins, cholesterol, triglyceride, thyroid-stimulating hormone, cortisol, and many more. All these are the end points of genes and genome. It is thus safer to simply use the term clinical molecular medicine.

Molecular medicine in an interdisciplinary approach intricately linked to life science research. It allows the medical student and clinicians to understand normal and pathological cellular processes at the molecular level. There are many examples of molecular applications to the contemporary medical practice, which have funda- mentally changed diagnostic and therapeutic applications. The focus has now shifted from simply symptomatic management to the molecular pathology of human diseases. This is aided by new drug discovery and develop- ment dependent upon unraveling of the molecular processes and pathophysiology specifically involving the molecular targets. However, the new drug development is a long-term painstaking and expensive effort that starts with basic and preclinical research followed by successive clinical trials and finally approval for therapeutic use by a statutory authority.

Molecular medicine is central to a number of undergraduate and postgraduate teaching programs worldwide. In addition, it is an integral part of well-established teaching courses, particularly related to many aspects of medicine. This textbook offers the entire spectrum of molecular medicine in a clinically oriented manner using relevant clinical cases and scenario. Conceptualization and planning of the book required scrutiny of the avail- able evidence that provides insight to normal and pathological cellular processes at the molecular level.

This allowed to the selection of the topics that are covered in this book. The focus has been on the molecular per- spective of the pathophysiology, improving the diagnosis and the targeted molecular therapy.

This is an edited textbook comprising many chapters. The broad and diverse range of topics included in this book required contributions from many experts on different areas of molecular medicine. However, all efforts are made to present a homogeneous textbook in a uniform and consistent style. This is a clinically oriented book with relevant scientific factual and applied information on related molecular systems. As far as possible, authors have included pertinent clinical cases with discussion on the molecular systems underpinning the pathophysiol- ogy and clinical manifestation. Most chapters, except for those covering the basic cellular and molecular biology, are arranged in a consistent format including the introduction, clinical cases, discussion with reflections on the molecular systems underpinning the clinical scenario, overview of the relevant molecular biology and pathophys- iology, targeted molecular diagnosis and therapy, summary points, and relevant references with guide to further reading. Each chapter includes numerous color illustrations and summary of critical genes and molecules. References are kept to as low as possible with important cross-references to help the reader to understand com- plex interdependencies between the different fields of molecular medicine. Among many examples the monoclo- nal antibody Herceptin not only provides a comparatively new treatment option for aggressive breast cancer but is also a recombinant protein drug that is difficult to produce. Nevertheless, the successful application of this molecular evidence is one of the paradigmatic applications of pharmacogenetic testing. There are now many such applications for the treatment of cancer of lung, skin, and colon.

This textbook on clinical molecular medicine is set out in three sections—the fundamentals of cell and molecu- lar biology, the molecular systems in human disease, and the molecular therapeutics. As far as possible, practi- cally all chapters follow a set pattern as described in the preceding paragraph. Some of the novel diagnostic and therapeutic applications included form the basis of genomic and precision medicine that are essential compo- nents of clinical molecular medicine. Novel treatment modalities are included based on new drugs targeted at specific molecular level, stem-cell and somatic-cell therapy, RNA interference, and the CRISPR/Cas9 gene edit- ing. The concluding section of the book includes a chapter on the ethical dimensions of molecular medicine.

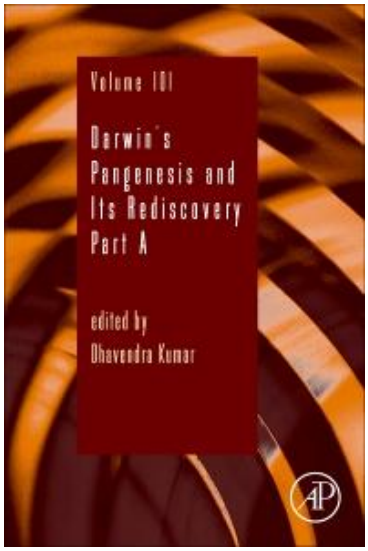
It is hoped that readers and users of this textbook will enjoy the journey through the field of molecular medi- cine and share the enthusiasm for this fascinating subject. The success of this book would be reflected in building a firm base and developing skills in the practice of clinical molecular medicine.

Dhavendra Kumar, Editor

12. 'Darwin's Pangenesis and its Rediscovery', Advances in Genetics Volume 1 & 2

Charles Darwin's theory of biological evolution includes a unique concept of hereditary factors. This laid the foundation of modern genetics and genomics. The two volumes on 'Darwin's Pangenesis', edited by Professor Kumar, provide in depth analysis of this theory. These monographs are part of the 'Advances in Genetics', Academic Press, Elsevier

12.1 'Darwin's Pangenesis and Its Rediscovery' Part A, Volume 101

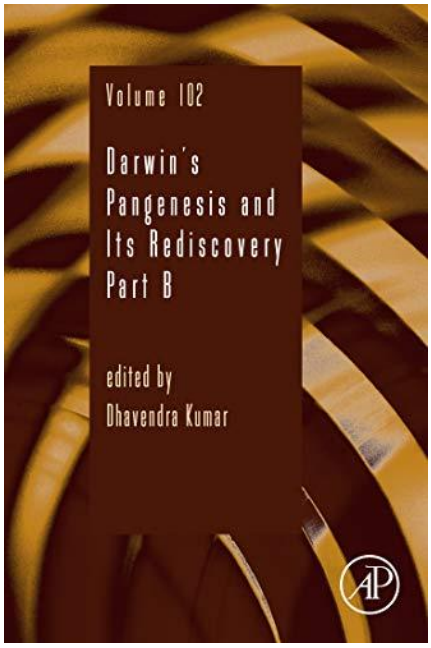


Darwin's Pangenesis and Its Rediscovery Part A highlights the findings of Darwin's Pangenesis, an expanded cell theory and unified theory of heredity and variation that strengthened his theory of evolution and explained many phenomena of life. Now, new advances and the discovery of circulating cell-free DNA, mobile RNAs, prions and extracellular vesicles are providing new breakthroughs, thus increasing evidence on the inheritance of acquired characters, graft hybridization, and many other phenomena that Pangenesis suggests. Sections of note in this volume include the rationale, criticisms, influence and recent molecular evidence of Darwin's Pangenesis, as well as its relation to the inheritance of acquired characters, which is often included under the blanket term "transgenerational epigenetic inheritance."

Key Features

- Presents a comprehensive approach to Darwin's Pangenesis, which is so little understood that few have recognized its far-reaching importance, but seems today surprisingly modern
- Links Darwin's hypothetical gemmules with circulating cell-free DNA, mobile RNAs, prions and extracellular vesicles, shedding new light on an old theory
- Includes section on Darwin's Pangenesis in relation to the Lamarckian inheritance of acquired characters, a central debate in the history of genetics

12.2 'Darwin's Pangenesis and Its Rediscovery' Part B, Volume 102



Darwin's Pangenesis and its Rediscovery Part B explores Darwin's Pangenesis, an expanded cell theory and unified theory of heredity and variation from over 150 years ago that strengthened his theory of evolution and explained many phenomena of life. Now, new discoveries on circulating DNA, mobile RNAs, prions and extracellular vesicles are providing striking evidence for the chemical existence of Darwin's imaginary gemmules. In addition, new evidence for the inheritance of acquired characters, graft hybridization, and many other phenomena that Pangenesis supposedly explains are progressing, and are hence explored in this comprehensive volume.

Specific chapters in this new volume include Darwin and Mendel: The Historical Connection, Darwin's Pangenesis and Graft Hybridization, Darwin's Pangenesis and Medical Genetics, Darwin's Pangenesis and Certain Anomalous Phenomena, and Natural Selection and Pangenesis: The Darwinian Synthesis.

- Presents the only book on Darwin's Pangenesis, an expanded cell theory and a unified theory of heredity, variation, development and reproduction
- Highlights Darwin's tremendous contributions to genetics, as well as Mendel's legacy and limitations
- Includes sections on Darwin's Pangenesis in relation to graft hybridization, medical genetics, evolutionary theory, along with many other updates

13. Advances in Genetics, Serial Editor, Dhavendra Kumar

13.1 Volume 105, Academic Press, Elsevier, 2020

Serial Editor : Dhavendra Kumar , William Harvey Research Institute Bart's and The London School of Medicine & Dentistry London, UK

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Preface

Advances in genome sequencing and supporting informatic technologies largely focus on DNA coding and noncoding regions of the genome. Other areas of interest include single-nucleotide polymorphisms, copy number sequence variations, epigenome and evolutionary conserved genome variations. Specific coding genome alterations and variations information are now widely used in diagnosing wide ranging genetic conditions. It is also rolled into therapeutic applications, specifically targeted therapy.

Perhaps the most intriguing and challenging part of the genome is the transcriptional factors that work closely with the complex RNA systems and the ribosomal peptide assembly platforms. There is now huge amount of data and information available on diversity of RNA structure and function. Some of this information has found its way into clinical genomics and applied plant genomics. However, there is lot more to understand and learn from the complex RNA systems.

The present issue includes two articles related to the RNA homeostasis. The article on the role of RNA interacting proteins in modulating plant–microbe interactions is an impressive example of applied plant genomics. The article on oomycete class of microorganisms deserve appreciation as it highlights the relevance of plant genomics in the context of natural food wastage caused by infecting or invading microorganisms. Authors draw attention to the importance of oomycete genome sequences, coupled with proteomic and transcriptomic (RNA) analyses, for understanding the oomycete genome biology, particularly the metabolism and pathogenic capability. The other article related to the common X-linked fragile X-syndrome (FRAXA) highlights the importance of RNA homeostasis essential for the assembly of the FMRP ribonucleoprotein complexes.

The current volume includes three articles relevant for understanding the complex genomic and molecular mechanisms underpinning the electrophysiological manifestations in developmental malformations related to the potassium ion channel discordance (channelopathy), application of yeast genetics for unraveling the complexities of amyloid and prion protein dementia largely ignored as opposed to the Alzheimer's dementia, and molecular mechanisms of antibiotic drug resistance relevant for the discovery of novel and next generation genome driven antibiotic drugs.

xii Preface

It is anticipated that readers and investigators would find the varied selection of articles in this issue stimulating and relevant to their respective areas of interest. It is possible that some of the articles could be expanded and reproduced as a thematic volume. Your views, reviews, and critical appraisal would undoubtedly help the Editor and Publisher in making an informed decision.

DHAVENDRA KUMAR, Serial Editor
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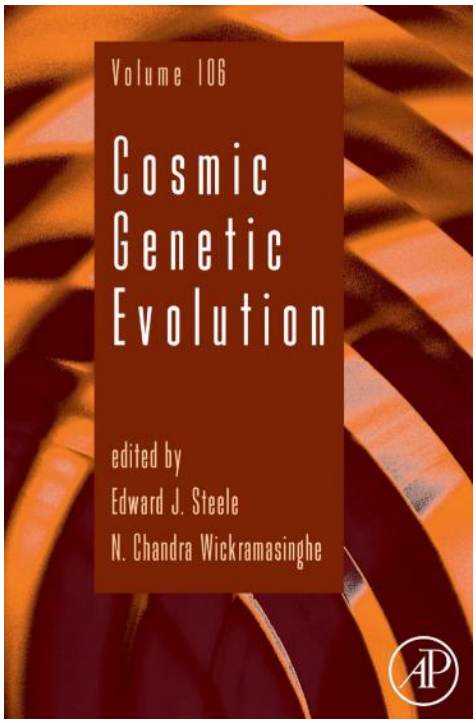
Queen Mary University of London
London, United Kingdom

13.2 Advances in Genetics, Volume 106: "Cosmic Genetic Evolution"

Guest Editors: Edward J. Steele & Chandra Wickramasinghe;

Serial Editor- Dhavendra Kumar



This is a unique book that goes into deeper on the origin of life linked to astrology and examines the evidence on the extra terrestrial basis of life.

Preface

" The origin of Life and Astrobiology"

Dhavendra Kumar, Serial Editor, Advance in Genetics, Academic Press, Elsevier

'Advances in Genetics', Volume 106: "Cosmic Genetic Evolution"
Guest Editors: Edward J. Steele & Chandra Wickramasinghe

Charles Darwin is historically renowned for his theory of evolution as the basis of variation of biological life that exists around us. Similar views were also echoed by the contemporary biologist, Alfred Russel Wallace, who is credited with independently conceiving the theory of evolution through natural selection. His paper on the subject was jointly published with some of Charles Darwin's writings in 1858. Despite strong opposition of the contemporary Christian Church of the time, gradually the natural selection theory for the biological evolution was accepted and remains pivotal to explain both inter- and intra- species variation. However, a small section of theologists, philosophers and biologists continue to hold different views for the origin of life and its developments into numerous species and variation. Both schools, however, believe and acknowledge the genetic basis of life within the realms of nucleic acids, the ribose nucleic acid (RNA) and the deoxyribose nucleic acid (DNA). The fundamental questions remain- what must have been the earliest form of life on Earth? and what is the relationship to life beyond Earth, if it exists at all?

Molecular biologists agree that the earliest form of life must have been based on the RNA molecule, with DNA evolving later following successive chemical processes to facilitate the RNA functions. It is argued that the earliest life would have been heterotrophic, arising from and metabolically processing prebiotic organics as proposed in the Oparin-Haldane theory. In this context, it is important to consider the abiogenesis theory that life on Earth arose from non-life more than 4 billion years ago. Abiogenesis proposes that the original life forms were very simple and gradually became increasingly complex. It probably preceded biogenesis, in which life is derived from the procreation of other life. Abiogenesis became impossible once the present composition of the Earth was achieved. The abiogenesis theory is neither proved nor disproved. The cosmic origins of life discussed in the many articles in this volume remains at the forefront of modern discussions.

In the 1920s, the famous British biometric scientist John Haldane and Aleksandr Oparin, the Russian biochemist independently set forth similar ideas for the origin of life on Earth. Both believed that organic molecules could be formed from abiogenic materials in the presence of an external energy source, for example the ultraviolet radiation, in combination with very low atmospheric oxygen, ammonia, water vapour, and probably other gases. Both agreed that the earliest form of life probably first appeared in the warm oceans of Earth and were heterotrophic, nurtured by preformed nutrients from chemicals in existence on early Earth, or brought in by comets compared to being autotrophic, generating food and nutrients from complex interactions of the sunlight, including cosmic radiations with inorganic materials. Oparin believed that the life developed from microscopic spontaneously formed spherical lipid molecules held together by electrostatic forces, probably the earliest form of cells. These molecules most likely functioned as enzymes, essential for the biochemical metabolic reactions necessary for life's evolution. Haldane, unfamiliar with Oparin's thoery, believed that simple organic molecules formed first and in the presence of ultraviolet light became increasingly complex, ultimately forming cells. Haldane and Oparin's ideas formed the foundation for much of the research on the origin of life, specifically formation of cells.

The Haldane-Oparin theory on the origin of life was tested to a limited extent by two American chemists. Harold Urey and Stanley Miller. They successfully produced organic molecules from some of the inorganic components thought to have been necessary for the appearance of life, the prebiotic phase. The Miller-Urey experiment included combination of warm water with a mixture of water vapour, methane, ammonia, and molecular hydrogen exposed to the atmospheric electrical discharges in the form of lightening. Miller and Urey found that simple organic molecules, including amino acids (the building blocks of peptides), had formed under the simulated conditions of early Earth. The Miller-Urey experiment demonstrated that organic molecules could form from abiogenic materials under the constraints of Earth's prebiotic atmosphere. Later research showed that amino acids can spontaneously form small protein molecules (peptides). It is also shown that the RNA molecule can be artificially synthesised from nucleotides (nitrogen containing compounds or bases] linked to sugar and phosphate groups. In fact, in addition to carrying and translating genetic information, RNA acts like a catalyst, a molecule that increases the rate of a reaction without itself being consumed. It is, thus, logical to accept that multiple forms of RNA existed in the prebiotic phase of abiogenesis that led to the formation of life on Earth or in any wider context.

It has been suggested that peptide nucleic acid (PNA) might have been the first genetic material that preceded the RNA and DNA. PNA forms very stable double helical structures and even stable triple helices. However, the chemical nature of PNA does not allow it be a sustainable genetic material necessary for replication, transfer of genetic information or its reorganization. Activated PNA monomers tend to cyclize easily and thus formation of oligomers is very difficult under prebiotic conditions. Further, and PNA hydrolyses rather rapidly and thus restricts the chances of it ever being accumulated in sufficient quantity, for instance deep in the primitive oceans.

The concept of sunlight (ultraviolet radiation) and energy sources from other planets in the cosmos (cosmic radiations) influencing the origin of life on Earth, or indeed anywhere in the cosmos, falls within the field of Astrobiology. The main question remains on the likelihood of the existence of life beyond the confines of Earth or perhaps in the wider cosmos.. Astrobiology deals with the processes that may lead to the origin and evolution of life on Earth. Scientists continue to focus firstly on sites for understanding the processes of chemical (prebiotic) evolution (Titan, asteroids, and comets), and secondly on targets for searching for life beyond Earth (Mars, Venus, Europa, Enceladus, and others). Mars is one of the most popular targets due to the fact that early Mars and early Earth had a similar history. The quest for life on Mars is one of the most important missions of the modern astrobiology. Several ethicists and philosophers have strong reservations in relation to ethical, social and legal concerns that fall within the new discipline of ***astrobioethics***. Perhaps the main stumbling block of research in life on Mars is the anticipation of a close similarity to life on Earth.

Most astrobiologists are guided by the following broad requirements and principles on the origin of life-

(1) The elements of life, carbon, hydrogen, oxygen and nitrogen (CHON)

(2) CHON + energy (e.g., UV from stars, atmospheric lightning discharge) = monomers (Miller-Urey micro molecules)

(3) Monomers + aqueous environment (to protect pre-biotic organics from destruction by UV) + concentration/ assembly/ordering = polymers.

(4) Some such polymers presumably incorporated both gene-like information and enzyme-like catalytic activity (ribozymes). The information content in the enzymes being of a super-astronomical magnitude opens the way to the concept of a cosmological origin of life and the ideas of panspermia discussed by Sir Fred Hoyle and Prof. Chandra Wickramasinghe.

(5) Earliest life, wherever it started, would thus have been heterotrophic and thermophilic

The concept of cosmic genetic evolution emerged from discussions with the guest editors of this thematic volume. It is an extension of astrobiology to explore the extent of ultraviolet radiation (sunlight) and range of complex cosmic radiation systems implicated in genetic or genomic variation and function. The cosmic radiations (cosmic rays) include high-energy protons and atomic particles (nuclei) which move through space at nearly the speed of light. They originate from the sun, from outside of the solar system, supernova explosions of star, and from distant galaxies. These pass through the ozone layer and upon impact with the Earth's atmosphere, cosmic rays can produce cascade of secondary particles capable of striking the Earth's surface.

The fundamental questions remain-

- Whether cosmic rays are capable of inducing spontaneous benign or deleterious genetic changes (mutations and variants)?
- How far the cosmic ray phenomenon along with the introduction of new cosmic viruses could account for successive evolution of life on Earth?
- Could cosmic radiation be an important factor in the emergence of different forms of biological life and variations?
- How far does the impact of cosmic rays on the Earth might account for the creation of new viral variants capable of causing human disease, for example the Corona/ Covid-19/ SARS-CoV-2 virus?

The guest editors and other contributing authors have produced this impressive volume on a very unusual subject full of past and present hypotheses. Information and supporting arguments are most relevant and will form the basis for further discussion and design of new experiments and investigations. They all deserve to be congratulated on this exciting

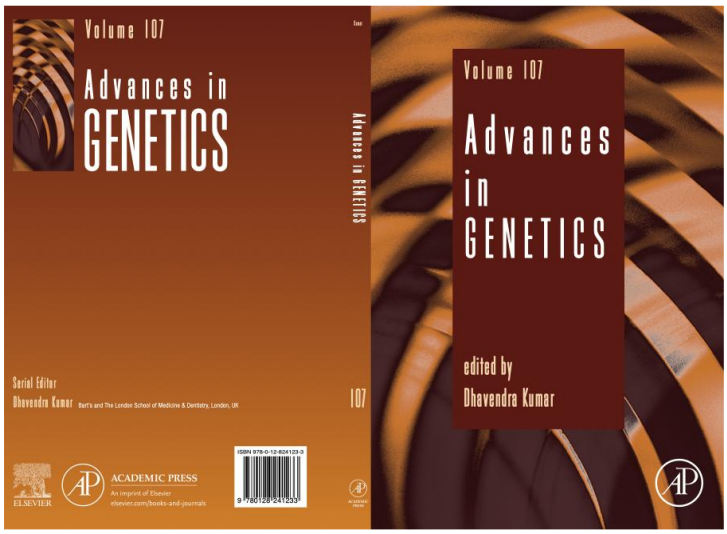
achievement. Now authors, editors and publishers shall wait for acceptance and appreciation of this unique contribution to the genetics literature.

Disclaimer and Acknowledgements

This article is based on author's own perceptions, understanding and amateur knowledge of cosmology and astrobiology. Some of the ideas and concepts are derived from author's informal discussions with Professor Chandra Wickramasinghe, the Co-Editor of this thematic volume. His thoughtful insights and guidance are greatly appreciated. The author prefers to avoid add literature references as the subject is widely discussed in diverse digital open access public domains.

The author would be delighted to deal with any questions or observations related to this article (d.kumar@qmul.ac.uk ; genomicmedicineuk@gmail.com).

13.3 Advances in Genetics, Volume 107



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Preface:

The 107th volume of *Advances in Genetics* is now with us. It has probably taken longer than anticipated, largely due to unavoidable circumstances surrounding the Sars-CoV-2 (COVID-19) pandemic. Millions got infected and sadly several people globally perished. It's an old recurrent thinking that a crisis breeds the opportunity. The Covid-19 pandemic offered scientists, technologists and healthcare professionals life-time opportunity to put all personal, professional and material resources in the quest of effective and efficient targeted laboratory diagnosis, drug therapy and vaccine development. Microbial genetics and genomics, specifically the pathogenomics, have emerged as the most promising of the *OMICS* sciences sector. The reverse transcriptase polymerase chain reaction (RT-PCR) based Covid-19 laboratory testing is echoed all over and an ordinary person on any street anywhere in the World has some knowledge of this test. Further the viral mRNA (messenger RNA) based new vaccine development has raised hopes of millions across the World. This development echoes excitement, hope and passion that was around following the discovery of penicillin followed by development of several other anti-microbials. We are now living and moving ahead with genetic and genomic applications in precision, predictive and preventive clinical medicine and healthcare.

The current volume includes a collection of diverse articles focussing on basic and applied genetics. Two articles discuss the role of nutritional regulation, particularly the micronutrients, in the postembryonic development and the bio-availability. The role of fungal

molecular genetics in blockbuster drugs development offers the reader to grasp the complexities of novel drug discovery and development.

One of the most challenging and vital fields of genomic medicine is undoubtedly unravelling of the genetic and genomic complexities in complex and common diseases. Despite limitations and low diagnostic yield, the genome wide association studies (GWAS) continue to hold on. Perhaps the most relevant outcome of GWAS is the *polygenic score* with enhanced power of prediction of personalised genetic risks and outcomes of the disease.
There are two articles in the current volume that deserve particular attention. The role of GWAS is revisited in an attempt to find the *proof of concept* for the genetic basis of circadian clock and pathological implications in mental health. The model of bronchial asthma, one of the well-known complex and common diseases, is selected in another article. It is a gentle and persistent reminder of the role of several hundreds low risk alleles and variants spread across the genome in filling the inevitable recurring and persistent gaps in our knowledge. This is the main crux of the matter in complex genomics. The reader might like to use this model to look around other common and complex diseases like type 2 diabetes mellitus, systemic hypertension and ischemic heart disease.

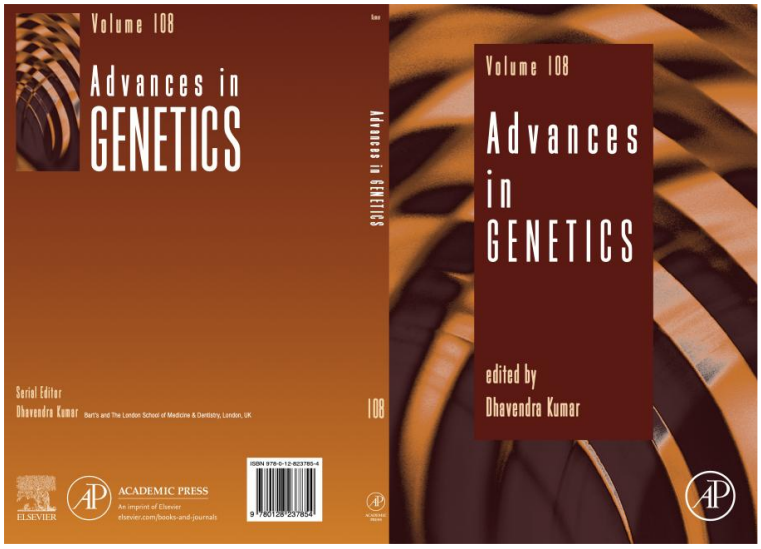
The article on founder genome variants in different populations cohort provides further stimulus to consider and appreciate the vital importance of the evolutionary conserved genome variants and population specific founder variants in designing and delivering the genomic and precision medicine.

Professor Dhavendra Kumar

The William Harvey Research Institute, Bart's and The London School of Medicine,

London, England, UK; November 2020

13.4 Advances in Genetics, Volume 108 'Precision and Personalised diagnosis and prevention'



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7. Recent advances in lung cancer genomics- applications in targeted therapy

Preface:
In the early stage of conceptualising and actioning on the current volume (Advance in Genetcis 108), no one had even dreamt of SARS-2/ Covid-19 pandemic. By the time we were able to put together contents and identify most appropriate faculty, early warning signs and unclear news had started buzzing around of a new Corona family virus that had affected hundreds in the Wuhan city in South West China. Towards the late 2019, we were able to put together most articles included in the current volume of Advances in Genetics. We chose to focus on genome based precision and personalised diagnosis and prevention at population level. At that time most clinicians, healthcare professionals and public at large had not consumed the idea of individualised genomic precision diagnosis and prevention at population level. During the first quarter of the Corona/SARS-2 pandemic, the RT-PCR diagnostic test got established as the most sensitive and reliable diagnostic tool [1]. However, for considerable period we could not work out a precise treatment strategy. Within the next few months, research laboratories around the globe emerged with claims of vaccine development. Amongst these, the mRNA derived vaccine became the front runner [2]. Both RT-PCR precision diagnosis and mRNA SARS-2/Corona/Covid-19 vaccine are examples of genome led personalised precision diagnosis and population prevention. It might look

serendipitous, the current volume appearing at the height of Covid-19 infection control with similar message, however in different diseases and applications.

The current volume includes carefully selected articles authored by a team of highly skilled scientists and clinicians. Preventive population genomics offers the prospect of population stratification for targeting screening and prevention and tailoring care to those at greatest risk. The *BRCA* model provides thirty years of insight and experience of how to conceive of and construct precision breast cancer care and serves as an initial model for preventive population genomics. Population-based *BRCA*-testing in the Jewish population is feasible, acceptable, reduces anxiety, does not detrimentally affect psychological well-being or quality of life, is cost-effective and is now beginning to be implemented in most breast cancer clinics. Population-based *BRCA*-testing and multigene panel testing in the wider general population is cost-effective for numerous health systems and can save thousands more lives than the current clinical strategy.[3] In the clinical diagnostic setting, there is always the need for novel technologies with high order sensitivity and specificity.

The translational research in diagnostic genomics has led to the development of three potential technologies- liquid biopsy, single-cell RNA sequencing and spatial transcriptomics. [4] These three novel genomic technologies offer robust detection and accurate diagnosis in cancer as cornerstone for precision oncology. These technologies are now increasingly applied for better molecular understanding of cancer and as well as many other heterogeneous genetic diseases.

Targeted precision molecular therapeutics is an established component of precision medicine. There are now new drugs available targeting the epithelial growth factor receptor (EGFR), vascular endothelial growth factor receptor (VEGF), mTOR, KRAS, BRAF and many more. One such new class of targeted drugs in the armamentarium is Poly ADP Ribose Polymerase (PARP) inhibitors (PARPi), which inhibit the enzyme PARP ,thus interfering with DNA repair. This strategy utilizes a pre-existing genomic lesion in tumors with homologous recombination repair defects, including BRCA mutations. [5] In this context, discussion on the prostate cancer, one of the significant causes of male mortality, is important and justified. Prostate cancer heritability is attributed to a combination of rare, moderate to highly penetrant genetic variants as well as commonly occurring variants conferring modest risks [single nucleotide polymorphisms (SNPs)]. Some of the former type of variants (e.g. *BRCA2* mutations) predispose particularly to aggressive prostate cancer and confer poorer prognoses compared to men who do not carry mutations. Molecularly targeted treatments such as PARP inhibitors have improved outcomes in men carrying somatic and/ or germline DNA repair gene mutations. Both germline and somatic prostate cancer research have significantly evolved in the past decade and will lead to further development of precision medicine approaches to prostate cancer treatment as well as potentially developing precision population screening models. Ongoing clinical trials are exploring other molecular targeted approaches based on prostate cancer somatic alterations. [6]

Genomic characterization of lung cancer has not only improved our understanding of disease biology and carcinogenesis but also revealed several therapeutic opportunities. Targeting tumor dependencies on specific genomic alterations (oncogene addiction) has accelerated the therapeutic developments and significantly improved the outcomes even in advanced stage of disease. Multiplex gene testing has become mandatory in view of constantly increasing number of therapeutic targets and effective treatment options. Influence of genomic characteristics on response to immunotherapy further makes comprehensive genomic profiling necessary before therapeutic decision making. This

approach is pivotal for managing the non-small cell lung cancer (NSCLC). Current lung cancer management is the perfect example of "precision-medicine" in clinical oncology. [7]

The prevalence of non-communicable diseases has been on an upward trajectory for some time and this puts an enormous burden on the healthcare expenditures. Lifestyle modifications including dietary interventions hold an immense promise to manage and prevent these diseases. Recent advances in genomic research provide evidence that focussing these efforts on individual variations in abilities to metabolise nutrients (nutrigenetics) and exploring the role of dietary compounds on gene expression (nutrigenomics and nutri-epigenomics) can lead to more meaningful personalised dietary strategies to promote optimal health. [8] Finally, the focus shifted on the microbiome with abundant new products targeted at specific molecular loci. Several novel natural products endow the capacity to suppress the hike of superbugs, and help us to avoid the burgeoning condition of antibiotic resistance. There is a wide gamut on different sources of microbes that endure the tendency to synthesize novel compounds, and curtail the spread of rising superbugs. In addition, there are classes of secondary metabolites with their route of biosynthesis by different microbiota residing in different animals, insects, reptiles and humans. [9]

Authors and editor of this volume believe to have made a small contribution to the enormous and rapidly advancing knowledge base in the burgeoning field of precision, personalised and preventive genomic medicine. All those who contributed, in whatever manner, are gratefully acknowledged. Any resemblance or replication of factual information is coincidental and unintentional simply to convey and elaborate the concept of genomics led precision and personalised evidence-based medicine.

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Professor Dhavendra Kumar

The William Harvey Research Institute, Bart's and The London School of Medicine,

London, England, UK; July 2021

14. 'Genomic and Precision Medicine in Clinical Practice'- Lead Editor for this **24 volumes** series covering practically all aspects of emerging disciplines within the domain of genomic medicine. The series is commissioned by Elsevier, the World's leading Life Sciences publisher.

I Published Titles

14.I.1 Genomic Medicine- Skills and Competencies

Ed. Dhavendra Kumar

Many aspects of genomic applications in science, biotechnology, clinical medicine and healthcare require core and specialist knowledge, skills development and competencies for carrying out a number of tasks. There are now several knowledge-based courses and

opportunities for skills and competencies development and assessment. This volume convers all major aspects of genetic and genomic education training that are currently offered and evaluated targeted at researchers, physicians, nurses, genetic counselors, bioinformatics technicians and other professionals.

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Preface:

'True education must correspond to the sur- rounding circumstances or it is not a healthy growth.'

Mahatma Gandhi

Scientific advances, knowledge, and ap- plications are dynamic processes that need to be purposeful and yield benefits to the humankind, environment, and the society at large. Since the completion of the Human Genome Project coupled with rapid ad- vances in OMIC sciences and technologies, practical applications of genomics are now increasingly harnessed. There are several ex- amples around; undoubtedly, the successes of combating and preventing

SARS-CoV2 or the COVID-19 pandemic would remain with us for long time. The diagnostic prowess of the reverse transcriptase polymerase chain reaction (RT-PCR) and prevention potential of the ribose nucleic acid (RNA)-derived anti-Corona virus vaccines are now globally appreciated. Every common human, irre- spective of skin color, ethnic origin, and geo- graphic location, has become aware of these genomic applications in medicine, health, and socioeconomic welfare.

While we all agree on extraordinary bril- liance and aptitude of scientists and tech- nologists leading to new discoveries and innovative applications, we need to remind ourselves that widespread and beneficial applications require special skills and com- petencies of the frontline workforce. There

is no denial on the need for structured and instructive education and training pro- grams to equip the right kind of people trusted for delivering the science and tech- nology. There is an urgent need to create and maintain efficient and effective skilled and competent workforce for delivering the precision genomic medicine and health care.

This book, one of the volumes in the *Genomic and Precision Medicine in Clinical Practice* series, provides theoretical and practical aspects of genomic education and training. The focus is on specific skills and competencies expected from any member of the multidisciplinary team entrusted to de- liver the specialized health care. The spec- trum is very broad to include clinicians, nurses, counselors, therapists, clinical and laboratory technicians, and community and public health professionals, among others. Each one of these professionals functions within the specific remit and limitations. However, they all must possess core scien- tific knowledge and practical working skills as expected from a member of the multidis- ciplinary team. Emphasis is laid on digital medium teaching and virtual simulations for acquiring and enhancing range of skills and competencies. Sections of this book also dis- cuss the ethical and legal aspects of genomic education and training.

In view of the gaps that currently exist between the developed, developing, and un- derdeveloped nations, sections of the book deal with efforts targeted to fill the gulf be- tween nations. The reader is also reminded about governmental and nongovernmental global programs in genomic education and training, specifically aimed at narrowing the wide gap in skills and competencies among the genomic medicine and healthcare profes- sionals and providers. Needless to say that it would be unfair to assume the finality of information included in the book. The book provides a basic framework and scaffoldings on which additional and new information would need to be added. Further, the reader and teachers alike would make the best use of it relevant to specific skills and compe- tencies expected in the genomic healthcare providers.

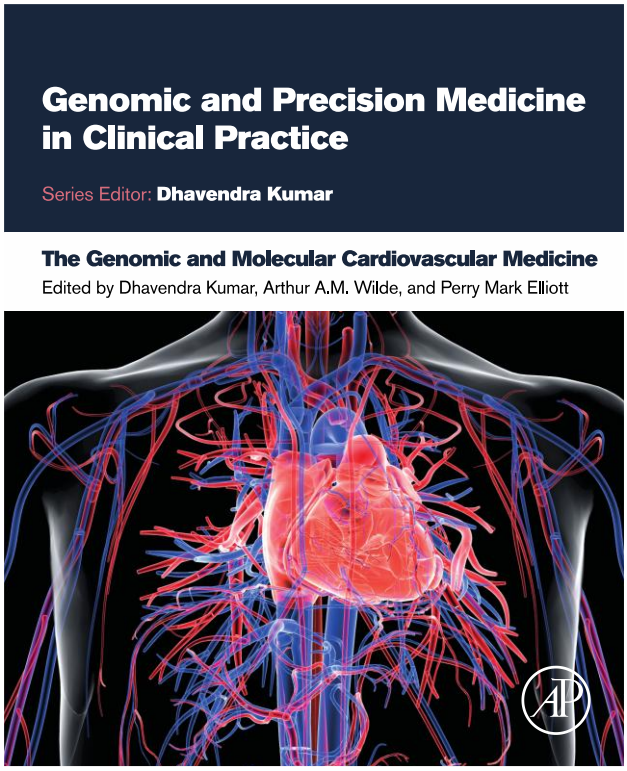
Dhavendra Kumar, Editor

London, United Kingdom

14.I.2 Genomic and molecular cardiovascular medicine

Eds: Dhavendra Kumar (UK), Arthur A.M.Wilde (The Netherlands), Perry M. Elliott (UK)

Cardiovascular diseases are collectively a huge challenge and one of the major causes of high level of morbidity and mortality in the developed world and the fast emerging economies of developing nations, like Brazil, China and India. Practically, every single cardiovascular disease is identified with complex etiology and pathogenesis. Genetic and genomic factors are now established underlying the causation of congenital heart disease, cardiomyopathies, arrhythmias, atrial & ventricular fibrillation, cardiac conduction disease, inflammatory and immunological diseases of the heart & blood vessels, inherited/ acquired connective tissue diseases involving the heart and blood vessels, coronary artery disease and hypertension of both systemic and pulmonary arterial/ venous circulation. This volume provides in detail the current understanding and evidence for genetic and genomic bases of the cardiovascular disease.



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Preface

In 2010, Kumar and Elliott developed the first textbook on clinical cardiovascular genetics (Principles and Practice of Clinical Cardiovascular Genetics; ISBN-10:0195368959 & ISBN-13: 978-0195368956, Oxford University Press, NY, USA). It was an ambitious project given many unproven hypotheses, incomplete evidence, fragmented scientific concepts and controversial clinical applications. Nevertheless, the project was completed with the profound help of several experts from clinical cardiology, cardiovascular surgery, clinical genetics, genetic counselling, basic genetics and genomics, laboratory genetics and many other health professionals. Fortunately, we were encouraged to receive positive feedback from medical, scientific and allied health professionals. Seven years later, Kumar and Elliott co-authored/edited the second edition (Cardiovascular genetics and Genomics- Principles and Clinical Practice, Springer-Nature; ISBN 978-3-319- 66112-4; ISBN 978-3-319-66114-8).

Since these editions, exponential growth in genetics and genomics, including multi-OMICS, has contributed to ad- vances in medical practice and healthcare policy. The practice of cardiovascular medicine and surgery now incorporates genetics and genomics and has led to significant changes to the training curriculum and professional development necessary for enhancing the scientific basis of the clinical cardiology practice. This development is in line with other medical specialist fields, such as oncology, medical ophthalmology, rheumatology, neurology and many more.

The transformative power of genetics in clinical medicine has been anticipated for decades, but the realisation of genuine and meaningful change has been slow, not least in the field of cardiovascular disease where most therapeutic advances have been in diagnostics, devices

and conventional medicinal chemistry. However, in the second decade of the 21st century, the tipping point has finally been reached. By harnessing the power of high-throughput analyses, computing and innovative in vitro models, cardiovascular medicine is on the brink of a step change in disease management based upon the targeting of specific aetiologies rather than the downstream consequence of cardiac dysfunction.

It is in this context that the authors of this textbook (third in the series) have joined together to present a comprehensive review of advances in our understanding of diseases affecting the cardiovascular system. The scope is broad, spanning fundamentals of cell biology to the deeply practical aspects of patient care. The author list includes recognised experts in their field and healthcare practitioners with years of experience in managing patients and families with genetic cardio- vascular disease. It is our sincere hope that this textbook will support the next generation of scientists and clinicians as they embrace the new genomic era in cardiovascular disease.

Editors Dhavendra Kumar London, England, UK

Perry Elliott

London, England, UK

Arthur Wilde

Amsterdam, The Netherlands November, 2023

14.I.3 'Genomics, Populations and. Society- Ethical, Social and Legal aspects'

Eds: Dhavendra Kumar & Ruth Chadwick

This volume deals with contentious and sensitive ethical, moral and social issues surrounding the scientific, clinical and healthcare delivery of genetics and genomics for the benefit of individual, family, community and the population at large. There are many institutional, organizational and professional good practice guidelines that are important for both professionals and the public. Some of the issues involve ownership of the data, patents, intellectual property, consent and confidentiality. Many governments and collective national organizations, for example European Union, have designed regulatory and statutory instruments to safeguard peoples and the public from potential harm of genomic technology applications.

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Preface

In 2016, we were bold enough to address the complexity of close links of genomics with society. Many of our colleagues agreed to help and contributed to the first edition of Genomics and Society. It was a huge challenge with inadequate and anecdotal available information. We were uncertain what aspects should be prioritized as each element is pertinent. Nevertheless, we embarked on the quest and managed to attract contributions from our colleagues with diverse knowledge and skills. The finished product was a relief and was accorded an encouraging welcome. The review in the European Journal of Human Genetics is the current evidence for meeting our objectives with some degree of satisfaction.

Since the first edition of our book, the whole field of ethical, legal, and social issues (ELSI) in Genomics and related emerging scientific and biotechnological fields are ines- capable and deeply rooted. It is now inconceivable to plan and offer any form of genomic services to people and society without serious considerations of ELSI. One of the conten- tious subjects in genetics and genomics is population diversity, marred with controversies and heterogeneous concepts. Since the completion of the human genome and available next-generation sequencing technologies, the diversity of humans can now be scientifi- cally explored irrespective of geographic, language, ethnic, and sociocultural perspectives. These aspects were acknowledged and appreciated during the SARS2-COVID pandemic when the common man on the street argued about genetic variation as the basis of out- comes, particularly the mortality as several hundreds and thousands perished, and mil- lions survived with variable medium and long-term morbidity.

Historically, global populations have welcomed and embraced every advance in sci- ence and technology with excitement, doubts, despair, ability to harness, and affordability. People from every single societal unit or ethnic background are keen to know more and more about genomic applications, particularly in healthcare and socioeconomic well- being. There is now the inevitable question of affordability and access faced by diverse populations in low and middle-income countries (LMICs). Global organizations, includ- ing the World Health Organization (WHO), Human Genome Organization International (HUGO), United Nations Educational and Scientific Organization (UNESCO), Global Genomic Medicine Collaborative (G2MC), Global Association for Genomics and Health (GA4GH), and Global Genomic Partnerships UK, are united to bring genomics and related technologies closer to the ordinary person anywhere on the World map.

The current volume, appropriately named Genomics, Populations and Society, addresses all issues included in the first edition. It goes further to discuss implications and impact of advances in genomic and OMIC diagnosis in common and rare diseases, high-order sensitivity and specificity to detect and treat many infectious diseases, and the availability of new drugs and devices. There is a great deal of assurance for equity and accessibility, economic security and viability, preservation of ethnic and sociocultural identity, data protection and ownership, digital health, and artificial intelligence. We are mindful of the fact that industry and private partnerships would be crucial for the globalization of genomics; however, difficult it might be given unavoidable socioeco- nomic and sociopolitical gulf between affluent western nations and LMICs.

We are grateful to world-class authors and contributors who have given their valuable time and space for writing superb text for this volume. We are very pleased and humbled to present this volume to professionals, society, and individuals around the world. It is inev- itable that by the time this book is made available to people, many new advances in knowl- edge and technology will be added. However, we are content that this book shares factual information and addresses core issues related to genomics and OMICs applications to medicine, healthcare, society, and populations at large. Finally, we are humans and thus gaps and errors remain ours alone. We eagerly wait to know the outcomes and place of this volume in genetics and genomics literature.

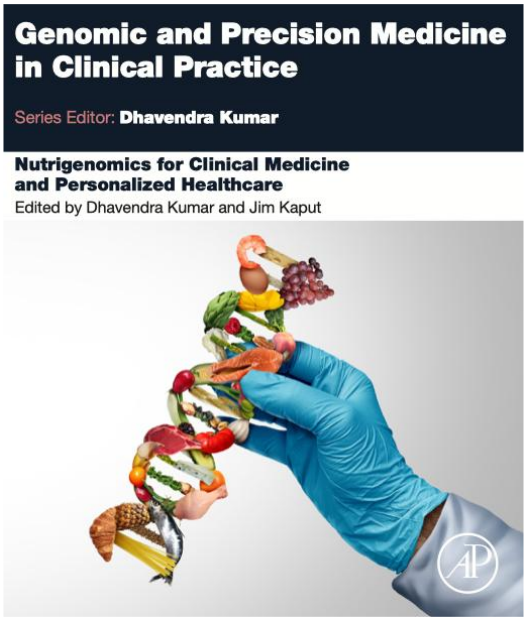
Editors

Dhavendra Kumar Ruth Chadwick

II Titles under development:

14.II.1 Nutrigenomics for clinical medicine and personalized healthcare
Eds. Dhavendra Kumar (UK) and Jim Kaput (USA)

This volume is dedicated to genetic and genomic aspects of nutritional factors underpinning optimal physical fitness and health. Individual's genetic and genomic make up and functionality determines how a particular nutrient is digested, assimilated and metabolized by the body. The ultimate point of any nutrient lies in the final utilization by the target tissue or organ of very specific biochemical ingredient harvested from the metabolic pool. Many aspects of the genome determine the nutritional value of a given nutrient, for example the glycaemic index of carbohydrates, bio-availability of nitrogenous compounds from protein rich foods, lipid absorption and transport from the gut and transport of iron and other trace metals important for cellular functions.



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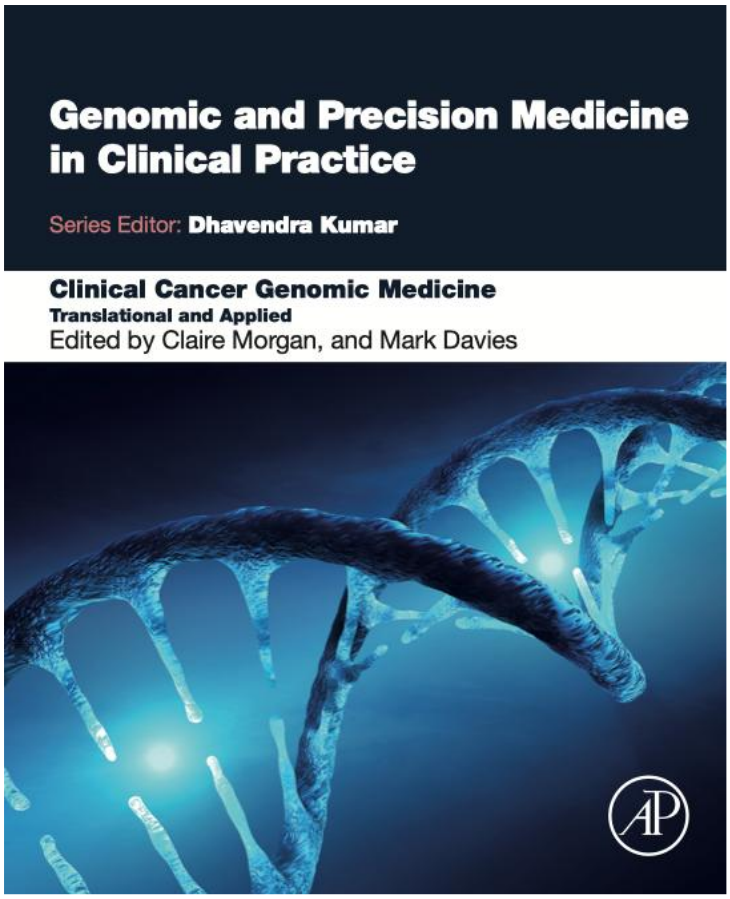
14.II.2 Clinical Cancer genomic Medicine

Editors: Claire Morgan and Mark Davies

The cancer is a genetic disease involving a number of genes, molecules and cellular structures. In most cases, these pathological changes result from life-long exposure to toxic, infectious and immunological factors. There is increasing evidence for underlying pre-existing, inherited or acquired, mutations and variants in a number of genes and their regulatory elements. The seminal 'two hit' theory explains the fundamental genetic and genomic basis of cancer aetiology and pathogenesis. This volume covers all major aspects of genetics and genomic aspects of cancer development, diagnosis, and management including the fast emerging stratified targeted molecular therapy in a number of common cancers.



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4. Cancer Evolution – Trevor Graham. Institute of Cancer Research, London.
5. Cancer and the microbiome- the Oncobiome-Paul Facey, Swansea.
6. Cancer immunogenomics - Awen Gallimore, Cardiff University.
7. Cancer pharmacogenomics – Dan Carr, MRC Pharmacogenomics, University of Liverpool
8. Genomic Technologies for Tumour Profiling - Phillipe Taniere, Birmingham.
9. New emerging technologies- The liquid biopsy – Tim Forshew, UCL, London, UK
10. Gene and genome editing - Ramsay Bowden, Medical Genetics, Cambridge.
11. Bioinformatics for Cancer Genome Analysis – Ezequiel Martin, Bilbao, Spain.

Section II: Clinical cancer genetics and genomics

12. Classification and epidemiology of the genetic and inherited cancer- hereditary cancer family syndromes- Shirley Hodgson, St George's Hospital Medical School
13. Breast cancer genetics & genomics- Gareth Evans, Genomic Medicine, St. Mary's Hospital & Univ. Manchester.
14. Ovarian, endometrial and related gynaecological cancers (David Church, Medical Oncologist Oxford- Endometrial; Neil Ryan (Bristol- Gynae Oncologist); Ranjit Manchanda (Cancer Research, QMUL)
15. Gastrointestinal malignancies- oesophagus, colorectal, hepato-biliary and pancreatic- Julian Sampson (Cardiff) plus others
16. Central nervous system tumours-Florian Siebzehnrubl. Cardiff University.
17. Neoplasia of endocrine system (Solitary and multiple)- Ruth Casey, Cambridge.
18. Ocular tumours- retinoblastoma- Catriona Duncan, Retinoblastoma Service, The Royal London Hospital & GOSH, London, UK
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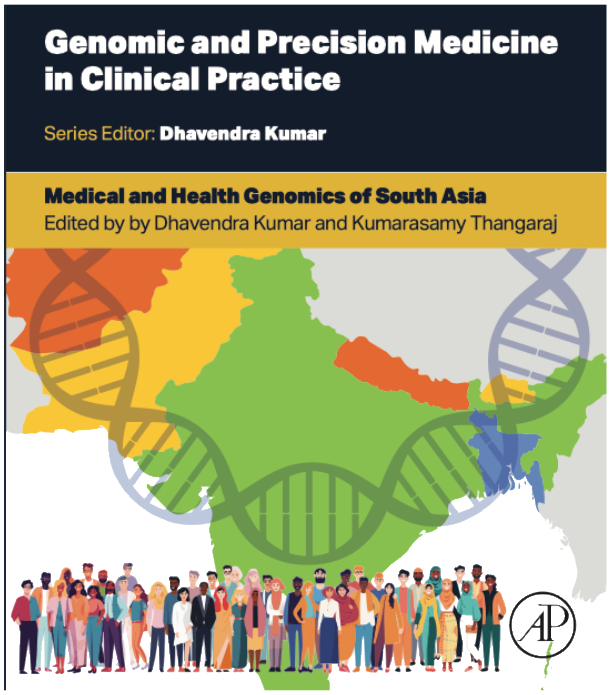
14.II.3 Medical and Health Genomics of South Asia
Eds: Dhavendra Kumar and Kumarsamy Thangaraj

Since the complete sequencing of the human genome, many aspects of genomic applications have emerged, notably in medicine and healthcare. Most of these developments are western centric with benefits harnessed by 'high income' nations. There is acute shortage of information and population specific knowledge base applicable to 'low and middle income nations' or politically described as 'emerging economies of the developing world'. This new book proposes to fill the gap for massively heterogeneous South Asian (including South-East Asians) peoples to assist integration of genomic advances in medical and healthcare practices. The book is in line with the '*Genetic disorders of the Indian subcontinent*' (Kluwer-Springer,2004,ISBN-10-1402012152] and the '*Genomics and Health in the Developing World*' (Oxford University Press, 2010, Monographs on Medical Genetics' series, ISBN-13-978-0195374759], both edited and co-authored by Professor Dhavendra Kumar. Both these books were developed and written by the team of experts from all over the world, specifically in several developing nations. The central theme being the genetic and/or genomic variation and population heterogeneity in the context of inherited or potential genetic diseases.

The proposed new book focuses on basic genomics and OMIC sciences as applied to human health, the human population anthropological and genomic diversity of South Asian peoples, the epidemiology of genetic and genomic diseases, harnessing gains of genomics to combat major health challenges in South Asia, in depth analysis on the status of genomic healthcare infrastructure, and closely examine the pertinent social, ethical, legal and economic instruments required to implement genomic medicine and genomic healthcare . It is designed on the multi-author edited format. Specific sections on introduction to common and rare genetic or hereditary diseases, current and rapidly evolving genetic and genomic

applications in medicine and healthcare, and the socio-cultural, economic, ethical, legal and regulatory factors prominently feature as well. The underlying aim and remit of the book is to produce a leading reference text resource on detailed annotated genomic information pool correlated with the diverse South Asian population heterogeneity.



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III Other proposed titles under consideration

14.III.1 The Human genome- Organisation and Function

This volume covers basic scientific and biological aspects of the human genome in its entire structure and function.

14.III.2 Laboratory Genomic and Molecular Medicine

This volume covers all laboratory methods of genome sequencing, an essential component of the genomic and precision medicine. Description and interpretation of the genome sequence changes and variation are central to the applied and translational genomics.

14.III.3 Microbial genomics and Pathogenomics

This volume covers genomic structure of major categories of microbial organisms with emphasis on all major pathogens underpinning infectious diseases. It also includes a section on genome based drugs and vaccines discovery and development.

14.III.4 Clinical genomics and genetic counseling

This important volume sets out principles and practice of clinical genomics and genetic counseling that are established specialist medical disciplines. Genetic & Genomic physicians, genetic/ genomic specialist nurses and genetic counselors are skilled professionals dealing with a number of common and rare genetic diseases with the focus on genetic/genomic diagnosis. In addition, other tasks include assessing the genetic risks and impact on close and extended family members, assisting and delivering the diagnostic and predictive genetic/ genomic testing, actively contributing to the management and treatment of a number of inherited/ genetic diseases as a key member of the multi-disciplinary team and actively contributing to the genetic/ genomic education and training of fellow clinical and healthcare professionals.

14.III.5 Genomic and Molecular Dysmorphology

This volume deals with clinical dysmorphology with particular reference to heterogeneous rare diseases of diverse etiology and pathophysiology. Most, by definition, are rare assessed by the incidence and prevalence. Genetic and genomic factors are heterogeneous and variable in these disorders. Apart from a number of physical congenital anomalies, many such diseases manifest with complex, life threatening functional morbidity. In this volume emphasis is given on mutations & variants in specific genes and the impact and pathological significance of genomic structural changes (single nucleotide polymorphisms, copy number variations, genomic microdeletions and genomic microduplications).

14.III.6 Genomics of complex disorders

There are many common medical multi-system disorders with complex aetiology and pathophysiology. In most cases, the precise causation is unknown. Examples include obesity, type 2 diabetes mellitus, age-related macular degeneration, Alzheimer's dementia, epilepsy, schizophrenia, bipolar depression, coronary artery disease,

bronchial asthma, essential hypertension and some common skin conditions such as eczema and psoriasis. Conventionally most of these conditions are described as multi-factorial determined by the complex interactions of underlying several hundreds and thousands of genetic/ genomic factors with a range of environmental factors and challenges, commonly referred to as the polygenic inheritance pattern. The advent and increasing use of the genome sequencing have led to much better understanding and appreciation of the heritability in many complex diseases.

14.II.7 Reproductive and fetal genomics

One of the major outcomes of the genetic and genomic medicine is the primary prevention of the genetic risks through informed choices and making decisions on reproductive options. In addition, diagnosis and interventions for male factor infertility and female infertility help the aspiring couple to consider appropriate route for achieving a successful pregnancy. Many procedures are available backed up by genetic and genomic testing including maternal serum screening for chromosomal aneuploidies, non-invasive prenatal diagnosis, conventional prenatal diagnosis by chorionic villous biopsy and amniocentesis and fetal blood sampling. Newer genomics led methods include pre-implantation genetic screening (PGS) and testing (PGD). This volume is dedicated to focus on all genomic aspects of reproductive and fetal medicine.

14.II.8 Ophthalmic genomics

Blindness at all ages is a global health problem with huge socio-economic impact. Apart from infections, vitamin A nutritional deficiency, immunologic eye conditions, toxic exposures, accidents and occupational hazards, genetic and genomic factors are implicated in a number of congenital and later onset medical conditions manifesting with progressive vision loss. This volume covers common Mendelian and complex eye genetic disorders with discussion on genomic variation and links with age-related degenerative eye conditions.

14.II.9 Neurology and Neuropsychiatric genomics

Genetic ad genomic factors are abundant in the pathogenesis of a number of early and late onset neurological and neuropsychiatric disorders. In addition to classic single gene neuro-muscular diseases, there are many complex diseases of polygenic/ multi-factorial nature where recent whole genome exome and full sequencing have revealed single nucleotide polymorphisms, copy number variation and novel specific gene changes. This approach has led to many critical genomic regions etiologically important for a range of neuro-psychiatric conditions. This volume provides critical and balanced review on the clinical status of genomic neurology and neuropsychiatry.

14.II.10 Mitochondrial genomics

In addition to the nuclear genome, the mitochondrial genome is a major component of the human genome. The nuclear DNA (nDNA) is distinct from the mitochondrial DNA (mtDNA) where intervening non-coding sequences (introns) are absent and coding sequences are critical for the assembly of a number of transfer RNAs (tRNA) and ribosomal RNAs (rRNA). The mtDNA molecule is compact and arranged in circular manner. Most mtDNA is confined to energy rich tissues and organs, like brain, eyes, heart and muscles. Specific mutations and variants in the mtDNA are known for a number of complex multi-organ disorders. These are matrilineal and could not be passed on by an affected male. Moreover, the distribution of mtDNA wild and mutated copies may differ within different organs and tissues, termed as heteroplasmy. However, similar clinical picture could result from nDNA sequence changes that impact on the mitochondrial function. This volume presents the whole field of mitochondrial genomics with clinical examples encountered in contemporary medical practice. Discussion on preventive and therapeutic aspects of mitochondrial disorders is also highlighted.

14.II.11 Clinical Immunogenomics

This volume deals with genetic and genomic aspects of the structure and function of the whole immune system. Apart from few rare immune deficiency disorders, majority conditions result from complex antigen and antibody interactions that are to large extent depend on many genes and polymorphic variants underpinning the T-cell dependent immunologic function. In addition to many auto-immune and iso-immune diseases, genetic and genomic factors play a significant role in the monoclonal antibody production that are central to targeted therapy for few cancers.

14.II.12 Therapeutic genomic medicine- Gene therapy (including genome editing) and Cell therapy (stem cell and somatic cell)

This volume deals with many treatment modalities for genetic diseases and circumventing or correcting the genetic or genomic aberrations that underpin complex medical conditions or adverse and unwanted outcomes of the drug therapy, particularly for neoplasia. Most gene therapy trials have failed to yield satisfactory or even any promising outcomes. Now the emphasis is laid on gene/ genome editing using the Cas9/CRISP-R approach. However, these are mostly in very stages of development. Genomic basis of the cell therapy, using stem cells derived from either embryonic or somatic cells, has gained momentum and currently explored in many clinical trials. These novel approaches feature in this volume.

14.II.13 Epigenomics and Medicine- structure, function and human diseases

Within the genome, a number of regions, in close proximity to the promoter areas of genes, make an important part of the genome system identified as the epigenome. This region, through complex molecular mechanisms, regulates switching on and

turning off genes confined to most somatic cells. Such molecular mechanisms include methylation and histone modifications. Some of these mechanisms are specific to 'parent of origin', the basis of 'genetic imprinting'. Some inherited disorders are determined through parental genetic imprinting and are important for phenotypic variation. The field of epigenomics has gained importance and applications in 'transgenerational transmission' of certain physical and behavioural phenotypes and outcomes of therapy. This volume covers some of these important aspects of epigenetics and epigenomics.

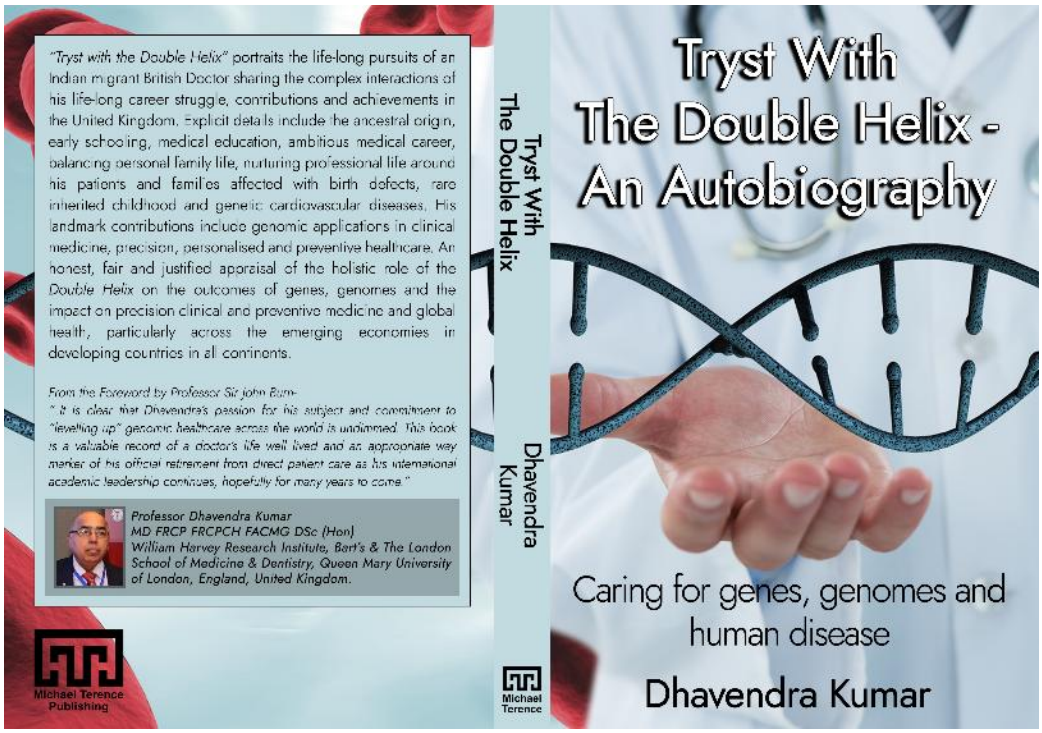
14.II.14 Toxicogenomics and Ecogenomics

Adverse physical and functional outcomes of exposure to toxins (including poisonous substances) largely depend up on the nature, duration, pattern, dosage and adjuvant factors. To some extent, this might also depend on the stage of development, age, gender and probably the genetic or genomic make-up of the individual. Increasingly, importance of the individual's genomic variation is agreed crucial for the outcome, for example anti-convulsant teratogenic effects, fetal anomalies born to diabetic mothers, risks of neonatal onset neoplasia argued with parental occupational exposures to hydrocarbons and many other examples. Increasingly, there is concern attached to environmental pollution, global warming, deforestation and many other ecological changes. Individual genomic variation is believed to be central to adverse outcomes. This volume features the genomic basis of adverse physical and behavioural outcomes to toxins and ecological changes.

14.II.16 Pharmacogenomics and Targeted Pharmacotherapy

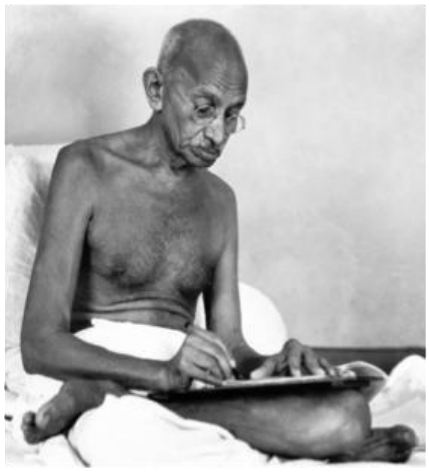
In this volume, basic and applied aspects of pharmacogenetics and pharmacogenomics are discussed. This field has gained major importance in genomic and precision medicine that aims to deliver personalized evidence-based pharmacotherapy. There is now abundant genomic variants data and evidence on many drugs for both positive (safe and effective benefits) and negative (adverse drug reactions and unwanted side effects) outcomes. Recent applications of specific and highly expensive anti-cancer and other medications have established importance of genetic/ genomic testing for efficient and effective targeted molecular therapy. This approach is also discussed under the broad remit of stratified and personalized medicine.

15. 'Tryst with the Double Helix'- An autobiography: Caring for Genes, Genomes and Human Disease. Michael Terrence Publishing, Kindle Books, Dec. 2020



The author, Prof. Dhavendra Kumar, revisits his life, family and peers and describes in detail his journey and quest on the double helix, the fundamental unit of the biological life. Key aspects of the autobiography are included here.

Dedication



"Scientific knowledge requires constant probing into the why and wherefore of every little process that you perform"

Mahatma Gandhi
(Mohan Das Karamchand Gandhi)

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Foreword

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Tryst With The Double Helix - An Autobiography
by Dhavendra Kumar

It is an honour and a pleasure to be invited to introduce this autobiography by my friend and long term colleague Dhavendra Kumar. Our lives have followed a parallel path in the specialty of Clinical Genetics; I began formal training at the Hospital for Sick Children Great Ormond Street, London with Professor Cedric Carter in 1980, a few months after Dhavendra arrived in England and began his training in Sheffield. We were fortunate to have arrived at the beginning of what was a golden era for clinical genetics, when the DNA revolution was finally impacting on diagnosis but was still heavily dependent on clinical acumen to target limited resources.

For most of the world, little has changed. While Dhavendra was making his contribution to the advances in the latter part of the 20th century, healthcare in Low and Middle Income Countries saw little impact. The autobiography documents the challenge and opportunity in India along with discussion of how he and his family were shaped by the environment there, not least in the prestigious Lucknow's King George's Medical College where young doctors can be now appreciated and win an award in his name.

As the 20th century became the 21st, the term Genomics became commonplace; looking at the "big picture" was the all-embracing theme but entirely complimentary to the approach of genetics in studying clinical patterns among familial traits, just as routinely looking at chromosomes had stood alongside clinical examination in our early careers. The difference

made by the power of next generation sequencing began to impact on an ever broader spectrum of clinical care and Dhavendra records how his own practice shifted to follow this trend and how he focused on the major clinical need of applying these new technologies to the care of families with an inherited predisposition to cardiac disease.

The focus on Cardiac Genetics became Dhavendra's strongest professional focus as his clinical practice evolved with moves from Sheffield to Oxford and on to the Institute of Medical Genetics in Wales, finally being rewarded with an honorary chair at the prestigious William Harvey Research Institute at the Barts and London School of Medicine & Dentistry to recognise his lifetime contribution. He records how his love of India and academic contributions to the practice of genetics there came together in his role as editor of the Oxford Monograph *Genomics and Health in the Developing World* and later with his ongoing engagement with the Human Variome project to develop his Global Familial Heart Challenge.

The most striking feature of this autobiography is Dhavendra's drive and commitment to writing so many books; in an era of instant access to online information, it is worth noting the continued value of books in science. Whether from a single author or editorial efforts to corral busy clinicians and scientists into producing timely chapters, it is easy to forget how valuable these distillations of knowledge and experience can be for the student and healthcare practitioner alike. Equally important is the discipline their composition imposes on clinical academics, forced to distil their opinions and test them in print.

It is clear that Dhavendra's passion for his subject and commitment to "levelling up" genomic healthcare across the world is undimmed. This book is a valuable record of a doctor's life well lived and an appropriate way marker of his official retirement from direct patient care as his international academic leadership continues, hopefully for many years to come.

About the Author

Professor Dhavendra Kumar
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-Institute of Life Sciences, School of Medicine, Swansea University, UK

My parental home was in the northern Indian city of Moradabad, in the State of Uttar Pradesh, where I was born. After finishing primary and education secondary education in the State run Government Intermediate College, Moradabad, I studied Medicine and postgraduate medical training in Paediatrics at the King George's Medical College, Lucknow, Uttar Pradesh, India. In 1979, I moved to Britain aspiring higher specialist training in Paediatrics or a related medical field.

As an acknowledged genetic and genomic clinician, accredited in the UK and USA, I practised clinical genetics with special interests in genetic diseases of children, inherited conditions of heart and blood vessels, genomic medicine and genomic applications in global healthcare. Following my retirement from the National Health Service, my clinical interests in genetics and genomics continue with more focus on consultancy and advisory sectors.

Professionally acknowledged and complimented now as an author and editor of several textbooks and monographs in the field of clinical genetics, cardiovascular genetics and genomic medicine & healthcare. Main titles include ***'Genetic Disorders of the Indian Subcontinent'***, '***Principles and Practice of Genomic Medicine'***, '***Cardiovascular Genetics & Genomics- Principles and Clinical Practice'***, ***'Genomics and Health in Developing World' and 'Clinical Molecular Medicine-Principles & Practice'***. My two books, '***Oxford Specialist Handbook on Inherited Cardiac Disease'*** and '***Medical & Health Genomics'*** were highly commended at the British Medical Association Annual Medical Book Awards. Current genomic editorial roles include, Chief Serial Editor for '***Advances in Genetics***', editorial board of many biomedical journals and the founding *Editor-in-Chief* of the new cardiovascular medicine journal- '***Genomic and Molecular Cardiology***'. The new genomic medicine series, '***Seminars in Clinical Genomic and Precision Medicine***' is the highlight of my continued efforts in bio-medical scientific publishing.

Fast emerging virgin field of the cardiovascular genomic medicine is exciting and I am passionate for raising its awareness and importance in the context of inherited cardiovascular conditions (ICC) in the clinical cardiology practice. My peers and colleagues acknowledge my passion for the benchmark practice of 'multi-disciplinary care for inherited/familial heart disease'. In this context, I founded and lead the '***Global Familial Heart Challenge***' project for promotion; early detection, management and prevention of familial/ inherited heart diseases globally.

The niche area of genomic education and training is attractive to me with opportunities for new post graduate courses (MSc, Diploma and Certificate) in the Cardiff University, the University of South Wales, Swansea University and equivalent courses sponsored by the Health Education England. My commitment for genetic and genomic education is evident by the ***Indo-UK Genetic Education Forum*** that I founded and lead. This project is expanded as the ***UK India Genomic Medicine Alliance*** (***UKIGMA***) contributing to India's efforts in areas of genomics and bio-technology. I am fortunate to continue and expand my links with the mother India through active participation in few collaborative projects, mainly the *Genome India, UK-India Health Data and Bio-informatics Joint Centre, and Global Summit of Indian Overseas Researchers and Academicians – the* ***Vaishvik Bhartiya Vaigyanik 'VAIBHAV'*** *Summit 2020.*

In keeping with my roots and natural inclination, I am passionate for high quality healthcare in developing nations, particularly harnessing the benefits of genetics, genomics and biotechnological advances and new

developments. The new project, the ***Global Consortium for Genomic Education (GC4GE)*** aims to enhance and empower healthcare providers in the developing world through genetic/genomic education and training. Pursuant to this initiative, I am actively engaged with a number of global genomic medicine initiatives of the Human Genome Organization International (***HUGO***), Global Genomic Medicine Collaborative (***G2MC***) and Genomic Alliance for Global Health (***GA4GH***). I founded and lead the **Genomic Medicine Foundation (UK)**, promoting genomic applications in medicine, healthcare and socio-economic welfare through scholarship and fellowship.

Acknowledgements

It is uncommon for someone to progress and build a life-long career without inspiration and support of family, friends and colleagues. I am no exception. I was fortunate to have very good schoolteachers who encouraged me and offered timely advice at different stages. The early part of medical school period was difficult but later on I came across good teachers, particularly Prof. KP Bhargava, the Head of Pharmacology and Therapeutics, King George' s Medical College (now University). He not only guided me on the subject but also encouraged me to edit the first issue of the Journal of the *King George's Medical College Pharmacological Society*. This was my first 'hands-on' experience of writing and editing that later on manifested with desire to write and edit for a bigger audience. During the postgraduate paediatric training, I owe deepest regard and gratitude to the late Professor P.C. Bajpai, who as a mentor guided me to plan and structure the project for my MD thesis. Unfortunately, he passed away before I could finish the MD. The other two deserving names include the Late Prof. N.L. Sharma, Head of Paediatrics and the Late Prof. P.K. Misra, excellent clinicians and teachers, offered me advice on developing clinical and academic career in Paediatrics.

Moving on from Paediatrics to Medical Genetics was a challenge and risky business. I had no idea of genetics as it was not taught at all even at the MD level, where only occasional reference was made of basic inheritance patterns and few common chromosomal disorders. I was fortunate to be surrounded by a big team of laboratory scientists and gradually build up my genetic knowledge base. Among many colleagues, Diana Curtis, Tony Potter, Gordon Lowther, Ann Dalton, Margaret Smith deserve appreciation and acknowledgement. Dr. Charles Eric Blank, my boss and the Head of the Sub-Department of Medical Genetics, University of Sheffield and Director of the Centre for Human Genetics was instrumental to put me on the British Clinical Genetics platform. He was unique as a medically qualified human geneticist with strong mathematical skills that he always enjoyed to apply in simple clinical situations. Not only I learned basic human genetics, I gained a lot from the clinical freedom that he allowed me to enjoy throughout my long tenure in Sheffield.

There were many others outside my work base who helped me to establish in medical genetics including Dr. John Fitzsimmons

(Nottingham), Prof. Ian Young (Leicester), Prof. Mike Patton (London), Prof. Andrew Read (Manchester), Prof. Dian Donnai (Manchester), the Late Prof. Robin Winter (London), Prof. Judith Hall (Vancouver, Canada), Prof. Julian Sampson (Cardiff) and Prof. Sir Peter Harper (Cardiff). The list is too long to mention here. I will always remain indebted to them and many others not listed here.

In February 2003, I was invited as a Guest Speaker at the Annual Conference of the Indian Society of Human Genetics held in the city of Jammu in the northern Indian state of Jammu & Kashmir. The souvenir gift happened to be a brass double helix mounted on the globe. I always cherished it and used the double helix model in the genetic clinic. While searching for the cover design for this book, I decided to take its photo with my stethoscope, a perfect illustration of my long career as a basic medical doctor caring for genes, genomes and human disease.

The most successful and rewarding period of my career began in Oxford where brief encounters with Prof Sir David Weatherall and other eminent geneticists and medical academics allowed me to focus into entirely new directions. Prof. Weatherall's visionary and brilliant approach to the whole field of clinical genetics and genomics has been instrumental in planning and producing many books and setting up new genomic journals. In the clinical context, I owe my gratitude to Dr. Susan Huson, the Consultant in Clinical Genetics in Oxford, who offered me professional space and invaluable support. Her confidence in me and friendly manner had no match.

I am grateful to several people in Cardiff and other parts of Wales. I am indebted to Drs. Jonathan Gray, Sally Davies, Annie Procter, Mark Rogers, Ian Frayling and Prof Daniela Pilz. Prof Julian Sampson provided much necessary academic impetus to me and supported my many activities that helped me to perform better on the national and international platforms. Prof. Angus Clarke is perhaps the most loyal and understanding colleague, who not only contributed many chapters in my books but offered timely wise advice whenever I needed. Prof. Maggie Kirk, Director of the Genomic Policy Unit at the University of Glamorgan (now University of South Wales) very kindly included me in her academic team as the Visiting Professor. This affiliation proved to be extremely helpful in developing the 'multi-disciplinary team' model for delivering the inherited heart conditions service. Prof. Ruth Chadwick, the Director of the Cardiff & Lancaster University Centre for Social and Economic Applications of Genomics (CESAGEN) welcome me as an external observer helping me to develop

invaluable insights into social, cultural and economic aspects of genomic medicine.

During all struggles and tasting successes, I always remembered my father who passed away at the very early stage of my career in medical genetics. He had high expectations from me but could not live long enough to relish and appreciate whatever I have managed to achieve. I dedicate my books to his lasting memory. Blessings of my mother and my elder brother were always with me who supported me throughout the medical undergraduate course.

Last but not the least, I have no words to express deep affection and gratefulness to Anju, my wife and dearest life-companion who quietly but firmly supported me throughout in the long pursuits of building career as a clinical geneticist. My children Ashish and Nikita were always looking on me with clear hope and confidence that their father would not disappoint them.

Finally, I am always grateful to many friends, colleagues, and many unknown people who blessed me for my successful life and career.

1:

The Prologue

Many people around us, particularly with limited knowledge of science, talk loosely about *DNA* or inadvertently state, '*it's all in genes*'! I often wonder if they had any idea about genes and what actually happens in real life? Do they know about the Watson-Crick's *double helix*? How many would have slightest idea of the Nobel Laureate Har Gobind Khurana's *genetic code*? We are now going through the exciting phase of *genomics era*. People and politicians rather loosely talk about genomics led *precision and personalized medicine*. Not surprisingly many more are excited on prospects of genomics helping to create designer babies, offering cure for untreatable cancers and many diseases and doing unimaginable wonders. Young students of life sciences and related technologies get very excited just to imagine that they too could study genetics and genomics and be part of all these fantastic new scientific developments.

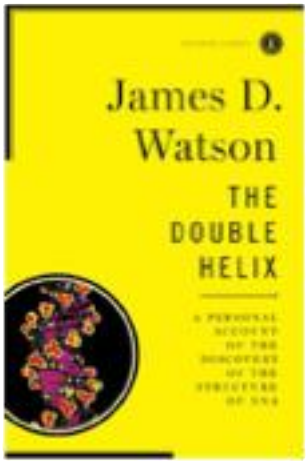


Figure 1.1: Front cover of 'The Double Helix' by James D. Watson, the co-discoverer of the double helix, with personal account of events leading to the model of DNA double helix
(Downloaded from the online Public resource)

I had never imagined that the large part of my working life would be spent studying the marvels and dealing with many challenges of the double helix, perhaps one of the most precious particles on earth, probably next to atom of the physical matter. Like many others, I also had heard about mixed accounts related to the discovery of the DNA double helix. One evening, I accidentally saw part of the Hollywood movie made on events and personal account of James Watson himself (Figure 1.1). My first impression of simple line drawing of it was not too impressive but nevertheless very intriguing and stimulating (Fig. 1.2).

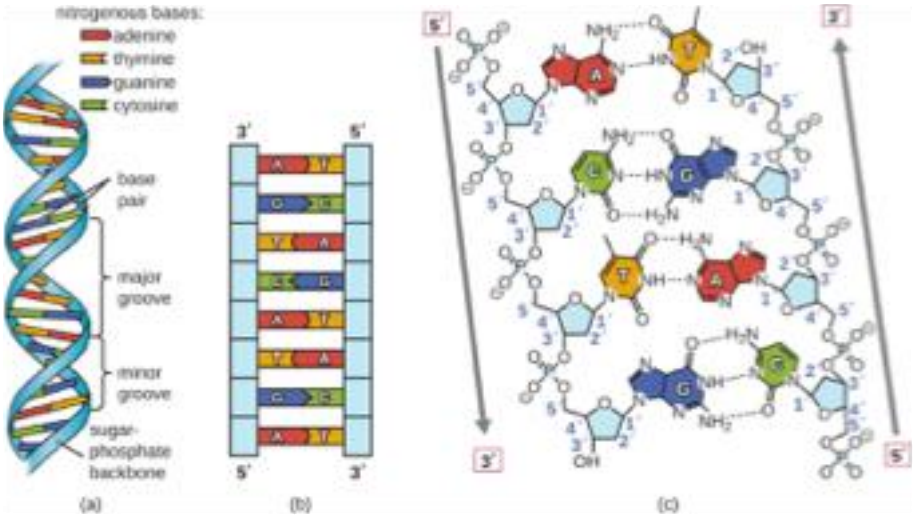


Figure 1.2: Watson-Crick Model of the Double Helix; note arrangement of the four bases (nucleotides) in perfect order- adenine-thymine & cytosineguanine supported by the sugar (deoxyribose) and phosphate backbone. (Courtesy of Google Images).

It took many years before I could fully grasp the structure and functional impact of the double helix. In fact it has not yet finished. In addition, I became aware that the whole genetic and genomic structural arrangement in the nucleus is multi-helical supercoiled chromosome assembly starting from the basic double helix (Figure 1.3). It remains a big challenge how to make the best use of different helical structures in diagnosis and management of diverse range of genetic diseases. Perhaps I was in a unique position as a clinician and not a career life sciences scientist. I dwelt with it on several occasions with different objectives trying to find answers and explanations for my patients and their close relatives worried about the potential risks of an incurable genetic disease. After having spent 40 years unraveling the enigma of the double helix, my wife, family and friends

compelled me to share my own experiences and challenges on pursuing a long helical career around the famous double helix of the core of genetics.

Series of my recollections and reflections provide a glimpse of my family, my early schools years, experiences and challenges as a medical student, aspirations and hurdles of a junior doctor, ambitions and unclear paths for building a career in Medicine and conducting the right kind of research. As a growing young boy in a small town, called Moradabad in Uttar Pradesh, I had many such dreams but never thought I was destined to explore DNA and the double helix closely even without being a real scientist or biotechnologist.

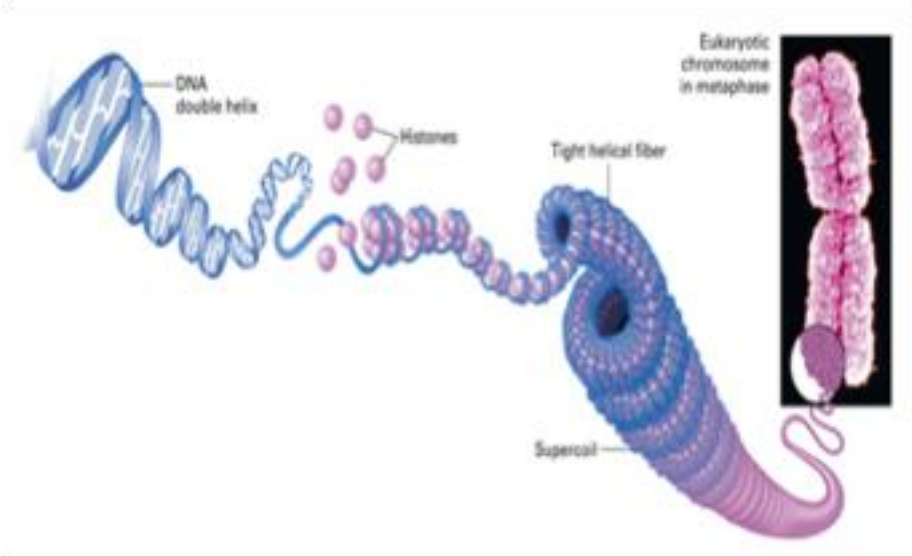


Figure 1.3: From the DNA double helix to tight helical supercoiled chromosome assembly in the eukaryotic cell
(Courtesy of the Institute of Medical Genetics, Cardiff University, UK)

Little insects, earthworm and plants always fascinated me. As a young inquisitive boy, I used to wander around parks, gardens and bushes browsing around and collecting some of these interesting creatures. However, I had no idea about how these beautiful living objects shared the most fundamental component called genes. When the Head of Biology in the Government Intermediate College in Moradabad agreed to sponsor me for the Science Talent Search examination conducted by the National Council for Education, Research and Training (NCERT), I began search for a project. I quickly decided to work on the beautiful butterfly. My head

teacher was equally very excited and offered me few practical tips. I carried through this interest and entered the famous medical college in Lucknow. I do recall, questions about genes and genetics were reserved for those who were picked up for the distinction. I had some idea about genetics and occasionally discussed with my classmates. However, I was never asked a question in any MBBS examination.

During my tenure in the Department of Paediatrics as a Resident Doctor and postgraduate MD student, I came across children presenting with rare and unknown genetic diseases. Most were labelled as *idiopathic*, clearly indicating a significant gap amongst all of us around that time. One case reminds me even today. This little baby, apparently disguised as a boy, had undetermined male or female external genital development. Clearly parents and the family were very distressed and received many illogical explanations. I was intrigued and spent some time on this child. My supervisor agreed that it could be one of the *hermaphrodite syndromes*? I wrote a detailed summary and referred the baby to an expert in All India Institute of Medical Sciences in New Delhi. It turned that baby, a female, had some degree of virilization due to a genetic defect. The baby's external genitalia development was corrected by relatively inexpensive steroids administration. I suppose it was my first clinical experience of a genetic syndrome. At that time I had not realized that it was the beginning of my long quest and life with genes, genome and genetic diseases.

It just happened that I have spent practically whole of my working life dealing with and talking about genes. As a medical geneticist it was my job, career focus and livelihood to live and raise my family. During the long tenure spanning forty years, I came across unusual looking children with varied chromosome abnormalities, babies born with malformed organs, young adults developing incurable diseases, common and rare cancers in the family, parents and families grieving following the loss of young children and adults dying suddenly from inherited heart disease and adults suffering from incurable dementia and nervous system diseases. The list is too long to fit in the available time and space.

This book is about my own biographical landscape of life-long quest for understanding the molecular biology of human health and disease. During the long pursuit dealing with several different kinds of inherited conditions, the most striking observation is the tremendous clinical variation and underlying varied pathogenesis. Heterogeneity, particularly the clinical and genetic, is the rule for most inherited disorders. To some extent this might also be true for non-inherited diseases.

I often reflect on progressing with new advances in genetics, particularly the laboratory diagnosis. My experience goes back to very early basic chromosome preparations, then moving on to striking chromosome painting and eventually to the contemporary chromosome microarray analysis. Following the completion of the Human Genome Project, the technology changed dramatically leading to the genome sequencing. It replaced very time consuming, labour intensive and inefficient genetic testing methods. I grew up with all these changes and could foresee which one had the potential for eventual acceptance in Medicine.

It is humbling to feel that my family, close friends and peers acknowledge me as an expert in medical genetics and genomic medicine. I am not sure if I am worthy of all these grateful appreciation and accolades. However, I feel strongly that it was certainly an act of destiny to put me right place and alongside probably the best people full of wisdom and knowledge of human and medical genetics. My publications and books are testimony of my contributions or services as a clinical geneticist with rapid unfolding of horizons of genomic medicine and healthcare.

My north Indian ethnic background and upbringing in a middleclass family helped me a lot in adapting to many facets of medicine and particularly to genetics. Moving away soon after MD in Paediatrics at KGMC was disappointing since I had hoped to carry on practicing and developing my clinical-academic career. The fact remains that I was destined to work and live in the UK. I tried to move to USA but it did not materialize despite obtaining the Board certification in clinical genetics. Many friends and colleagues simply assign it the pre-fixed appointments of life.

Working and living in a developed country like Great Britain with lots of European influence have been a real challenge. The huge gap that exists even today between developed and less developed nations is striking. I never felt comfortable with usage of terms like *developing nations* or *emerging economies*. Nevertheless, these descriptions always reminded me of the gap that needed to be filled or narrowed. I am fortunate to have found ways to explore and express my views on the importance of genetics and genomics for the benefit of people in these countries. My two books (*Genetic Disorders of the Indian Subcontinent* & *Genomics and Health in the Developing World*) are testimony to this belief.

Through the ***Tryst with the Double Helix***, I wish to recall key platforms and share my experiences of my long journey from the streets of Moradabad to the elegant campus of the King George's Medical College (now University), Lucknow and onwards to many cities and medical

institutions across England and Wales in the United Kingdom. I learned on the job about genes, genetics, genomics and many other related aspects. The *Double Helix* is not only the fundamental structural concept of the nucleic acid DNA, it also reminds us that one needs to be supported and nurtured to stand firm. For me the double helix is metaphorical. I often tell my close friends that it has been truly fascinating to grow and live life on the double helix or even multi helix. My *real life* examples and personal involvement with the challenges of incurable rare genetic diseases are unparallel. It's even more exciting for a clinician to progress with the faith and conviction of achieving the ultimate goal of effective and efficient medical and healthcare outcomes of genetics and genomics.

Through this biography, I have presented my clinical and professional experience and academic/ scientific contributions in many diverse aspects of human and medical genetics. The evidence and description of my clinical genetic experience is discussed in three separate sections. The first part includes selected published papers and articles with supporting evidence from the public domains as evidence for the scientific impact and clinical utility of my work. The second part includes evidence from a number of professional roles and activities that I was engaged with on different occasions. I have included examples where in my own judgement I was able to contribute reasonably enough to justify the time space used. The third section is about my current and future activities related to genomic medicine and healthcare with emphasis in developing nations.

With around four decades of clinical genetic experience in diverse categories of human morbidity and mortality anyone in my position might wonder whether it was worth it. The simple answer is absolutely YES! However, I am unsure I have fully grasped the molecular basis of common and rare human disorders that are conveniently called genetic diseases. I am sure many others like me do wonder and would carry on working with patients, families, clinicians, scientists, researchers and other professionals hoping to find answers and explanations with the help of new genomic technologies and bioinformatic tools. For me, I have the life-long mission for contributing to the global health care equipped with my life-long experiences and some understanding of human genetics and genomics. I look forward to achieving this through the new Genomic Medicine Foundation (UK) working in collaboration with international agencies including UNESCO, WHO, HUGO and the Global Alliance of Genomics for Global Health.

I sincerely hope and anticipate that my personal account and evidence presented would be in keeping with my life-long mission for understanding

Dhavendra Kumar 7

the molecular (genetic) basis of human disease for facilitating the evidence-based practise of clinical genetics and genomics. This mission is infinite and requires many lives. It will be up to my peers, genetic & genomic community and related professionals to conclude if I have used my time reasonably good enough to justify many years pursuing the above mission.

In finishing this introductory statement, I am reminded by the famous quote- "*ARS LONG VITA BREVIS*"- translated as '**ART IS LONG AND LIFE IS SHORT**', that is engraved on a large stone at the entrance of the Sheffield University Medical School, where I began my mission and career in Medical Genetics. My saga of the *Double Helix* will never end and someone else would come forward to take baton with more examples and impressive record.

XI FOUNDED AND EDITOR-IN-CHIEF OF GENETICS/ GENOMICS JOURNALS-

1. ***The HUGO Journal*** (formerly- Founding Editor in Chief ***Genomic Medicine***), Springer, Dordrecht, The Netherlands.

The HUGO Journal- Official Journal of the Human Genome Organisation

In August 2007, a new bio-medical journal ***Genomic Medicine*** was launched to capture the key developments in genome sciences and technologies relevant to medicine and human health. Since then, several major journals emerged also to compete in the same conceptual space. Because, many of the leading biomedical journals are affiliated with major organizations (for example, the EMBO Journal, Journal of ASHG, Journal of ESHG, National Academy of Sciences, etc.), the future of Genomic Medicine depended on successful partnership with an institution or organization. In 2008, the Human Genome Organisation

(HUGO), one of the leading international science organizations, entered discussions with Springer (the publisher for Genomic Medicine), and the Editorial leadership of Genomic Medicine, to assume responsibility for the journal. This proposal was formally accepted by the governing HUGO Council held at the HGM2008 conference in Hyderabad, India (2008), and by the broad editorial board of Genomic Medicine. This merger was viewed as mutually beneficial to ensure a unique place for a journal in the competitive area of genomic medicine, and to provide HUGO with a publication vehicle for its concepts and ideas. The journal was renamed The HUGO Journal and re-branded as the official publication for this international organization. The initial leadership of the journal was to be shared by Dhavendra Kumar (University of Cardiff), and Edison T. Liu (President, HUGO).

The scope and remit of The HUGO Journal is very wide and includes:
Genomic sciences and human disease: e.g., pharmacogenomics, cancer genomics, genetics of Mendelian disorders, genetics of complex diseases
Genome structure and genetic variation
Comparative genomics between humans and other organisms
Microbial genomics of organisms pertinent to human disease
Population genetics
Human evolution and migration
Genome-to-systems strategies in systems biology
Genomic technologies
Genomics and genetic epidemiology
Computational genomics
Ethical, legal, and societal research relevant to genomics and human genetics
Science policy analyses pertinent to genomics and genetics
Genomic and genetic research from emerging and developing countries
[Kumar and Liu (2009). The emergence of the HUGO Journal. Hugo J. 2009 December; 3(1-4):1–2]

2. "***Applied and Translational Genomics",*** Elsevier, Online & Open Access

Founding Editor-in-Chief of *Applied &Translational Genomics*, a new open access biomedical journal providing a forum for discussion and publication of cutting edge research and new developments in all aspects of applied and translational genomics. The remit of the journal is

broad to provide a wide coverage across applied genomics and translational genomic research and applications in medicine, health, biotechnology and bio-economy.

The journal publishes reviews and original research papers in many genomic areas including- Comparative genomics • Applied bio-systems • Applied biotechnology (laboratory development and support) • Clinical cytogenomics (molecular cytogenetics) • Clinical genomics (diagnostics) • Genomic and personalized medicine (evidence-based medicine) • Public/population health (Screening and targeting selected population; large scale infection control and preventive measures) • Pharmaceutical industry (new drugs and vaccines) • Pharmacogenomics • Plant and crop genomics (Agricultural genomics) • Marine genomics • Animal and Veterinary genomics • Bio-economy • Education and media (professional and public education; bio-information through on-line/media resources) • Ethical, legal and social issues in translational genomics • Legal and Regulatory including Intellectual property rights

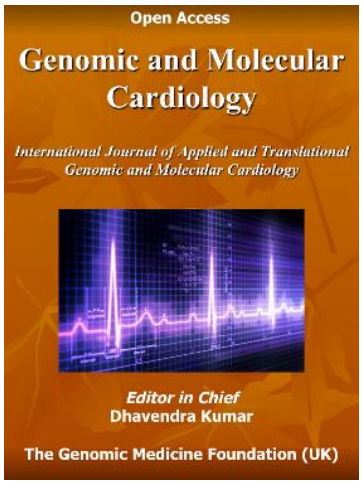
3. "***Current Trends in Genomic Medicine***", Genomic Medicine Foundation (UK)

Founding Editor in Chief: Open access journal for publishing state of the art articles and research papers on recent advances in genomic medicine

The '**Current Trends in Genomic Medicine'** is a new international journal aimed at providing and communicating knowledge and developments in the field of the science of genetics and genomics as applied to human health. It will include major issues in the fast developing practice of medical and clinical genomics, drug discovery and development, and other related developments relevant to promoting human health and prevention of disease. Emphasis will also be on ethical, moral and legal matters as applied to genomics and human health. A separate section will cover public interests, including media coverage of key and controversial topics related to public health and government policies on genomics based health service.

4. ***" Genomic and Molecular Cardiology***"- Genomic Medicine Foundation (UK)

Founding Editor in Chief: Open access journal for publishing state of the art articles and research papers on recent advances in applied cardiovascular genetics and genomics.



The '**Genomic and Molecular Cardiology'** is an open-access online journal publishing original research, meta analyses, reviews, case commentaries and updates on recent development focusing on genetic and genomic aspects of wide range of cardiovascular conditions. Apart from genomic aspects, the journal also features molecular basis of diverse cardiovascular conditions with particular emphasis on inherited cardiovascular conditions.

The journal particularly focuses on delineation of the clinical phenotypes, new genes and variants, genotype-phenotype correlations, basic and clinically applied molecular genetics, next generation sequencing and new therapeutic developments (drugs & devices). The original cardiovascular research will highlight the omics: proteomics, metabolomics, functional genomics and systems biology – as well as clinical trials in the burgeoning field of pharmacogenomics related to cardiovascular medicine.

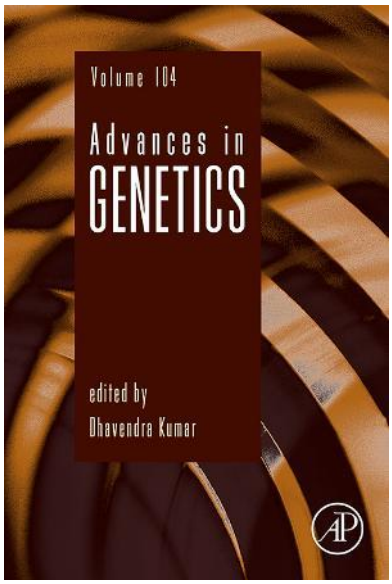
The journal also features current and comprehensive reviews in the areas of recent advances in cardiovascular development, Mendelian cardiovascular conditions, new diagnostic and therapeutic progress, and controversies in cardiovascular genetics. A dedicated news section summarizes the new developments in the field, highlighting articles likely to impact the management of cardiovascular disorders. Other features include clinical case reports and studies, book reviews, and letters to the editor.

5.Editorial roles in other Journals

1. Series Editor- 'Advances in Genetics', Academic Press, Elsevier, The Netherlands 2016 to 2021; volume 101 to 108

Current Serial Editor of this original and highly reputed reviews serial focussing on key and seminal areas of genetics and genomics research. Commencing from volume 101, the series has so far published five volumes encompassing molecular evolution, plant genetics, cancer

genetics and developmental genetics. The series includes both thematic (Volumes 101 & 102) and mixed reviews (Volumes 103, 104, 105 & 106). Other volumes under development include thematic volume 106 on Cosmic Genetics and general volume number 107.



2. Associate editor- Journal of Translational Medicine, Springer/ BMC
Section Lead for Clinical Genetics- 2000 to 2018

Journal of Translational Medicine is an open access journal publishing articles focusing on information derived from human experimentation so as to optimise the communication between basic and clinical science.

3. Associate editor- Journal of Genetics, Indian Academy of Sciences, Springer
Section Lead- Clinical Genetics from 2015 to 2019

The *Journal of Genetics* is among the oldest English language journals in genetics. The journal covers all areas of genetics and evolution, including molecular genetics and molecular evolution. The journal retains its traditional interest in evolutionary research that is of relevance to geneticists, even if it is not explicitly genetical in nature. It publishes research papers and reviews articles on current topics, commentaries and essays on ideas and trends in genetics and evolutionary biology, historical developments, debates and book reviews. The journal also publishes 'Resources', which are brief reports on the development and use of molecular markers for assessing genetic variability, short notes on useful software or modifications to techniques, and descriptions of pedagogical aids and methods in genetics teaching.

4. Associate Editor- The Physician, Official Journal of the British Association of Physicians of Indian Origin (BAPIO); from 2018 to date

The journal covers all areas of genetics and evolution, including molecular genetics and molecular evolution. The journal retains its traditional interest in evolutionary research that

is of relevance to geneticists, even if it is not explicitly genetical in nature. It publishes research papers and reviews articles on current topics, commentaries and essays on ideas and trends in genetics and evolutionary biology, historical developments, debates and book reviews. The journal also publishes 'Resources', which are brief reports on the development and use of molecular markers for assessing genetic variability, short notes on useful software or modifications to techniques, and descriptions of pedagogical aids and methods in genetics teaching.

5. Editorial assistance through peer review

- Journal of Medical Genetics
- European Journal of Medical Genetics
- Clinical Genetics
- The Lancet
- American Journal of Medical Genetics
- European Journal of Human Genetics

XII PRESENTATIONS (CONFERENCES/ LEARNED SOCIETIES/ SYMPOSIA/WORKSHOPS)

Regular contributions and presentations made at scientific and professional meetings throughout my tenure in medical/ clinical genetics. (From 2004 onwards)

2004

- 'Genetics of the cardiovascular disorders in childhood': First Asian Genomics Workshop, 12-22 April, Shenzhen, PR China.
- 'Genetic variation among the Indian subcontinent populations', First Asian Genomics Workshop, 12-22 April, PR China
- 'The spectrum and heterogeneity of genetic disorders among people from the Indian subcontinent', First Asian Genomics Workshop, 12-22 April, PR China.

2006

- 'The role of Wnt7A in human limb development' Sheridan E, Woods CG, Stricker S, Seeman P, Stern R, Cox J, Roberts E, Springer K, Scott S, Karbani G, Malik S, Bond J, Kumar D, Al-Gazali L, Mundlos S. BSHG Annual Conference, 18-20 September 2006 (Spoken presentation; contribution original clinical case report)
- 'Hypertrophic cardiomyopathy in Fabry disease presenting with sudden cardiac death.' Adila AlKindy, D Kumar, S Davies. BSHG Annual Conference, 18-20 September, York (Poster presentation; contribution- data from Fabry disease clinical audit)

2007

- Notch 3 gene mutation associated with Sneddon's syndrome- a complex disorder of unknown etiology with variable clinical features overlapping the phenotype of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy [CADASIL]. (Poster) D. Kumar, J. Holroyd, I. Frayling, I. Ferguson (ASHG meeting 2007 San Diego, USA).

2008

- The multi-disciplinary approach to delivering the specialist clinical cardiovascular genetic service in Wales. Dhavendra Kumar,1 Sally Davies, 1Annie Procter,1Ian Frayling,1Phillip Thomas, 2, Ian McDowell,3, Julian Sampson, 41. All Wales Medical Genetics Service, Institute of Medical Genetics, University Hospital of Wales, Heath Park, Cardiff, Wales, UK; 2. Department of Cardiology, Morriston Hospital, Swansea and Chair- Cardiac Services Network for Wales, Wales Assembly Government, Cardiff, UK; 3. Department of Biochemistry and Director-Laboratory Medicine, University Hospital of Wales, Cardiff, UK; 4. Academic Head, Institute of Medical Genetics, Cardiff University, UK and Director, Wales Gene Park, Cardiff University, Heath Campus, Cardiff, UK (Poster) BSHG 2008, 15-17 September, York.
- Dealing with sudden unexpected cardiac death- a new challenge. Mrs. Mary Nicol, D Kumar, C Owen, P O'Callaghan. (Poster) BSHG 2008, 15-17 September, York
- Dhavendra Kumar. 'The genomic basis of evidence-based medicine'- oral presentation at the 'Clinical Genomics symposium', satellite meeting for 13th Human Genome Meeting of the Human Genome Organisation, New Delhi, 25 Sept. 2008.

2009

- Genetic Counselling for Inherited Cardiovascular Conditions: A Comparison between Wales (UK), Australian and North American Practice. Nicol, M(1),Kumar, D (1),Procter, A (1),Edwards, A (1); Care, M (2) and Macciocca, I (3) (1)All Wales Medical Genetics service, Institute of Medical Genetics, University Hospital of Wales, Cardiff(2) Department of Medical Genetics, The Fred Litwin Family Centre, Mount Sinai Hospital, Toronto Canada; (3) Victoria Genetics Services, Murdoch Children's Research Institute, Children's Hospital, Melbourne Australia;
- Poster presentations at-
  1) British Society of Human Genetics, 2009, Warwick, England, UK
  2) American Society of Human Genetics 2009, Honolulu, Hawai, USA
- A focus group study of health care professionals involved in the care of families in Wales affected by sudden arrhythmic death syndrome (SADS). Bethan Handerson1 , Dhavendra Kumar2, Mary Nicol 2 , Kate Brain3, Rachel Iredale4, Angus Clarke2,31. Bangor University; 2. Institute of Medical Genetics, University Hospital of Wales, Cardiff; 3. Institute of Medical Genetics, School of Medicine, Cardiff University, Cardiff; 4. Genomics Policy Unit, University of Glamorgan, Wales. BSHG 2009, Warwick, England.
- Dhavendra Kumar 'Personalised medicine in the genome era', Plenary presentation at the 'the 2009 South African Society of Human Genetics, Stellenbosch, SA.

2010

- 'Molecular genetics of chronic heart failure', Plenary presentation at the 'World Congress of Heart Failure', Chandigarh, India, 5 Feb 2010.
- "Evidence-based medicine and translational research", Plenary presentation at the seminar on 'Emerging complexity in medicine: how to translate the new scientific

knowledge into better patients care?', organized by Institute Superriori Sanita (Italian National Institute of Health), Rome, 12-13 April 2010.

- Introductory presentation and Chair of the Workshop 'Genetics and Genomics for developing countries' at Human Genome Meeting 2010, Montpellier, France, 18-21 May 2010. HGM is the annual official meeting of the Human Genome Organisation
- Genetic counseling and testing in inherited monogenic cardiac disorders: interviews with patients and their families. Siv Fokstuen (Geneva, Switzerland), Dhavendra Kumar (Cardiff,UK), Jean-Louis Blouin(Geneva,Switzerland), Angus Clarke (Cardiff,UK). Oral presentation by Dr Fokstuen at the European Society of Human Genetics meeting, 12-14 June 2010, Gothenberg, Sweden
- "The views of health professionals regarding the management and care of families affected by sudden arrhythmic death syndrome". Bethan Henderson1 , Kate Brain2, Dhavendra Kumar3, Mary Nicol 3 , Rachel Iredale4, Angus Clarke2,3 1. School of Psychology, Bangor University; 2. Institute of Medical Genetics, School of Medicine, Cardiff University, Cardiff; 3. Institute of Medical Genetics, University Hospital of Wales, Cardiff; 4. Genomics Policy Unit, University of Glamorgan, Wales Poster presentation at European Society of Human Genetics meeting, 12-14 June 2010, Gothenberg, Sweden
- "Dealing with sudden cardiac death- a comparison between Welsh (UK), Australian and North American practice." M.C.Nicol, D.Kumar, A.Clarke, I.Macciocca and M.Care. European Society of Human Genetics, 12-14 June 2010, Gothernberg, Sweden.
- 'Autism in developing countries', Plenary presentation at the International Conference on Autism, Jersualem, Israel, 4-6 July 2010

2011

- 'Inborn errors of metabolism and therapy of genetic disorders', Chair, Human Genome Meeting 2011, Human Genome Organisation, Dubai, 16 March 2011.
- 'Molecular genetics of heart failure' at the International symposium on current trends in clinical genetics and genomic medicine, 21-24 March 2011, Chettinad Health University, Chennai, India.
- 'Personalised medicine in the genome era' at the International symposium on current trends in clinical genetics and genomic medicine, 21-24 March 2011, Chettinad Health University, Chennai, India.
- 'Non-classic inheritance' at the 'Current practice of genetic and genomic medicine', 26-27 March 2011, Apollo Indraprastha Hospital, New Delhi, India.
- 'Clinical approaches to inherited disease- neuromuscular disorders' at the 'Current practice of genetic and genomic medicine', 26-27 March 2011, Apollo Indraprastha Hospital, New Delhi, India.
- 'Dealing with family history of cancer' at the 'Current practice of genetic and genomic medicine', 26-27 March 2011, Apollo Indraprastha Hospital, New Delhi, India.
- 'Targeted molecular therapy' at the 'Current practice of genetic and genomic medicine', 26-27 March 2011, Apollo Indraprastha Hospital, New Delhi, India.

- ’Screening first degree relatives for hypertrophic cardiomyopathy: Experience of a multidisciplinary inherited cardiovascular conditions service. Poster presentation at the BSHG annual conference, 5-7 September 2011, Warwick University.

2012

- ’Malformation syndromes and obesity’, Oral presentation at the symposium- ’Genes and Human Malformations’, The Centre for Human Genetics, Bangalore, India. 27-29 Feb 2012.
- ’Personalized medicine in the genome era’, Invited Lecture at the Annual Meeting of the Indian Society of Human Genetics, Chandigarh, India. 3-6 March 2012.
- ’Molecular genetic approach to chronic heart failure’, Plenary lecture, Annual Meeting of the Indian Society of Human Genetics, Chandigarh, India. 3-6 March 2012.
- ’Advances in Rare Genetic disorders, Session organiser & Chair,2012 Human Genome Meeting of the Human Genome Organisation (HUGO), Sydney, Australia. 10-14 March 2012.
- ’International Consortium for Cardiovascular Genomics’, Co-Chair/ Lead on behalf of the Human Variome Project, Biennial meeting, UNESCO, 10-13 June 2012, Paris.
- ’Molecular genetic approach to complex heart disease’, Invited Lecture, Annual Conference of the Sri Lanka Medical Association, Colombo, 2-6 July, 2012.
- ’Genetic basis of birth defects surveillance and registry’, Invited Lecture, Sri Lanka Medical Association, Colombo. 2-6 July 2012.
- ’Genomics & Bio-Economy’, Platform presentation, The Second International Genomics Conference, Cardiff, UK. 13-14 September 2012.
- ’The cardio-genetic multi-disciplinary team (CG-MDT) approach to genetic screening for structural inherited cardiac conditions (ICCs): A hundred families’ experience from The University Hospital of Wales.”, Poster presentation, 2012 British Society of Human Genetics, Warwick University, 17-19 September 2012.
- ‘ECG patterns in Inherited Cardiac Conditions; Session Chair on behalf of the Association of Inherited Cardiac Conditions- AICC, at the 2012 Heart Rhythm Congress, Birmingham, UK. 23-26 September, 2012.
- ‘Delivering the specialist services for Inherited cardiac conditions in Wales’, Invited lecture, SADS-UK symposium on ‘Sudden Cardiac Death’ at the Royal College of Pathologists, London, UK. 20 October 2012.

2013

- ’Clinical and molecular aspects of inherited paediatric tumours’, 23-25 January 2013, Indian Cancer Genetics Conference, ACTREC, Mumbai, India
- ’Targeted molecular therapy in clinical oncology’, 27-29 January 2013, Next revolution of genetics and genomics, New Delhi, India.
- ’Genetic, genomics and clinical medicine’, 31 Jan. 2013, Current trends in genetic and genomic medicine, Lucknow, India

- ’Targeted molecular therapy for cancer’, 31 Jan. 2013, Current trends in genetic and genomic medicine, Lucknow, India
- ’Genes, genome and clinical medicine- the paradigm of obesity’, 4th Feb. 2013, Ranbaxy Science Foundation Symposium ”Gains of Genomic Research in Biology and Medicine”, Institute of Immunology, New Delhi, India.
- ’Harnessing genomics for the developing world’, Public Lecture, 19th Annual Scientific Symposium and Research Awards, Ranbaxy Science Foundation, 4th February 2013, New Delhi, India.
- ’Challenges of pre-implantation genetic diagnosis in clinical medicine’, 13-18 April, 17th Human Genome Meeting/21st International Congress of Genetics, Singapore.
- ’Teaching genetics in the 21st century’, 13-18 April, 17th Human Genome Meeting/21st International Congress of Genetics, Singapore.

2014

- ‘The Molecular Basis of Birth Defects’, International Birth Defects & Ophthalmic Genetics Conference, 9-11 Feb, 2014, Colombo, Sri Lanka
- ‘Overview and Classification of Brain and Spinal Cord Malformations’, International Birth Defects & Ophthalmic Genetics Conference, 9-11 Feb, 2014, Colombo, Sri Lanka
- ‘Vascular complications in inherited connective tissue disorders’. International Birth Defects & Ophthalmic Genetics Conference, 9-11 Feb, 2014, Colombo, Sri Lanka
- ‘Metabolic and Mitochondrial Genetic Eye Diseases’, International Birth Defects & Ophthalmic Genetics Conference, 9-11 Feb, 2014, Colombo, Sri Lanka
- ‘Ocular malformation in inherited metabolic & mitochondrial disorders’, Indian Ophthalmic Genetics Conference, 15-16 Feb. 2014, Narayana Nethralaya, Bangalore, India.
- ‘Public health approach to inherited blindness’, Indian Ophthalmic Genetics Conference, 15-16 Feb. 2014, Narayana Nethralaya, Bangalore, India.
- ‘Molecular perspectives of chronic heart failure- implications for management’, Seminar ‘Genes and Genome’, 21 Feb 2014, Department of Human Genetics, Guru Nanak Dev University, Amritsar, India.
- ‘Impact of genomics on the health in developing countries’, 20-22 Sept. 2014, Annual Conference of the British Society of Human Genetics. Liverpool, England, UK
- ‘Targeted molecular therapy in clinical medicine- a paradigm of personalized medicine’, 9-11 October 2014, Innovations in Molecular Medicine, Budapest, Hungary
- ‘The molecular basis of managing the chronic heart failure’, 20-21 Nov. 2014, International Conference on Next Generation Sequencing, Oxford Global Genetics, London, UK.

2015

- **'Inherited Cardiovascular Conditions- Opportunity and Challenges**', "CURRENT TRENDS AND GENETICS IN CARDIAC ARRHYTHMIA AND HEART FAILURE" [ICHF 2015], 31Jan-1 Feb. 2015, Chandigarh, Punjab, India.
- **'Molecular approaches to arterial/ aortic dilatation & rupture',** "CURRENT TRENDS AND GENETICS IN CARDIAC ARRHYTHMIA AND HEART FAILURE" [ICHF 2015], 31Jan-1 Feb. Chandigarh, Punjab, India.
- **Teaching and Training of medical genetics and genomics in emerging developing nations** , 'THE GENETIC AND GENOMIC PRACTICE OF MODERN CLINICAL MEDICINE' HIMALAYAN INSTITUTE OF MEDICAL SCIENCES, DEHRADUN, UTTARAKHAND, INDIA, **3 FEBRUARY 2015**
- **'Human Heredity, Genes and Genome: Historical Facts',** "Our Genes and Genomes- Past, Present and Future", 4th February 2015, Hemwati Nandan Bahuguna Medical Education University, Indian Forest Research Institute, Dehradun, Uttaranchal, India.
- **'Spectrum and patterns of genetic disorders in clinical practice',** "GENETICS & GENOMICS IN MODERN CLINICAL MEDICINE", King George Medical University Research Showcase, 9-10 Feb. 2015, Lucknow, Uttar Pradesh, India.
- **'Targeted molecular therapy and Stratified Medicine',** "GENETICS & GENOMICS IN MODERN CLINICAL MEDICINE", King George Medical University Research Showcase, 9-10 Feb. 2015, Lucknow, Uttar Pradesh, India.
- **'Genomics in clinical practice- The model of Stratified Medicine and Personalised Cancer pharmacotherapy',** 2nd. Next Generation Sequencing Conference, part of the 8th Global Discovery and Innovation Forum, 13-14 May 2015, London, UK
- **'NGS diagnostics for Inherited Cardiovascular Conditions',** Global Next Generation Sequencing Forum, Berlin, Germany, 5-8 October 2015.
- **'Genomic approach to managing chronic heart failure',** World Bio-Data Congress, Sanger Genome Centre, Hinxton, Cambridge, 20-21 October, 2015.
- **'Genetic basis of heart disease, diabetes and cancer', Public Lecture,** All India Institute of Medical Sciences, Jodhpur, Rajasthan, India, 10 Dec. 2015.
- **'Abnormal development', Open Student Lecture,** All India Institute of Medical Sciences, Jodhpur, Rajasthan, India, 11 Dec. 2015.
- **'The Rasopathies', Invited Lecture, Second Annual Conference of the Society of the Indian Academy of Medical Genetics,** All India Institute of Medical Sciences, Jodhpur, Rajasthan, India, 12-13 Dec. 2015.
- **'Targeted molecular therapy', Key note Lecture, Second Annual Conference of the Society of the Indian Academy of Medical Genetics,** All India Institute of Medical Sciences, Jodhpur, Rajasthan, India, 12-13 Dec.. 2015.
- **'Molecular approach for managing chronic heart failure'**, **Invited lecture**, Lari Heart Centre, Department of Cardiology, King George's Medical University, Lucknow, India, 18 Dec. 2015.

- '**Stratified and personalized therapy in Cancer'**; **Invited Lecture**, Department of Surgical Oncology, King George's Medical University, Lucknow, India, 19 Dec. 2015.
- **'Abnormal morphogenesis- clinical and genetic perspectives'**, **Invited Lecture**, Department of Paediatrics, King George's Medical University, Lucknow, India, 19 Dec. 2015.
- '**Reproductive genetics and genomics- clinical perspectives'**, **Invited Lecture**, Grand Round, King George's Medical University, Lucknow, India, 19 Dec. 2015.
- '**The Clinical Medicine in the OMICS Age'**, **Guest of Honour Invited Lecture**, King George's Medical University, Lucknow, India, 21 Dec. 2015.

2016

- **'Cardiovascular phenotypes in Inherited Metabolic Diseases',** Third International Conference on Birth Defects (ICBD-2016)"Molecular and Metabolic Basis of Developmental Disorders'; Clinical Workshops- 1) Clinical Dysmorphology 2) Fetal and Prenatal Genomics 3) Clinical Cancer Genetics

  7-10 December 2016, AIIMS New Delhi, India; Jointly Organized by

  INDO-UK GENETIC EDUCATION FORUM & SOCIETY OF THE INDIAN ACADEMY OF MEDICAL GENETICS (SIAMG), 7-9 December 2016.

- '**Pediatric Tumours- Clinical Genetic Approach'**, 3rd Indian Cancer Genetics Conference jointly held with the Indo UK Genetic Education Forum, ACTREC, Tata Memorial Cancer Research Centre, Mumbai, India. 13-14 December 2016.

- **"THE CLINICAL MEDICINE IN THE OMICS AGE',** Seminar on Genomics in Clinical Practice, Seth GS Medical College and KEM Hospitals, Parel, Mumbai, India. 15 December 2016.

NB- Presentations from 2017 onwards are listed in a previous section.

XIII CITATIONS - ACADEMIC AND PROFESSIONAL

A. Citation for the India-Padma Award nomination 2024

Professor Dhavendra Kumar is an internationally renowned and acclaimed clinical geneticist and genomic physician. He was born in Moradabad (UP) in a modest middle class family. He studied in the Government Intermediate College, Moradabad, followed by Medicine (MBBS) & MD (Paediatrics) in King George's Medical College (University), Lucknow. He had a brilliant track record as a student with three Gold Medals. His scientific & academic achievements are recognised as Fellow of UK, Ireland & USA professional Colleges (FRCP, FRCPI, FRCPCH,, FACMG). IN addition he is conferred by the global Indian diaspora community with the HIND RATAN award and Doctor of Science (Honaris Causa) by KGMU. He serves several Universities as

Honorary Professor in South Asia (5), UK (3), USA (1) & China (1). He is honoured to serve the 'Vaishwik Bharatiya Vaigyanik Summit (VAIBHAV)' led by the Prime Minister Rt. Hon. Shri Narendra Modi. Recently, he received the Life Time Achievement Award from the Global Association for Physicians of Indian Origin.

He is reputed as superb genomic clinician, particularly cardiovascular inherited diseases. Apart from being holistic excellent clinical geneticist, he has extensively contributed to the medical genetics and genomics literature as evident from his excellent publications. His award winning high profile books (30) and journals (5) confirm the reputation as a devout enthusiastic author & editor. He has worked closely with the WHO Non-Communicable Disease program and the Science Council for promoting genomic healthcare globally, particularly in low & middle income countries (LMICs). He founded the nongovernmental organisation, the Genomic Medicine Foundation UK (www.genomicmedicine.org), specifically to support genomic education and genomic healthcare in collaboration with global agencies like the Human Genome Organization International (www.human-international.org).

He is respected across the Indian subcontinent for his painstaking efforts and hard work spanning over 20 years wholly committed to raising awareness and enhancing knowledge and skills of Doctors, Nurses and allied healthcare professionals dealing with birth defects, genetic diseases and genetic health risks. His programme, the Indo-UK Genetic Education Forum, offered opportunity for scientists and medical geneticists from Europe, north America, Australasia and South East Asia to collaborate closely with Indian and South Asia institutions. This project continues with the UK India Genomic Medicine Alliance (UKIGMA), led by Professor Kumar, aimed 'to organise and lead a professional group of like-minded clinicians and healthcare professionals for promoting and supporting the genomic medicine across the Indian subcontinent. This project is actively involved with key genetic/genomic centres in New Delhi, Chandigarh, Mumbai, Chennai, Bangalore, Manipal, Mysore, Hyderabad, Lucknow, Amritsar and Colombo. The alliance regularly organises high profile learning and research events for birth defects, cancer genetics, cardiovascular genetics, pharmacogenomics, preventive genomics and genome ethics. The genomic education is prioritised with MSc Biotechnology (Jammu), Medical Genomics (Mysore) and Genetic Counselling (Amritsar).

He has been instrumental for the iconic 'Centre for Precision Medicine and Healthcare-CPMH' in KGMU (Lucknow), a unique first of its kind academic unit, aimed at research, innovation and medical applications of multi-OMICS and artificial intelligence in key areas of healthcare-Infection, metabolism, inflammation, cancer and rare diseases. He founded the eponymous KGMU 'Young Investigator Award' for promoting quality by the Junior Faculty in all areas of healthcare. He is leading the KGMU 'genomic medicine elective' for 7th semester MBBS students, approved by the National Medical Commission. This initiative is planned to other medical colleges. His similar efforts have strengthened genomic education agenda in Australia, South Africa and Latin America. His recommendations, as the external adviser, to the South Africa Medical Research Council have led to development of integrated genomic medicine centre in Cape Town and other cities. As the Senior Consultant Adviser to the Apollo Group of Hospitals, he leads the Apollo Genomics Institutes located in major metropolitan cities (Delhi, Ahmedabad, Bangalore, Hyderabad, Kolkata, Mumbai & Chennai), offering 'state of the art' genomics led precision & personalised medical &

preventive healthcare. His work is commended by leading Indian newspapers quoting leadership in cancer genetics, rare familial blindness, genetic, and genetic basis of sudden death in sports. Professor Kumar is the most deserving and distinguished Padma Award nominee supported by his patients, colleagues, fellow scientists, professionals and the general public throughout UK, India, South Asia, and South Africa.

Significant contribution made by this person

- Professor Dhavendra Kumar has served for 42 years UK NHS medical genetic service centres. He is an expert clinical geneticist with special interest genetic/inherited cardiovascular conditions, genetic counselling, genomic & precision medicine & preventive genomic healthcare.
- He is passionate for genomic education in UK for training for junior doctors, nurses, midwives & genetic counsellors. His contributions to MBBS level genetics teaching, intercalated BSc Medical Genetics course, Post Graduate Diploma in Genomic Medicine, MSc in Genomic Medicine are exemplary. He is actively involved the International genomic education through the Wellcome-Sanger Genome Centre.
- His high impact research led to the delineation of new genetic syndromes and understanding the complex molecular mechanisms. Collaborative research has discovered new genes leading to precision genomic management. As the Research Director, he established protocols for conducting efficient, effective and ethical research. These skills reflect setting up the KGMU Professor Dhavendra Kumar Young Investigator Award.
- Professor Kumar is acknowledged as a prolific author and editor of 32 books covering most aspects of clinical genetics & genomic medicine. Notable titles include Genomics and Clinical Medicine, Genomic Medicine, Clinical Cardiovascular Genetics, Genomic & Molecular Medicine, Advances in Genetics, and Genomic Precision Medicine in Clinical Practice. Two books, Medical & Health Genomics and Specialist Handbook of Inherited Cardiac Disease received high BMA Medical Books Awards commendations. Three books (Genetic Disorders of the Indian Subcontinent, Genomics and Health in the Developing World & Genomics & Society) provide detailed information relevant to genomic healthcare in Low & Middle Income countries. He has founded 5 biomedical Journals and led as Editor in Chief (Genomic Medicine; HUGO Journal; Applied & Translational Genomics; Genomic & Molecular Cardiology and Current Trends in Genomic Medicine).
- He founded the UK India Genomic Medicine Alliance (UKGMA), widely acknowledged for raising awareness and promoting genomic healthcare across India & South Asia. This led to several current genetic education programs including MSc courses (Bangalore, Mysore; Manipal, Jammu & Amritsar) and the National Medical Commission approved MBBS genomic medicine elective course. As external Faculty adviser, he has established KGMU Centre for Precision Medicine KGMU, first of its kind in whole India.
- Professor Kumar is internationally renowned for his contributions to several global genomics networks (Australian Genomics; UNESCO Human Variome

Project; HUGO; WHO- Science Council & Advisory committee for Developing Countries). As external adviser to South Africa Medical Research Council, he contributed to the Centre for Genomic Medicine in the University of Cape Town. He continues with HUGO contributing to global genomic healthcare.

Impact/ Outcome of the work done by this person

Professor Kumar's work has made huge impact with major outcomes in many areas of genomic medicine & healthcare. He has facilitated developing clinical protocols for precision diagnosis & personalised management of rare genetic diseases and inherited cardiovascular conditions manifesting with sudden cardiac death including multidisciplinary genomic-OMIC medicine approaches for adult onset chronic morbid diseases like chronic heart failure, irregular heart rhythm diseases, and chronic joint diseases.

His genomic books are invaluable medical genetic literature resources. Many public health planners refer to Genetic Disorders of the Indian subcontinent; Genomics and Health in the Developing World; Genomics Population & Society for genomic aspects of healthcare planning, particularly in South Asia and other Low & Middle Income countries. Many medical colleges recommend his books in the undergraduate & postgraduate medical curriculum (Genomics & Clinical Medicine; Genomic Medicine; Clinical Cardiovascular Genetics & Genomics & award winning Oxford Handbook of Inherited Cardiac Disease and Medical and Health Genomics)

His initiatives have led to setting up key Genomic Medicine degree courses- PG Diploma in Genomic medicine & healthcare (Univ. South Wales UK), MSc Genomic Medicine (Swansea University UK), MSc Medical Genetics & Genomics (JSS Medical College Mysore), MSc Biotechnology (Shri Mata Vaishno Devi University Jammu), MSc Genetic Counselling (Shri Guru Ramdas University of Health Sciences Amritsar), MSc Genetic Counselling, Manipal Hospital Bangalore).

Professor Kumar's UK India Genomic Medicine Alliance is instrumental for establishment of leading medical genetic and genomic centres in many places across India (Chettinad Health University, Chennai; Manipal Higher Academy for Education, Manipal; JSS Higher Academy for Education, Mysore; King George Medical University, Lucknow & Sri Lanka (University of Colombo). He has established seven Apollo Genomics Institutes (Ahmedabad, Bangalore, Chennai, Delhi, Hyderabad, Kolkata, Mumbai) for the Apollo Group, India.

Professor Kumar is a founding member of the UNESCO Human Variome Project (www.humanvariomeproject.org). It represents the Global Variome with the Human Genome Organization International (www.hugo-international.org) and the Human Genome Variation Society. As Chair of the HUGO Education Committee he has developed key tools for global genomic education for teaching and training.

Provide a 4-line brief on why does this person deserves a Padma award*

Professor Kumar is a renowned internationally acclaimed clinical geneticist and genomic medicine physician respected for his life-long medical services managing wide ranging inherited diseases. As a prolific books author & editor, his contributions to the medical literature are exemplary. He is widely respected for his commitment

for genomic education, research and innovations. His passionate and commendable work raising awareness & promotion for genomic medicine & healthcare across India, South Asia and are unique and deserve proper recognition with an appropriate Padma Award.

Any other relevant information

In addition to extraordinary remarkable medical academic career as clinical geneticist & genomic medicine physician, Professor Kumar is a very humble and modest person who has pursued his life with dignity and self-respect. He is approachable to any one for advice and mentoring. He is respected for his dedicated community work related to multi-cultural activities. As the President of Indian community, he developed the Sheffield Hindu Temple and lobbied UK Government for providing multi-faith prayer facilities in educational centres and public places. During the Covid pandemic lockdown, as the President of the Cardiff Rotary Club, he served local communities with food, shelter and healthcare. He founded the India Wales Club serving the Indian diaspora resident in Wales and nearby England counties.

He has served as medical adviser to many charitable organisations, notably the Sudden Arrhythmic Death Syndrome UK and the Cardiomyopathy Association UK. He actively promoted and lobbied placement of life saving defibrillator devices in schools, sports clubs and public places across UK. He works closely with Indian NGOs for rare diseases and many other agencies committed for inherited diseases. In his retirement, he continues with his passion for raising awareness and promotion for novel science & technology approaches in medicine and healthcare across India and other South Asian nations including the Asia Pacific region. His new commitments include the multi-professional North India Genomic Consortium and the North East India Genomic Consortium promoting & educating medical & healthcare providers for genomic medicine & healthcare.

B. Entries in Google Scholar (www.scholar.google.com)

Selection of relevant entries include-

1. Evidence for digenic inheritance in some cases of Antley-Bixler syndrome?

bmj.com [HTML]… , D Sillence, D Kumar, C DeLozier-Blanchet, … - Journal of medical …, 2000 jmg.bmj.com. The Antley-Bixler syndrome has been thought to be caused by an autosomal recessive gene. However, patients with this phenotype have been reported with a new dominant mutation at theFGFR2 locus as well as in the offspring of mothers taking the antifungalagent.

Cited by 70 - Related articles - BL Direct - All 11 versions

2. From evidence-based medicine to genomic medicine

nih.gov [HTML]D Kumar - Genomic Medicine, 2007 - Springer Abstract The concept of 'evidence-based medicine' dates back to mid-19th century or even earlier. It remains pivotal in planning, funding and in delivering the health care. Clinicians, public health practitioners, health com- missioners/purchasers, health planners, politicians

and ...
Cited by 3 - Related articles - BL Direct - All 5 versions

3. Moebius syndrome.
nih.gov [PDF]D Kumar - British Medical Journal, 1990 - jmg.bmj.com ... Dhavendra Kumar Moebius syndrome consists of congenital complete or partial facial nerve palsy with or without paralysis of other cranial nerves (most commonly an abducens paralysis) and often associated with other malfor- mations of the limbs and orofacial structures. ...
Cited by 94 - Related articles - All 7 versions

4. Disorders of the genome architecture: a review
nih.gov [HTML]D Kumar - Genomic Medicine, 2008 - Springer Abstract Genetic diseases are recognized to be one of the major categories of human disease. Traditionally genetic diseases are subdivided into chromosomal (numerical or structural aberrations), monogenic or Mendelian diseases, multifactorial/polygenic complex
Cited by 2 - Related articles - All 4 versions

5. Congenital renal tubular dysplasia and skull ossification defects similar to teratogenic effects of angiotensin converting enzyme (ACE) inhibitors.
bmj.com [PDF]D Kumar, G Moss, R Primhak, R Coombs - British Medical Journal, 1997 - jmg.bmj.com. Skull ossification defects similar to teratogenic effects of angiotensin convertingenzyme(ACE)inhibitors Dhavendra Kumar, Gail Moss, Rob Primhak, Robert Coombs
Cited by 12 - Related articles - BL Direct - All 10 versions

6. [BOOK] Genetic disorders of the Indian subcontinent
D Kumar - 2004 - books.google.com
A CIP Catalogue record for this book is available from the Library of Congress. ISBN 1-4020-1215-2 (HB) Published by Kluwer Academic Publishers, PO Box 17, 3300 AA Dordrecht, The Netherlands. Sold and distributed in North, Central and South America by ...
Cited by 1 - Related articles - All 2 versions

7. [BOOK] Genomics and clinical medicine
D Kumar, DJ Weatherall - 2008 - books.google.com
OXFORD MONOGRAPHS ON MEDICAL GENETICS GENERAL EDITORS Arno G. Motulsky Peter S. Harper Charles Scriver Charles J. Epstein Judith G. Hall 16. CR Scriver and B. Childs: Garrod's inborn factors in disease 18. M. Baraitser: The genetics of neurological ...
Cited by 1 - Related articles - All 7 versions

8. Genomic medicine: a new frontier of medicine in the twenty first century

nih.gov [HTML]D Kumar - Genomic Medicine, 2007 - Springer
Although the concept of heredity has been in existence since ancient times, the science of genetics began to evolve only around 150 years ago. The Darwinian theory of evolution by natural selection made clear reference to hereditary factors that reflect at least some of the present-day ...
Cited by 3 - Related articles - BL Direct - All 4 versions

9. The clinical, pathological and genetic aspects of sporadic late onset cerebellar ataxia: observations on a series of ten patients
D Kumar, WR Timperley - Acta Neurologica Scandinavica, 2009 - interscience.wiley.com
... Hallamshire Hospital, Sheffield, England. Correspondence to Address Dr. Dhavendra Kumar Centre for Human Genetics University of Sheffield 117 Manchester Road Sheffield S105DN England. Copyright 1988 Blackwell Munksgaard. ...
Cited by 2 - Related articles - All 2 versions

10. [CITATION] Book Review: Genetics and You
D Kumar - American Journal of Medical …, 1997 - New York, Alan R. Liss, c1977- …

11. Genetic and Genomic Approaches to Taxonomy of Human Disease
D Kumar - Genomics and clinical medicine, 2008 - books.google.com
6 Genetic and Genomic Approaches to Taxonomy of Human Disease Dhavendra Kumar The philosophy of disease is complex and reflects the way an abnormal body state is perceived and understood on the back-ground of sociocultural, psychological, and biomedical factors.

12. [BOOK] Principles and Practice of Clinical Cardiovascular Genetics
D Kumar, P Elliott - 2010 - books.google.com
3 Oxford University Press, Inc., publishes works that further Oxford University's objective of excellence in research, scholarship, and education. Oxford New York

13. Genome Mirror-2006
nih.gov [PDF]D Kumar - Genomic Medicine, 2007 - Springer
Well before the completion of the Human Genome Project in 2003, geneticists had already known about errors in the human genetic code and their role in hereditary single-gene disorders. Apart from uncommon Mendelian diseases, hundreds of common and rare alleles ofseveral ... BL Direct - All 4 versions

14. Thoracic and Abdominal Aortic Aneurysms
SL Drinkwater, D Kumar, P Taylor - Principles and Practice of …, 2010 - books.google.com
12 Thoracic and Abdominal Aortic Aneurysms Susan L Drinkwater, Dhavendra Kumar, and Peter Taylor Introduction Aortic aneurysms involving the thoracic and abdominal aorta are

increasing in incidence. The majority of these occur spo-radically, but a small proportion has a family ...

15. [CITATION] Applications in Audiological Medicine
L Van Laer, G Van Camp, D Kumar - 2008 - en.scientificcommons.org ... Download, http://hdl.handle.net/1854/LU-802871. Publisher, Oxford University Press. Contributors, Kumar, Dhavendra. Repository, Ghent University Academic Bibliography (Belgium). Keywords, Medicine and Health Sciences. Type, info:eu-repo/semantics/bookPart. Cached

16. The Classification of Inherited Cardiovascular Conditions
D Kumar, R Newbury-Ecob - Principles and Practice of Clinical …, 2010 - books.google.com The Classification of Inherited Cardiovascular Conditions Dhavendra Kumar and Ruth Newbury-Ecob All major body systems have a complex anatomical and physiological arrangement to ensure smooth functioning throughout the life span.

17. Dhavendra Kumar (ed): Genomics and clinical medicine
D Donnai - Human Genetics, 2009 - Springer
This new text is published as part of the excellent series Oxford Monographs on Medical Genetics. It is extraordi- narily ambitious in its aims, which are to address the inXu- ence of variations in the human genome on disease occurrence and susceptibility as well as on disease ...

18. A case of lateral facial clefts with Fallot tetralogy, duodenal stenosis and intestinal malrotation: a new multiple congenital anomaly syndrome?
D Kumar - Clinical Dysmorphology, 1999 - journals.lww.com Multiple congenital malformations in a Caucasian female infant are described which include lateral facial clefts, malformed external ears, cleft palate, Fallot tetralogy, duodenal stenosis and intestinal malrotation. There were no associated limb or spinal anomalies. This case ...
BL Direct - All 2 versions

19. Dhavendra Kumar (Ed): Genetic disorders of the Indian subcontinent (2004)
C Deshpande - Human Genetics, 2006 - Springer
Genetic disorders of the Indian subcontinent is a com- prehensive and timely book that addresses the burden of genetic disorders in the people of the Indian subcon- tinent. The book is divided into three main sections. Section A deals with the demographic variation and regional ...
BL Direct

20. Keith DiPetrillo (ed):"Cardiovascular Genomics: Methods and Protocols". Springer Protocols—Methods in Molecular Biology

D Kumar - Human Genetics - Springer
This book is a collection of articles edited by Dr Keith DiPetrillo and published by Humana Press in collaboration with Springer Protocols as part of the Methods in Molecular Biology series. The title of the book is probably misleading. The preface directs to complex cardiovascular ...

21. CONGENITAL DEVELOPMENTAL ANOMALIES
D KUMAR - Genetic disorders of the Indian subcontinent, 2004 - books.google.com
CHAPTER 7 CONGENITAL DEVELOPMENTAL ANOMALIES DHAVENDRA KUMAR 1. INTRODUCTION Developmental abnormalities presenting as unusual single or multiple anatomic alterations are not restricted to any ethnic human population. Every year about 3% of all children born in ...
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22. Genome mirror-2007
nih.gov [HTML]D Kumar - Genomic Medicine, 2007 - Springer
The medical and health applications of genome sciences and technologies were a highlight of the programme for the last annual meeting of the American Society of Human Genetics (23–27 October 2007) held in San Diego, CA, USA. The importance of genomic medicine ...
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23. [CITATION] Book Review: Genetic Counseling in the Dawn of the 21st Century
D Kumar - American Journal of Medical Genetics, 2000 - JOHN WILEY & SONS LTD
BL Direct

24. NeuropsychiatricDiseasesII: Mood Disorders
D Kumar - Genomics and clinical medicine, 2008 - books.google.com
20 NeuropsychiatricDiseasesII: Mood Disorders Dhavendra Kumar Disorders of mood affect all people irrespective of age, gender, culture, religion, and social and working background. Although, women are thought to have two to three times higher prevalence of mood ...
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25. Genomic Perspectives of Human Development
D Kumar - Genomics and clinical medicine, 2008 - books.google.com
5 Genomic Perspectives of Human Development Dhavendra Kumar Disorders that affect tissue differentiation, organogenesis, and morphogenesis constitute a significant proportion of human genetic disease. These disorders may result from any of the known genetic mechanisms ...
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26. EPIDEMIOLOGY OF GENETIC DISEASES
IC VERMA, D KUMAR - Genetic disorders of the Indian …, 2004 - books.google.com CHAPTER 4 EPIDEMIOLOGY OF GENETIC DISEASES ISHWAR C. VERMA, DHAVENDRA KUMAR 1. INTRODUCTION The Indian subcontinent includes several developing countries-India, Pakistan, Sri Lanka and Bangladesh. The infant mortality rate in these ...
Related articles

27. GENETIC NEUROLOGICAL AND PSYCHIATRIC DISEASES
… KUMAR, MA PATTON, A KUMAR - Genetic disorders of the …, 2004 - books.google.com CHAPTER 16 GENETIC NEUROLOGICAL AND PSYCHIATRIC DISEASES DHAVENDRA KUMAR, MICHAEL A. PATTON, AJITH KUMAR 1. INTRODUCTION Recent advances in molecular biology have ushered in a new era of Neurology. In recent years, more and more genetic ...
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28. [CITATION] Neurogenetics, edited by SM Pulst
D Kumar - American Journal of Medical Genetics Part A, 2001 - interscience.wiley.com It is also possible that your web browser is not configured or not able to display style sheets. In this case, although the visual presentation will be degraded, the site should continue to be functional. We recommend using the latest version of Microsoft or Mozilla web browser to ...
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29. [CITATION] Molecular Mechanisms of Neurodegenerative Diseases, edited by Marie-Françoise Chesslet
D Kumar - American Journal of Medical Genetics Part A, 2002 - interscience.wiley.com It is also possible that your web browser is not configured or not able to display style sheets. In this case, although the visual presentation will be degraded, the site should continue to be functional. We recommend using the latest version of Microsoft or Mozilla web browser to ...
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30. [CITATION] Genetic counseling in the dawn of the 21st century. Christos S. Bartsocas and Peter Beighton, editors
D Kumar - American Journal of Medical Genetics Part A, 2000 - interscience.wiley.com It is also possible that your web browser is not configured or not able to display style sheets. In this case, although the visual presentation will be degraded, the site should continue to be functional. We recommend using the latest version of Microsoft or Mozilla web browser to ...

31. CITATION] REVIEWS-Book Review-//Molecular Mechanisms of Neurodegenerative Diseases
D Kumar - American Journal of Medical …, 2002 - New York, Alan R. Liss, c1977- …
David N. Cooper and Hildegard Kehrer-Sawatzki (eds): Handbook of Human Molecular Evolution

32.D Kumar - Genomic Medicine, 2008 - Springer
This handbook or set of handbooks forms part of Wiley's ambitious 'Encyclopaedia of Life Sciences' comprising 26 volumes that cover wide-ranging aspects of biological sci- ences. It is also available as an 'on-line' version (www.els. net).

33. [CITATION] Dhavendra Kumar (Ed): Genetic disorders of the Indian subcontinent (2004): Kluwer Academic Publishers, 608 pages, hard cover, ISBN 1-4020-1215-2 (…C Deshpande - Human Genetics, 2006 - Springer

34. Genome mirror 2008
nih.gov [HTML]D Kumar - Genomic Medicine, 2008 - Springer
There is continued interest in the possible causal links between alcohol and blood pressure. Although a wealth of data, both anecdotal and systemically collected, supports a direct causal link, several confounding factors play a significant role, notably age and gender. All 4 versions

35. What you always wanted to know about Huntington's disease
G Evers-Kiebooms, D Kumar, SD … - European Journal of …, 2010 - nature.com
This book is an update of the first edition published in 1999 and results from the author's long experience with Huntington's disease (HD) in a clinical genetic context as well as from his close collaboration with HD association. Most chapters start with a number of key points All 2 versions

36. David N. Cooper and Hildegard Kehrer-Sawatzki (eds): Handbook of Human Molecular Evolution: Wiley, Chichester, 2008, 1,717 pp,£ 295.00, ISBN 978-0-470-51746 …
D Kumar - Genomic Medicine, 2008 - ncbi.nlm.nih.gov
The two volumes cover more than 280 chapters, elegantly written by some 400 authors, all of whom are evidently well-informed and leaders in their chosen area of evolutionary genetics, comparative biology, genomics or human genetics. All 2 versions

37. The emergence of 'The HUGO Journal'
D Kumar, ET Liu - The HUGO Journal, 2009 - Springer
In August 2007, a new bio-medical journal Genomic Medicine was launched to capture the key developments in genome sciences and technologies relevant to medicine and human health. Since then, several major journals emerged also to compete in the same field.

38. DIABETES MELLITUS AND RELATED DISORDERS
D KUMAR, CB SANJEEVI, V RADHA, V … - Genetic disorders of …, 2004 - books.google.com
CHAPTER 21 DIABETES MELLITUS AND RELATED DISORDERS DHAVENDRA KUMAR, CARANI B. SANJEEVI, V. RADHA, V. MOHAN 1. INTRODUCTION Diabetes mellitus [DM] is a multi-system

complex metabolic disorder complicated with potentially severe manifestations. Related articles

39. [CITATION] Genetic Disorders of the Indian Subcontinent, edited by Dhavendra Kumar: book review P Beighton - South African Medical Journal, 2006 - Sabinet Online

40. [CITATION] Genetic disorders of the Indian subcontinent. Edited by Dhavendra Kumar. Dordrecht, The Netherlands: Kluwer Academinc Publishers, 2004. 608 p.
AS Teebi - American Journal of Medical Genetics Part A, 2007 - interscience.wiley.com It is also possible that your web browser is not configured or not able to display style sheets. In this case, although the visual presentation will be degraded, the site should continue to be functional.

41. CITATION] Genetic disorders among Arab populations
D Kumar - American Journal of Medical Genetics Part A, 1999 - interscience.wiley.com It is also possible that your web browser is not configured or not able to display style sheets. In this case, although the visual presentation will be degraded, the site should continue to be functional. Related articles - BL Direct

42. Clinical Medicine in the Genome Era: An Introduction
D Kumar - Genomics and clinical medicine, 2008 - books.google.com 10 Clinical Medicine in the Genome Era: An Introduction Dhavendra Kumar It was in Padua that medicine, long degraded and disguised, was now to prove her lineageas the mother of natural science, and the truth of the saying of Hippocrates.
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43. [CITATION] Genetics and you
D Kumar - American Journal of Medical Genetics Part A, 1998 - interscience.wiley.com BL Direct

44. [CITATION] Genomics and clinical medicine
Dhavendra. Kumar, DJ Weatherall - Oxford University Press
[PDF] Robert Godfrey (Bob) Saner
samj.org.za [PDF]TH Bothwell - South African Medical Journal, 2008 - samj.org.za ... Edited by Dhavendra Kumar. Pp. ... 2004. ISBN 1-4020-1215-2. In this excellent monograph, Dhavendra Kumar and forty expert contributors have provided a comprehensive overview of genetic conditions that have been identified in persons with origins of the Indian subcontinent.
View as HTML - All 2 versions

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XIV PAST ACTIVITIES AND ROLES

This section includes all clinical, academic, research and professional duties and commitments from 1 August 1980 to my retirement from UK NHS on 31 October 2017.

1. Clinical duties

i) Paediatrics: Five years post medical qualification and registration training in Paediatrics with 10 years' experience in Community Paediatrics.

ii) Medical/ Clinical Genetics:

Over 40 year experience (since 1980) in medical genetics including general clinical genetics, clinical dysmorphology (malformation syndromes), paediatric genetic disorders, neuro-genetics, cancer genetics and cardiovascular genetics.

During 1980 to 2004, I held various clinical positions as clinical assistant, associate specialist and locum consultant in the Centre for Human Genetics, Sheffield Children's Hospital and Department of Medical Genetics in Nottingham, Oxford and Exeter. In 1997,

I was accredited as Board Certified Clinical Geneticist with the American Board of Medical Genetics. Later I secured my UK Specialist Register in Clinical Genetics, the General Medical Council, UK.

2. Specialist genetic service development

This section (from 1 November 2004) includes my role and professional commitments as Consultant in Clinical Genetics, All Wales Medical Genetics (now Genomics) Service (AWMGS) based in the University Hospital of Wales, Cardiff, Wales, UK.

i)Clinical

General Clinical Genetics
Paediatric genetics- clinical dysmorphology
Clinical cardiovascular genetics
As the Lead Consultant for Cardiovascular Genetics service for Wales, I was actively involved in a number of clinical, academic and professional activities. I organised a multi-disciplinary team for developing an integrated 'All Wales Service for Inherited Cardiovascular Conditions" within AWMGS:
Actively pursued service development for Wales cardiac genetic service
Preparing the clinical service plan and protocols
Preparation of clinical care pathways/ protocols for clinical referrals, molecular genetic testing and managing family members with a history of 'sudden cardiac death'
Organizing the NHS multi-disciplinary team for providing a World class service for patients and families with inherited heart disorders across Wales
Active participation in setting up the National level service for families affected with sudden cardiac death in a close relative as laid down in the National Service Framework for England and Wales.
Organising & Leading the All Wales Cardiovascular Genetics Interest Group

ii) Teaching & Training

Undergraduate (MB) teaching Cardiff University School of Medicine (2007 to date) & Swansea School of Medicine (2007-2009)
Intercalated BSc in Medical Genetics, Cardiff University (2009 to date)
Educational supervisor- Clinical Genetics
MSc in Genetic Counselling, Cardiff University; 2006 to date
Co-Supervisor, PhD, University of Bristol & Cardiff (2009 to present)
External examiner D.Sc, Queens University Belfast, N-Ireland, 2010

iii) Management

Clinic referrals, appointments, supervision and follow up
Clinical audits

Clinical review meetings
Weekly Consultant meetings
Monthly Journal Club

iv) Research Management & Governance

R&D Lead for All Wales Medical Genetics Service, 2011- date
R&D Lead for the Specialist Services Division, Cardiff & Vale University Health Board (CVUHB), 2011 to date
Member of the CVUHB Research Governance Board, 2011- date.
Member of the Steering Committee, Research Design and Conduct Service (RDCS), National Institute of Social and Healthcare Research (NISCHR)

v) Cardiovascular genetics research

1. 'Aortic dilation prevention by Irbesartan in Marfan Syndrome (AIMS)- Lead investigator for Wales in this BHF funded multi-centre clinical trial coordinated by the Royal Brompton Hospital, London.
2. 'Genomic profiling in chemotherapy related cardiomyopathy', this study aims to carry out genomic profiling in chronic heart failure due to chemotherapy related cardiomyopathy using the next generation sequencing methods.
3. 'Molecular autopsy in sudden cardiac death' a collaborative multi-centre study with 'The Heart Hospital', London to explore the utility of molecular autopsy in assisting coroners in establishing the cause of unexplained sudden death.
4. 'Unmet needs of families in Wales affected by sudden arrhythmic death syndrome (SADS): A focus group and interview study'- this study aims at studying to identify unmet information and support needs of families across Wales who have experienced a sudden unexplained death in a close family member. Part of higher degree (D. Ed) thesis, the University of Bristol, UK.
5. 'Molecular heterogeneity of ion channel genes in sudden arrhythmic death syndrome (SADS)'- This study is focussed on extending molecular analysis in affected patients with SADS including whole genome sequencing.
6. 'Family and community experiences of sudden unexplained/cardiac death including the role of coroner', funded by the UK Education and Social Research Council (ESRC) and the Sudden Arrhythmic Death Syndrome (SADS-UK), charity; Centre for social and economic applications of genomics (Cesagen), Cardiff University, UK; this work is included in the Thesis for PhD, Cardiff University- conferred in July 2017.

3. Academic experience and profile

i) University of Lucknow, India

Prior to embarking and beginning my career pursuits in medical genetics, I was successful in securing a two years' grant (1977-1979) for cytogenetic studies in selected childhood mental retardation syndromes. The project was hosted by the Department of Paediatrics, King

George's Medical College (now University), Lucknow, UP, India. This project was funded by the Council for Scientific and Industrial Research (CSIR) of the Department of Science and Technology, Government of India. The project was jointly conducted with the help of the Director of the National Botanical Research Laboratory in Lucknow.

Since moving away from my alma mater, I maintained close links and kept myself informed with medical teaching and academic progress. In 2012, with the support of the then Vice Chancellor, I established and sponsored an award to acknowledge and recognise research and development of the young Faculty within 10 years of initial career. This award, popularly known as the '***Professor Dhavendra Kumar Young Investigator'*** award is conferred annually on one distinguished junior Faculty from any department of the King George's Medical University. It carries a Gold Medal and the Certificate with citation. In addition, the successful Faculty is invited to deliver the Oration sharing the outcomes and achievements of the research and setting out the vision for the future.

ii) University of Sheffield, England, UK

During my tenure in the Sheffield Children's Hospital (1980 to 2002), I worked as Honorary Tutor in Medical Genetics, the University of Sheffield. I pursued research in hereditary spinocerebellar ataxia and related disorders. The main purpose was to explore and collate evidence for clinical and genetic heterogeneity. This research project was funded by the NHS Locally Organised Research Scheme. The outcome of this work is evident from key publications (see Section 8-List of Publications). The whole research report and details are embedded in the thesis for Master in Medical Science (MMedSci) conferred in 1987 at the Convocation of the University of Sheffield, UK.

iii) University of Oxford, England, UK

I have had close links with the University of Oxford while working in the Sheffield Children's Hospital and as well as the Locum Consultant in Clinical Genetics in the Oxford Regional Clinical Genetics Service. Main activities include-

a) Collaborative research in Stickler syndrome with the Late Professor Bryan Sykes Connective Tissue Laboratory, Institute of Molecular Medicine, John Radcliffe Hospital, Oxford. This work led to a key publication (see Section 8.2- List of Publications).

b) Collaborative research with Professor Andrew Wilkie on molecular genetics of brachydactyly in his laboratory of the Institute of Molecular Medicine at the John Radcliffe Hospital, Oxford.

c) Join collaboration and consultation with the Late Professor Sir David Weatherall, Founding Director of the Institute of Molecular Medicine at the John Radcliffe Hospital (Oxford) for collating evidence and information on genetic disorders of the Indian subcontinent. This work is published as a monograph 'Genetic disorders of the Indian sub-continent' published by Kluwer-Springer (see Section 9- Journals and Books).

D) Joint collaborative research on genomics for healthcare. This project required frequent meetings and consultations with the Late Professor Sir David Weatherall, Founding Director of the Institute of Molecular Medicine at the John Radcliffe Hospital (Oxford). This work later

became the basis of two major books related to genomic medicine and healthcare (see Section9- Journals and Books).

iv) Cardiff University School of Medicine- Research and Development

1. As the CVUHB R&D Lead for Specialties Division (Clinical Board) and Medical Genetics, I gained an insight and knowledge on the R&D structure, functioning and administration of R&D including that of Cardiff University and local research ethics committee.
2. As a member of CVUHB Research Governance Group, I actively participated in various activities including reporting/ handling of serious adverse events and issues related to investigational medical products.
3. As the R&D Lead, I actively participated in financial management and Directorates' R&D allocations.
4. As the Principal Investigator of the multi centre clinical trial for Marfans syndrome (The AIMS study), I have knowledge and good understanding of organizing and managing clinical trials. Currently I am actively involved with the Clinical Research Facility team for day-day conduct of this trial along with co-investigators, Prof. Alan Fraser and Dr. Dirk Wilson.
5. I served as one of the key local investigators for participating/ engaging in multi centre research in Rare Genetic Diseases as part of the 'Musketeers' Agreement' on behalf of the National Institutes of Health Research (NIHR).
6. In addition, I also contributed to the am international genomic research through my contacts with the Human Genome Organization, Human Variome Project and a number of commercial pharmaceutical groups engaged in collaborative research including clinical trials.

4. Education and Training

i) Accredited courses, seminars and symposia

Actively pursued planning, developing, leading organisation of the following professional courses, seminars and conferences:

a) Genetic disorders and people from the Indian subcontinent-challenges for clinical services in the NHS. Two-day symposium organised in Cardiff, with Wales Gene Park, 22-23 November, 2005.

b) "Challenges of genetics and genomics for the Indian subcontinent", organised a pre-congress satellite symposium at the 11th International Congress of Human Genetics, 6-10 August, Brisbane, Australia.

c)"Challenges of cardiovascular genetics- The Cardiff symposium"- 22/23 November 2007 and 23/24 Nov. 2009 Cardiff. Two day educationally approved symposium to focus on recent developments, current practice and issues in delivering the cardiac genetic services in the UK.

d)"Clinical Medicine in the Genome Era", 26-27 February 2009, Cardiff. A two-day International symposium to review recent developments in genome sciences and technologies as applied to the practice of modern medicine.

e)"Short course on clinical cardiovascular genetics", 30-31 January 2010, Bangalore, India

f)"Current trends in Clinical Genetics & Genomic Medicine", 21-24 March 2011, Chettinad Health City, Chennai, India

g)"Current practice of genetic and genomic medicine", 26-27 March, Apollo Hospital, New Delhi, India

h)"Genetics and genomics in developing countries', 5-7 September 2011, Annual conference of the British Society of Human Genetics, University of Warwick, UK

i) "Inaugural meeting of the Association for Inherited Cardiac Conditions", 23 November 2011, Cardiff, UK

j) "The Third Cardiff Symposium on Cardiovascular Genetics", 24-25 November 2011, Cardiff, Wales, UK

k) "FH and Cardiac study day", part of the local training and continuous professional development programme for genetic counsellors and related health professionals; 26th January 2012, Institute of Medical Genetics, Cardiff.

l) "Genes and Human Malformations- Indian Birth Defects Conference", 27-29 February 2012, Bangalore, India; part of the Indo-UK Genetic Education Forum, jointly supported by CGS/BSHG and hosted by the Centre for Human Genetics, Indian Institute of Science, Bangalore, India

m) "The Second International Genomics Conference- Genomics for Healthcare and Socioeconomic progress", 13-14 September 2012, sponsored by the Human Genome Organisation-International and hosted by the Wales Gene Park, Cardiff University.

n) "The First Indian Cancer Genetics Conference", 23-25 January 2013, Advanced Center for Treatment, Research and Education for Cancer (ACTREC), Tata Memorial Cancer Trust, Mumbai, India; jointly organised by the Indo-UK Genetic Education Forum and ACTREC.

o) "The Next Revolution of Genetics and Genomics", 27-29 January 2013, Postgraduate Education Centre, Ram Manohar Lohia Hospital, New Delhi; jointly organised by the Indo-UK Genetic Education Forum with the Indian Academy of Medical Genetics and the Centre for Genetic Medicine, Sir Ganga Ram Hospital, New Delhi, India.

p) "Current Trends in Genetic and Genomic medicine", 31 January 2013, Dr Ram Manohar Lohia Post Graduate Institute of Medical Sciences, Gomti Nagar, Lucknow; jointly organised by the Indo-UK Genetic Education Forum

q) "Gains of Genomic Research for Medicine and Biology", The Ranbaxy Science Foundation Symposium, 4th February 2013, Institute of Immunology, New Delhi, India.

r) "The Fourth Cardiff Cardiovascular Genetics Symposium", organised by the Wales Gene Park, Cardiff University, 21-22 November 2013.

s) "International Birth Defects Conference", Jointly organised on behalf of the Indo UK Genetic Education Forum, Wales Gene Park and the Human Genetics Unit, The University of Colombo, Sri Lanka; 9-11 Feb. 2014.

t) Ophthalmic Genetics Seminar, 11 Feb 2014, Jointly organised on behalf of the Indo UK Genetic Education Forum, Wales Gene Park and the Human Genetics Unit, The University of Colombo, Sri Lanka.

u) Indian Ophthalmic Genetics Conference, 15-16 Feb 2014, Jointly organised on behalf of the Indo UK Genetic Education Forum, Wales Gene Park and Narayana Nethralaya, Bangalore. India.

v) "Genes and Genome", 21st Feb 2014, invited speaker to the Seminar organised by the Dept. of Human Genetics, Guru Nanak Dev University, Amritsar, Punjab, India.

x) "Joint UK-Dutch Clinical Genetics 2014", 17-19 March 2014, Leiden, The Netherlands.

y) Symposium on 'Genomics in Developing Countries', at the Annual Conference of the British Society of Genetic Medicine (BSHG), 17-19 September 2014, Liverpool Convention Centre, Liverpool, UK

z) "Familial heart and blood disorders- International symposium", 31 Jan-1 Feb 2015, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

Ab) "Seminar on Genomic and Molecular Medicine:, 3 Feb 2015, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India.

Ac) "Genetics and Genomics basis of Clinical Medicine", 9-10 Feb 2015, King George's Medical University, Lucknow, UP, India.

Ad) Clinical Genetics Society (UK), Spring Conference, 3rd March 2015, Royal College of Physicians, London.

Ae) "International Cardiovascular Conference- 5th Cardiff Cardiovascular Genetics Symposium and the Annual Meeting of the British Congenital Cardiac Association, 17-18 November, 2015, Cardiff, Wales, UK

af) "4th Joint UK Dutch Clinical and Cancer Genetics Conference & Joint UK Dutch Dysmorphology Club, 7-9 March 2016, Cardiff, Wales, UK.

Ag) Third International Conference on Birth Defects jointly with the Society of Indian Academy of Medical Genetics, 8-9 December 2016, All India Institute of Medical Sciences, New Delhi, India.

Ah) 'Clinical Workshops' on Clinical Dysmorphology, Clinical Cancer Genetics and Clinical Reproductive Genomics, 10Dec.2016, All India Institute of Medical Sciences, New Delhi.

Ai) 'Current Trends in Cancer Genetics', 12-14 December 2016, International symposium jointly with the Advanced Centre for Treatment Research and Education in Cancer (ACTREC), Tata Memorial Cancer Hospital, Mumbai, India.

Aj) 'Integration of Genomics in Medical Practice', 15 December 2016, International conference jointly with the Seth GS Medical College and KEM Hospital, Mumbai, India.

Ak) Invited speaker to the 'The lnternational conference on Genetic and Molecular Diagnostics in Modern Medicine, 17-18 December, 2016; Kamineni Institute of Medical Sciences, Hyderabad, India.

ii) UNIVERSITY OF SOUTH WALES- 'Diploma in Genomic Medicine and Healthcare'

Founding Clinical Director of the above distance learning online course, accredited by the Faculty of Life Sciences and Education, the University of South Wales, UK. This course offers medical practitioners and health professionals' opportunity to learn and develop skills in fundamental aspects of genomic applications in clinical medicine and healthcare. The course includes 6 modules (three mandatory) with the option of 'certificate' and planned to be extended to the Masters level (MSc).

5.Professional roles in genetics and genomics

1. UK Wide National projects & Contributions

a) Conference organiser for UK clinical Genetics Society (2014 to 2017)

b) Council member- British society of genetic medicine (2015-2018)

c) Field collaborator for the sanger genome centre project 'Decipher Development Disorders- DDD', 2007 to 2015

d) Member Wales Genomic Medicine Consortium, part of the UK 100,000 genomes project (2014 to 2018)

e) Represented Wales for the British Heart Foundation 'Miles Frost Hypertrophic Cardiomyopathy' project (2015 to date)

f) Represented Wales for the British Heart Foundation Inherited Cardiovascular Conditions Steering Group (2017 to date)

g) Founder member/ council member (formerly Trustee, Treasurer and National Secretary)- Association for Inherited Cardiac Conditions- AICC (2008 to 2018)

2. International engagement

a) Human Genome Organization

Since 2010 closely associated with the International Human Genome Organization (HUGO)- serve as the **HUGO Council Member**, founding editor in chief of **the HUGO Journal**, member of the **International Scientific Committee** for the annual Human Genome Meetings and actively participated in prominent HUGO initiatives for raising awareness and promoting genetics/ genomics education in the emerging economies of the developing world.

b) WHO- Grand Challenges of Genomics in Developing Countries

Served on the **International Advisory Committee to the World Health Organization's project- on Genetics & Genomics for the Developing Countries'**, (2010-2012) as part of the WHO Millennium Project. This included a 15 point plan that was included in the WHO

consultation document circulated to all Member Nations. Among many outcomes, recent global initiatives include plans for rare genetic diseases and pilot projects on the role of genomics in non-communicable diseases.

c) Indo-UK Genetic Education Forum

Set up and lead the **Indo-UK Genetic Education Forum**, an independent and voluntary group of dedicated British and European Clinical and Non-Clinical (Scientists) Genetics and Genomics professional interested in sharing and empowering genetics & genomics in South East Asian countries (Indian subcontinent). The Forum engages with senior clinicians, geneticists and related health professionals in major Centres and Institutions across India and Sri Lanka. Since 2010, the Forum has visited and delivered successfully many seminars, symposia and workshops on wide ranging subjects including congenital birth defects, inherited cardiovascular conditions, inherited metabolic diseases, neuro-developmental disorders, inherited eye diseases, pre-natal and feto-maternal medicine and laboratory genetics. The Forum has organised future seminars to educate and equip medical and bio-sciences teachers through '*Teaching the Teachers'* format workshops beginning January/ February 2015. The Forum has received overseas travel grants from the Wellcome Trust for two consecutive years (2014 & 2015). Governmental and Non-Governmental agencies in India and Sri Lanka have supported the Forum through grants and providing complimentary manpower and conference facilities. The visiting Faculty has always enjoyed and found the experience most humbling, challenging, rewarding and enjoyable.

The success of this initiative is evident from its expansion to a much broader role in promoting genomics in medicine and healthcare. I am now developing a new initiative encompassing the Forum and inviting many organizations, institutes, investigators and clinicians. The new project is appropriately named as the 'UK-India Genomic Medicine Alliance' (UKIGMA). Discussions are underway to seek funding from Wellcome-India DBT Collaboration and other agencies.

h) ***Wales Gene Park- International liaison***

Since 2007, closely associated with the Wales Gene Park and now serving as the Director of the International Programme. Main activities include organising and leading Biennial Cardiff Cardiovascular Genetics Symposium (the Fifth planned for 2015), Triennial Genomic Medicine & Health symposium (the Third planned for 2015), liaising with the Indo UK Genetic Education Forum, arranging and facilitating overseas visitors and providing a resource on International genetics and genomics programmes to Welsh medical, health and academic colleagues.

e) International Scientific Committee of the Human Variome Project- International Consortium for Cardiovascular Genetics & Genomics

The Human Variome Project is a major international initiative engineered and led by Prof. Dick Cotton in Melbourne, Australia. It is now approved and supported by UNESCO and WHO. I serve on the International Scientific Advisory Committee and closely associated with the Disease Specific Genetics Programme aimed at systematic

collection of major clinical phenotypes and correlation with gene mutations and variants. My role is with the inherited cardiovascular conditions. I have started organising the International cohort working in the field of cardiovascular genetics and genomics. Several groups across many continents are partners of the Consortium. The NIH funded Harvard Medical School led International Collaboration for Clinical Genomics has offered to work with the Consortium.

h) ***Advisor/ Facilitator for the International Visiting Fellowships of British Society of Genetic Medicine/ Clinical Genetics Society-UK***

I am actively involved with the International programme of the British Society of Genetic Medicine and its affiliated organisation the UK Clinical Genetics Society. My role is with the selection of annual visiting International Fellows. In addition, I am also working with others for developing an online module for Clinical Genetics teaching and assessment. This is expected to be self –sufficient and aimed at facilitating interested primary and secondary care medical and health practitioners in developing countries to practise equipped with basic competencies in clinical genetics.

g) Cardiff University-India Collaboration for biomedical education

Following the successes of the annual Indo-UK Genetic Education Forum seminars and workshops, I have developed professional links with several key professionals in the health and academic sectors. Apart from genetics and genomics, these senior people desire a strong base for biomedical education and research in South East Asia. Leading countries of the region (India and Sri Lanka) have set up policies and funded projects for creating massive and highly ambitious Advanced Bio-Technology and Bio-Medical Centres and Institutes. However, the progress is seriously hampered due to lack of adequately trained and skilled clinicians, health professionals, research scientists and laboratory staff. I have initiated small pilot projects with few Institutions in India including setting up an MSc in Genetics and Molecular Biology, providing teaching and supervisory input as the Visiting Professor. In addition, I am providing information and guidance for developing plans and strategy for Bio-Medical Research.

Recently, I arranged a visit of the Vice Chancellor of a new Medical Health University in Dehradun, the capital city of the State of Uttarakhand in North India. This visit, facilitated by the Cardiff University International Engagement and Innovation unit, has initiated dialogue and discussion for series of projects on new born screening, surveillance and registry of major birth defects, surveillance and prevention of oral cancer and supporting medical and bio-sciences teachers for enhancing skills and competencies based on the 'Teaching the Teachers' model. I am working with key people here in Cardiff and India for the successful launch of the Cardiff University-India Collaboration.

h) '**Promoting genetics and genomics in developing countries'**

Established close links with several genetic and clinical colleagues in India, China, The Philippines, Thailand, United Arab Emirates, Saudi Arabia, Israel, Brazil, South Africa

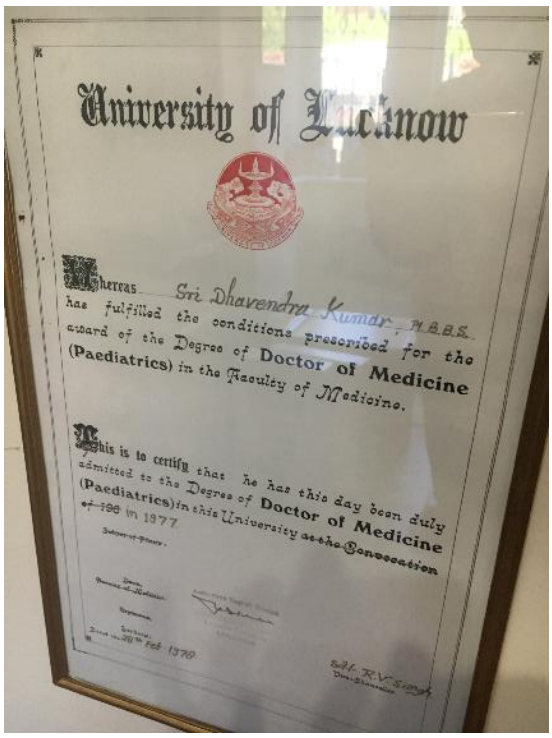
and Argentina. I led the dedicated session on this at the BSHG annual conference (5-7 September 2011) held in Warwick University. This is planned to move further ahead during the 2015 BSGM annual conference (22-24 Sept. 2014) in Liverpool.

i) Member, Expert Panel for **WHO Grand Challenges Project on Genomics and Public Health in Developing Countries,** July 2011 to date.

j) Founder/ Director of the **UK India Genomic Medicine Alliance (UKIGMA)**, on behalf of the Genomic Medicine Foundation UK Ltd. This alliance is now seeking collaboration for research, teaching and training related to human genomics in medicine and healthcare. Series of **Memorandum of Understanding (MOU)** are set up with key Academic Institutions and Universities across India and Sri Lanka.

XV CERTIFICATES, TESTIMONAILS AND PHOTOGRAPHS

i) Doctor of Medicine (MD) in Paediatrics


University of Lucknow

Whereas Sri Dhavendra Kumar, M.B.B.S. has fulfilled the conditions prescribed for the award of the Degree of Doctor of Medicine (Paediatrics) in the Faculty of Medicine.

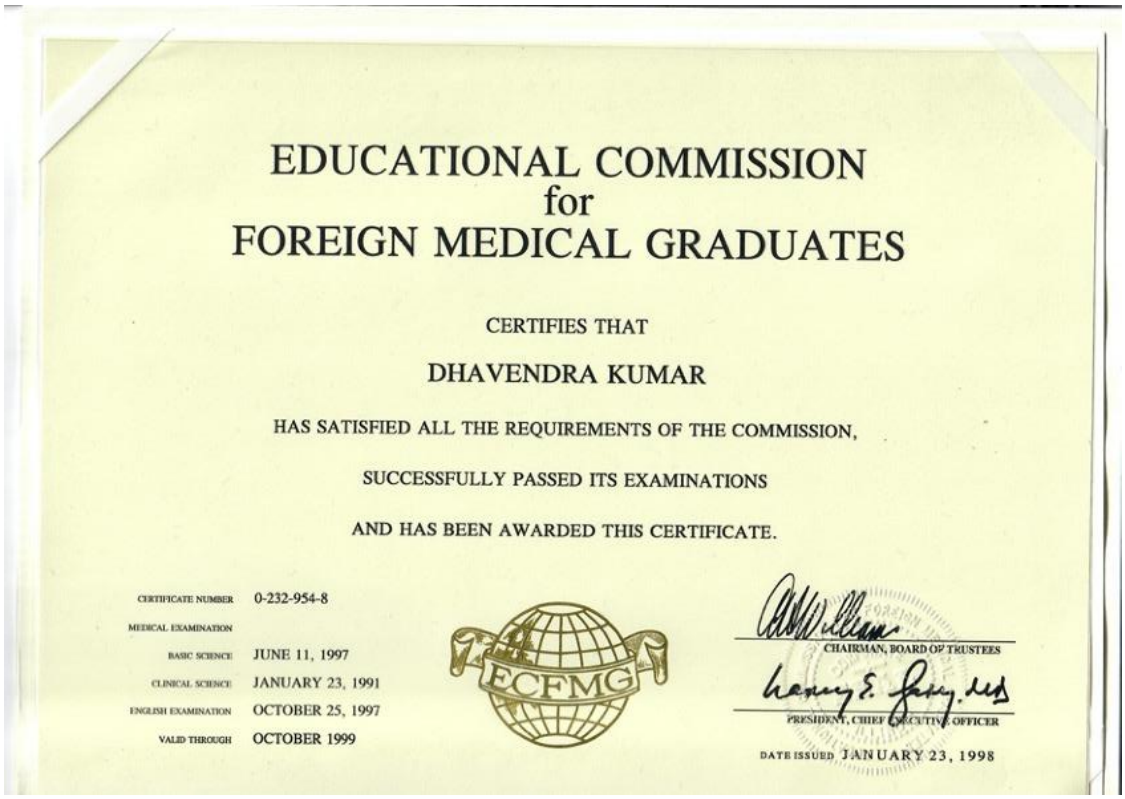
This is to certify that he has this day been duly admitted to the Degree of Doctor of Medicine (Paediatrics) in this University ~~at the Convocation of 198~~ in 1977

Subject to Proof.

Dated 20th Feb 1978

Sd/- R.V. Singh
Vice-Chancellor

ii) ECFMG Certificate



EDUCATIONAL COMMISSION
for
FOREIGN MEDICAL GRADUATES

CERTIFIES THAT

DHAVENDRA KUMAR

HAS SATISFIED ALL THE REQUIREMENTS OF THE COMMISSION,

SUCCESSFULLY PASSED ITS EXAMINATIONS

AND HAS BEEN AWARDED THIS CERTIFICATE.

CERTIFICATE NUMBER	0-232-954-8
MEDICAL EXAMINATION	
BASIC SCIENCE	JUNE 11, 1997
CLINICAL SCIENCE	JANUARY 23, 1991
ENGLISH EXAMINATION	OCTOBER 25, 1997
VALID THROUGH	OCTOBER 1999

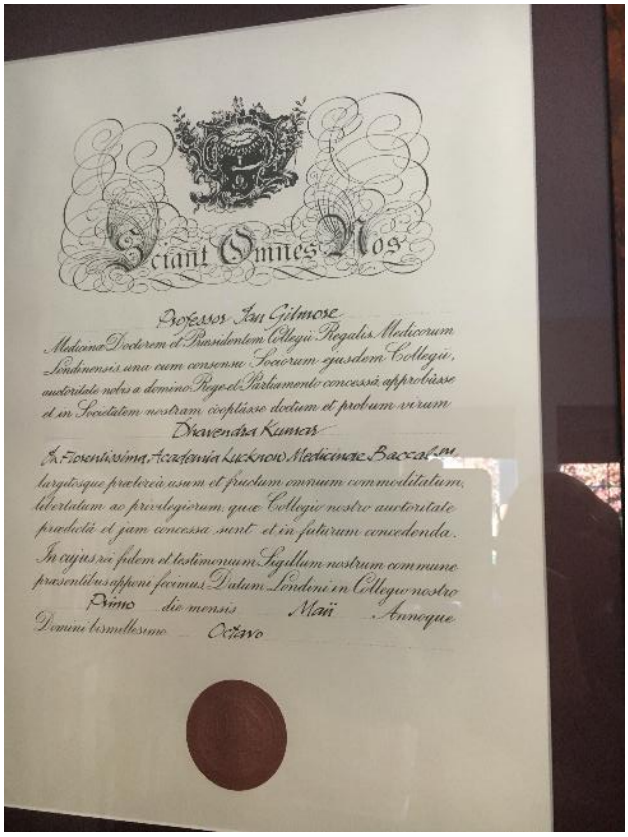
ECFMG

CHAIRMAN, BOARD OF TRUSTEES

PRESIDENT, CHIEF EXECUTIVE OFFICER

DATE ISSUED JANUARY 23, 1998

iii) Fellowship Royal College of Physicians, London (FRCP)



Sciant Omnes Nos

Professor Ian Gilmore

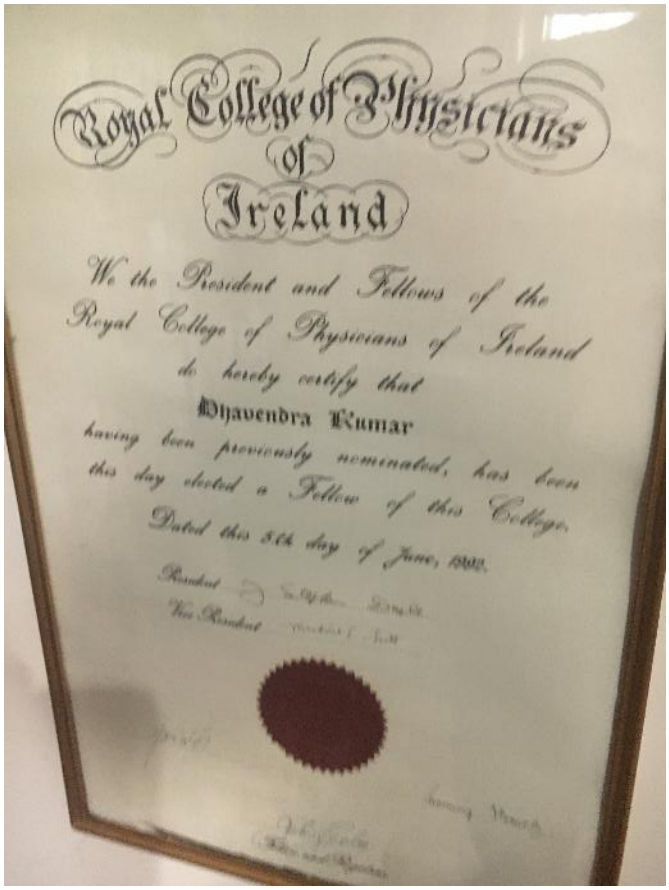
Medicinæ Doctorem et Præsidentem Collegii Regalis Medicorum Londinensis una cum consensu Sociorum ejusdem Collegii, auctoritate nobis a domino Rege et Parliamento concessâ approbâsse et in Societatem nostram cooptâsse doctum et probum virum

Dhavendra Kumar

In Florentissima Academia Lucknow Medicinae Baccalaureum largitosque præterea usum et fructum omnium commoditatum, libertatum ac privilegiorum, quæ Collegio nostro auctoritate prædictâ et jam concessa sunt et in futurum concedenda.

In cujus rei fidem et testimonium Sigillum nostrum commune præsentibus apponi fecimus. Datum Londini in Collegio nostro Primo die mensis Maii Annoque Domini bismillesimo Octavo

iv) Fellowship Royal College of Physicians Ireland (FRCPI)



Royal College of Physicians of Ireland

We the President and Fellows of the Royal College of Physicians of Ireland do hereby certify that

Dhavendra Kumar

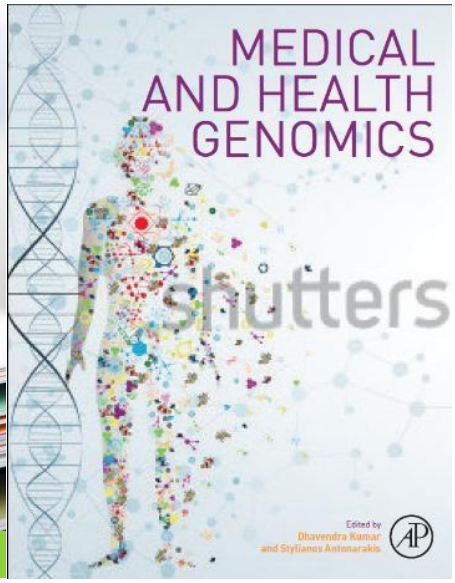
having been previously nominated, has been this day elected a Fellow of this College.

Dated this 5th day of June, 1992.

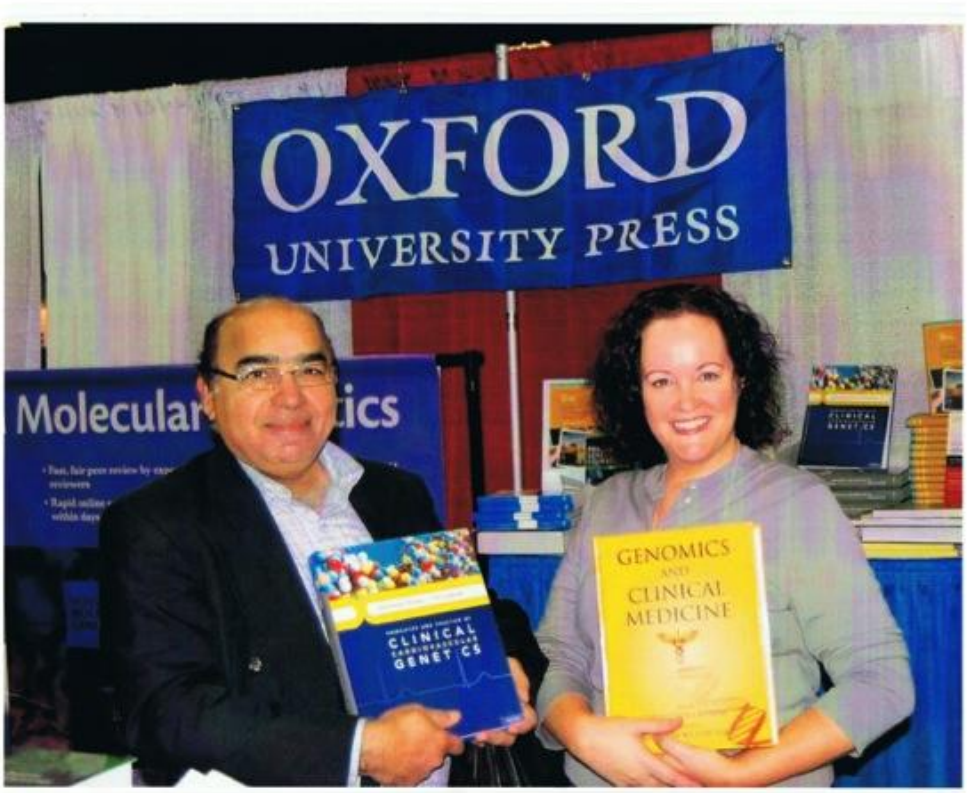
President

Vice President

v) BMA Medical Book Awards 2017



vi) Books presentation to the Director, Oxford University Press, New York



Presentation of Books and fecilitation by the Oxford University Press, New York At the 2011 American Society of Human Genetics Conference,Washington, DC

vii) Newspaper report on the Public Lecture delivered in India (February 2015)

जयपुर, बुधवार 11.12.2015 rajasthanpatrika.com सिटी पत्रिका patrika.com

आयोजन › एम्स में आनुवंशिकता पर जनचेतना व्याख्यान

कैंसर की जांच पर हुआ मंथन

Newspaper Report on the Public Lecture Delivered by Prof. Dhavendra Kumar 10 Feb.2015 at the All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.

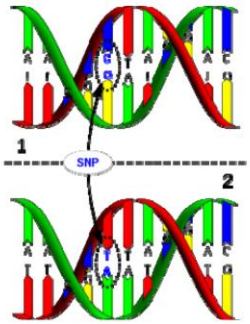
The report written in Hindi described the Main contents of the lecture discussing Role of Human Genomics in new precision Cancer diagnosis and treatment models Under development.

Prof. Kumar was the Chief Guest at the All India Medical Genetics Conference and the Visiting Academic Fellow at the Institute, One of the next generation of postgraduate Medical institutes in India.

viii) Presentation of the 'HIND RATTAN' (Jewel of India) Award

ix) Convocation ceremony for Doctor of Science (Honoris Causa)

"THE CLINICAL AND GENETIC HETEROGENEITY OF INHERITED HUMAN DISEASES- PERSONAL OBSERVATIONS AND INTERPRETATIONS"



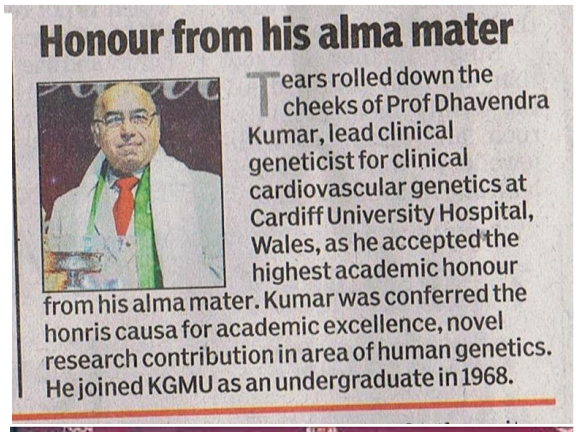
Submitted to
KING GEORGE'S MEDICAL UNIVERSITY, LUCKNOW, UTTAR PRADESH, INDIA

For the award of the degree of Doctor of Science (DSc)

Prof Dhavendra Kumar

MBBS (LUCKNOW), MD (PAEDS), DCH (RCPS-IRE), M Med Sci, FRCP(LOND), FRCP(IRE), FRCPCH (UK), DABMG (USA), FACMG (USA)

Institute of Cancer & Genetics (Formerly Institute of Medical Genetics), Cardiff University School of Medicine, University Hospital of Wales, Cardiff, UK & The Genomic Policy Unit, Faculty of Life Sciences and Education, The University of South Wales, Pontypridd, South Wales, UK
Cardiff, 31 May 2015



Honour from his alma mater

Tears rolled down the cheeks of Prof Dhavendra Kumar, lead clinical geneticist for clinical cardiovascular genetics at Cardiff University Hospital, Wales, as he accepted the highest academic honour from his alma mater. Kumar was conferred the honris causa for academic excellence, novel research contribution in area of human genetics. He joined KGMU as an undergraduate in 1968.

King George's Medical University
Uttar Pradesh, Lucknow

Doctor of Science (Honoris Causa)

conferred upon

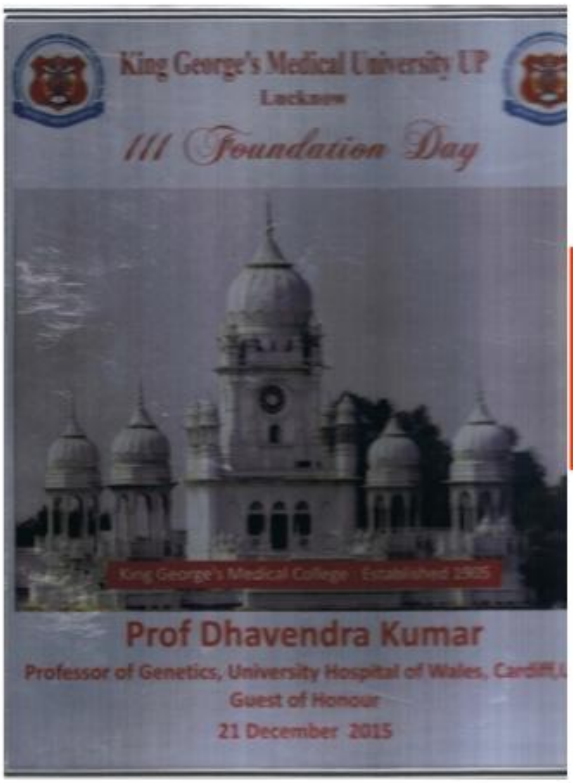
Prof. Dhavendra Kumar

Institute of Cancer & Genetics, Cardiff University School of Medicine, University Hospital of Wales, Cardiff, UK & The Genomic Policy Unit, Faculty of Life Sciences and Education, The University of South Wales, Pontypridd, South Wales, UK.

20 December 2015

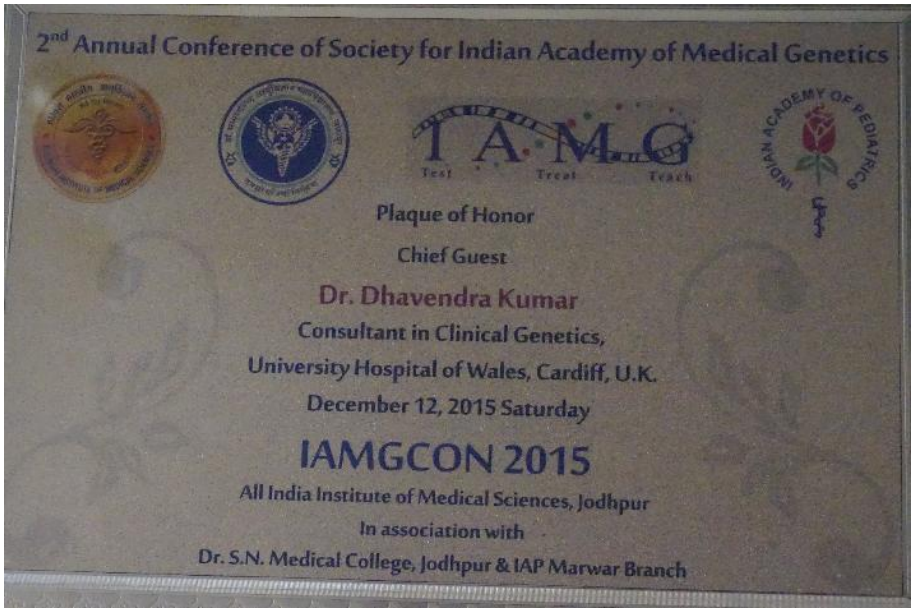
Vice Chancellor

x) Guest of Honour, 111th Foundation Day, King George's Medical University, Lucknow, India (2015)

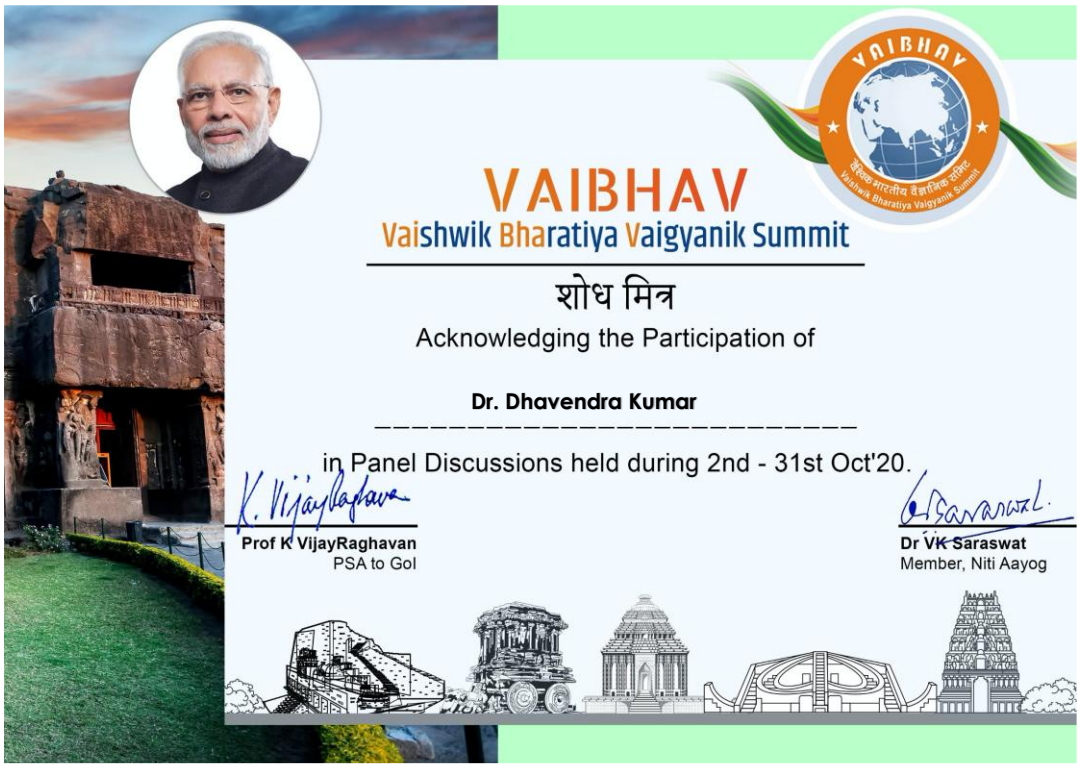


Photograph of the Ceremonial Plaque Presented to Prof. Dhavendra Kumar As the 'Guest of Honour' at the 111th Foundation Day of his Alma Mater The King George's Medical University Lucknow, Uttar Pradesh, India.

xi) 'Guest of Honour', Society of The Indian Academy of Medical Genetics, 2015

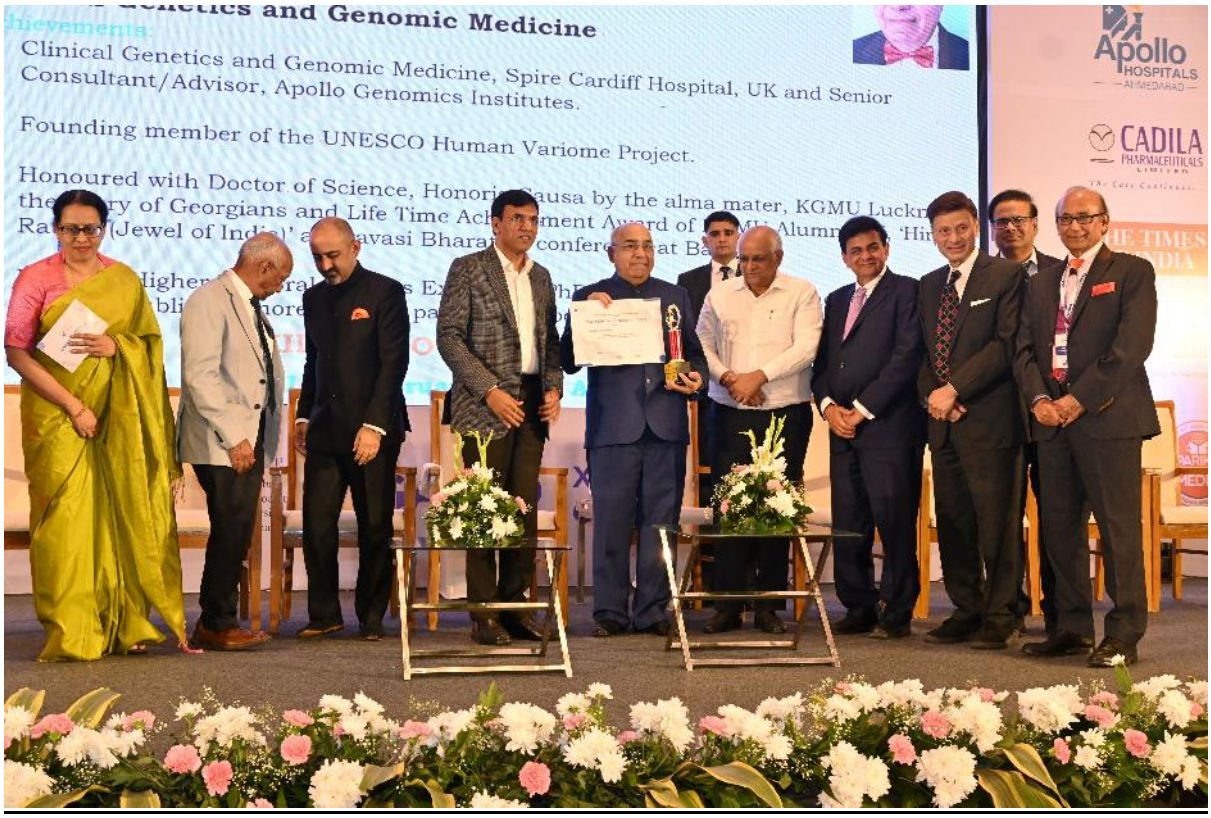


xii) Scientific summit of Oversease Scientists and Technologists, Government of India (VAIBHAV), 2020



xiii) Session Chair, Festival of Genomics & Biodata, Busines Design Centre, London, UK. 25-26 January 2023

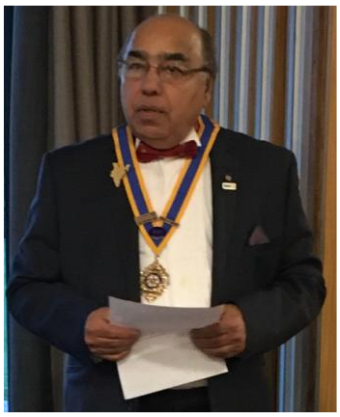
(xiv) Life Time Achievement Award, Global Association for Physicians of Indian Origin (GAPIO), 11 February 2023



XVI SOCIAL AND COMMUNITY SERVICE

i)Founder President- India Wales Club Ltd., Registered Charity No. 12586649; 2018 to date
"Independent charitable organisation for friendship and fellowship among Peoples of the Indian Heritage including families and friends"

ii) President- The Rotary Club of Cardiff, Charter date 1917; 2020 to date
As a Rotarian and President of one of the oldest Rotary Clubs in Britain, I actively led and contributed for the food bank during the Covid-19 lockdown. The Club is actively involved supporting the Cardiff Marathon and Disabled Sports activities & events.



XVII APPENDICES

1. Selected published papers and articles

1. Kumar, D. and Mittal, M., 2021. India's COVID-19 emergency: overarching conclusions belie facts. *Lancet*, *397*, p.1683. https://bookcafe.yuntsg.com/ueditor/jsp/upload/file/20210715/1626311944811091809.pdf;

'The Editors1 draw attention to India's economic capabilities, the challenges of a huge diverse population, and the dangers of false optimism amidst a second wave of SARS-CoV-2. However, some overarching conclusions belie facts and evidence.'

2. Kumar, D., 2021. The Genomic and Precision Medicine in Clinical Practice: Current perspectives and future directions. *The Physician*, *6*(3), pp.1-10.; www.physicianjnl.net; https://doi.org/10.38192/1.6.3.1

'An important milestone in the history of medical science is the recent completion of the human genome sequence. The progress on identification of approximately 22,000 homo sapiens genes and their regulatory regions provides the framework for understanding the molecular basis of disease. This advance has also laid the foundation for a broad range of genomic tools that can be applied to medical science.'

3. Nisselle, A., Janinski, M., Martyn, M., McClaren, B., Kaunein, N., Maguire, J., Riggs, E.R., Barlow-Stewart, K., Belcher, A., Bernat, J.A. and Best, S., 2021. Ensuring best practice in genomics education and evaluation: reporting item standards for education and its evaluation in genomics (RISE2 Genomics). *Genetics in Medicine*, *23*(7), pp.1356-1365. www.mq.edu.au;

'*Purpose Widespread, quality genomics education for health professionals is required to create a competent genomic workforce. A lack of standards for reporting genomics education and evaluation limits the evidence base for replication and comparison.'*

4. Elliott, P., Lambiase, P.D. and Kumar, D. eds., 2020. *Inherited cardiac disease*. Oxford University Press. www.books.oup.com ;

'Every year, thousands of people die or suffer chronic disability as the result of inherited diseases of the cardiovascular system. In many cases, diagnosis of inherited disease is delayed or missed owing to a lack of awareness, and an even greater number of relatives are exposed to unnecessary risk. This new edition of Inherited Cardiac Disease provides a comprehensive summary of the aetiology, presentation, and management of genetic disorders of the cardiovascular system. Fully updated to reflect the advances in molecular genetic technologies

and the publication of national guidelines for the management of families with inherited cardiac diseases, it retains the first edition's broad scope and applicability to all members of the multidisciplinary team, from specialists in cardiology and clinical genetics, to genetic counsellors, paediatricians, nurse specialists, and GPs who may come into contact with families presenting with inherited cardiac diseases. Containing both a short section on the general principles of cardiovascular genetics, individual disorders are then examined in detail, each featuring a clinical summary, diagnostic tests and special investigations, and treatments relevant to each inherited cardiac disease. Written in the succinct bullet-point style of the Oxford Specialist Handbooks, this new edition of Inherited Cardiac Disease delivers key information in an accessible manner, and is an invaluable guide to anyone who works with patients who are affected by inherited diseases of the cardiovascular system in their practice.'

5. Kumar, D., Steele, E.J. and Wickramasinghe, N.C., 2020. Preface: The origin of life and astrobiology. *Advances in Genetics*, *106*, p.xv. www.nih.gov

'*Charles Darwin is historically renowned for his theory of evolution as the basis of variation of biological life that exists around us. Similar views were also echoed by the contemporary biologist, Alfred Russel Wallace, who is credited with independently conceiving the theory of evolution through natural selection. His paper on the subject was jointly published with some of Charles Darwin's writings in 1858. Despite strong opposition of the contemporary Christian Church of the time, gradually the natural selection theory for the biological evolution was accepted and remains pivotal to explain both inter- and intraspecies variation. However, a small section of theologists, philosophers and biologists continue to hold different views for the origin of life and its developments into numerous species and variation. Both schools, however, believe and acknowledge the genetic basis of life within the realms of nucleic acids, the ribose nucleic acid (RNA) and the deoxyribose nucleic acid (DNA). The fundamental questions remain—what must have been the earliest form of life on Earth? What is the relationship to life beyond Earth, if it exists at all?'*

6. Kumar, D., 2020. The human genome and molecular medicine. In *Clinical Molecular Medicine* (pp. 3-16). Academic Press. https://www.sciencedirect.com/science/article/pii/B9780128093566000010; https://doi.org/10.1016/B978-0-12-809356-6.00001-0

'Since the discovery of the double helix structure of the nucleic acid, the focus of genetics moved ahead rapidly leading to the sequencing of human and many other genomes. This development, facilitated many genomic applications including medicine and healthcare. However, the developments in molecular biology and biotechnologies also led to introduction of molecular medicine. This chapter looks at the fundamentals of genomics in the molecular

context. It is expected that the reader will find contents of this chapter helpful in understanding and grasping the major components of clinical molecular medicine.'

7. Kumar, D., 2020. Molecular biology of acute and chronic inflammation. In *Clinical Molecular Medicine* (pp. 389-402). Academic Press. https://www.sciencedirect.com/science/article/pii/B9780128093566000228; https://doi.org/10.1016/B978-0-12-809356-6.00022-8

'*Inflammation is a natural response of tissues and organs following acute or chronic trauma, acute infection, or acute immune-mediated tissue damage. It is spontaneous and often positive and beneficial in response to acute injury or invading pathogen. The pathogenesis of acute and chronic inflammation includes complex molecular pathways involving several genes, genetic/genomic polymorphisms, peptides, and many other molecules. This chapter provides a clinically relevant overview on molecular complexities of inflammation.'*

8. Kumar, D., 2020. Integrated genomic and molecular medicine. In *Clinical Molecular Medicine* (pp. 535-543). Academic Press; https://www.sciencedirect.com/science/article/pii/B9780128093566000320; https://doi.org/10.1016/B978-0-12-809356-6.00032-0

'Despite tremendous advances in making an accurate diagnosis, most therapeutic programs lack precision and target the "average model patient." While "one-size-fits-all-approach" treatments can be very successful for some patients, it often fails for many others. However, this has changed with rapid scientific and technical advances facilitating the practice of evidence-based personalized precision medicine. The power of evidence derived from genomic and molecular scientific advances is undisputed. The whole process involves a stepwise approach in building the holistic picture referred to as stratified medicine with the ultimate aim of individualized or personalized therapeutic interventions. The new exciting opportunity for stratified and personalized medicine is introduced in this chapter. The chapter discusses the integrated organization and delivery of the genomic and molecular medicine service.'

9. Kumar, D., 2020. Molecular medicine of diabetes mellitus. In *Clinical Molecular Medicine* (pp. 267-288). Academic Press. https://www.sciencedirect.com/science/article/pii/B9780128093566000150; https://doi.org/10.1016/B978-0-12-809356-6.00015-0

'This chapter provides the overview and highlights clinically relevant aspects of genetic, genomic and molecular bases of all forms of diabetes mellitus that are essential for all categories of clinicians including public health and allied healthcare professionals.'

10. Kumar, D., 2020. Gene, genome, and molecular therapeutics. In *Clinical Molecular Medicine* (pp. 505-520). Academic Press.
https://doi.org/10.1016/B978-0-12-809356-6.00030-7;
https://www.sciencedirect.com/science/article/pii/B9780128093566000307

'Apart from understanding cellular and molecular mechanisms, the strength of molecular medicine is largely appreciated by diagnostic precision and exploiting molecular pathology for specific therapeutic interventions. In the previous chapters, information and discussion are confined to genetic and genomic basis of drug metabolism and drug response. In the current chapter, recombinant drugs and new therapeutic avenues targeting at specific genes, molecules, and cellular structures are discussed.
There are many such approaches largely confined to biomedical research. However, few are now approved for clinical use, and the list is fast expanding. The chapter includes separate sections on stem-cell therapy, gene therapy, antisense oligonucleotides, ribozymes, RNA interference, aptamers, and CRISPR/Cas9 gene/genome editing. In keeping with the size and scope of the book, scientific and experimental details are avoided. Emphasis is given to potential clinical applications. There are key references cited at the end of chapter to assist interested reader and student for further reading.'

11. Kumar, Dhavendra (2023). "Genomic Healthcare in Modern Medicine", Editorial, Special Issue 'Genomic Medicine', Apollo Medicine, Vol.20; Issue 2:91-92

Editorial

The Genomic Health Care in Modern Medicine

Dhavendra Kumar[1,2]

[1]Apollo Genomics Institutes, Indraprastha Apollo Hospitals, Sarita Vihar, Delhi, India, [2]William Harvey Research Institute, Queen Mary University of London, London, UK

The current special issue of the *Apollo Medicine* celebrates the progress made by genetics, particularly human genetics in modern medicine and health care. Among several key discoveries and innovations, the deciphering of the double helix structure of the deoxyribonucleic acid (DNA) by James Watson and Francis Crick in 1953 unquestionably remains the most significant milestone. This special issue is dedicated to this landmark discovery that conceptually revolutionized the cell and molecular biology with far-reaching implications. It offered the much-needed physical evidence for heredity and its correlation with physical and many other traits. We are now cherished with its applications and positive impact in managing the human disease and prospects of optimal human health.

The concept of heredity in living creatures dates back to the ancient times. Interpretations of hymns and inscriptions in the *Vedas*, particularly the *Rigveda,* refer to heredity. Scientists and the Vedic scholars have revisited the evidence collected from the Indus Valley Civilization consistent with the genetic evolution and recombination. It is claimed that some of the hymns when decoded relate to the complex processes such as the synthesis of chromosome, DNA replication, protein translation, and nucleotide pairing for nuclear reaction (https://www.dnaindia.com/bangalore/report-rig-veda-a-treasure-trove-of-transgenics-1506241). The team in the Council of Scientific and Industrial Research-Institute of Genomics and Integrative Biology is actively pursuing the role of the ancient Vedas in the context of modern genomic technologies (https://www.igib.res.in/?q = ayurgenomics/).

There are many anecdotes from the ancient Greek literature and mythology that relate to human heredity and health implications. Most of these are related to the times of Hippocrates around 380–350 BC. There is reference to "mothers who bear sons dying of bleeding when wounded in the war." Many acknowledge this as a clear reference to the classic X-linked hemophilia A. Perhaps the most pertinent evidence comes from the Aristotle's "Generation of Animals" book, in which the *heritable factors* are argued with the laws of inheritance, mainly during the act of reproduction (*Devin Henry, 2006. Aristotle on the mechanism of inheritance. Journal of the history of biology; doi 10.1007/s10739-005-3058-y.).*

There is an ongoing argument whether Aristotle's Greek philosophy favored natural selection theory for the biological evolution, later put forward by Charles Darwin? Despite the differing views on Charles Darwin's theory of evolution governed by the natural selection, many agreed with the concept of hereditary factors put forward in the Darwin's famous book "On the origin of species." Several years later, the evidence for dominant and recessive hereditary factors was provided by Gregor Mendel in his elegantly illustrated mathematical experiments on garden pea plants with different physical traits. However, this work was not appreciated for almost 60 years; when in the early 1900s, biologists became serious about the Mendel's laws of inheritance and the science of heredity. This generated tremendous interest on the mysteries of heredity material, possibly located in the nucleus of the cell.

During the early part of the 20th century, a large amount of data was generated on physical traits like height, and functional traits like intelligence, in the context of positive or negative heredity. The term "*eugenics*" was coined by Francis Galton, the great grandson of Charles Darwin. Whist this movement was full of good intentions, sections of the society started using this as the divisive and discriminatory tool both in the USA and UK, including the parts of the Europe. Later, the eugenic ideas and logic became the central theme of the Nazi Germany as evident from the doctrine of the *Race Hygiene* clearly targeted at Jews, Gypsies, and a few other minority sections, including people with physical and learning disabilities.

Despite the negative impact of the World War II and the eugenics movement, the progress in genetics and heredity continued. The period between 1950 and 1960, described as the *golden decade of genetics,* is decorated with discoveries and innovations in genetics, notably the Watson-Crick's double helix model of the DNA, Tjio-Levan's 46 chromosomes in the human cell, and Hargobind Khorana's triple nucleotide genetic code governing the assembly of amino acids for the peptide molecule synthesis. Since then the progress in genetics, later expanded to genomics, led to many more discoveries to the successful completion of the Human Genome Project in early parts of the new millennium. In 2003, advances in molecular technology allowed nearly 98% sequence of the human genome. The remainder 2% of the genome, comprising the repetitive DNA in telomeres (the terminal ends of the chromosomes) was eventually sequenced in 2022.

Although the practice of genetics in medicine became established in the early 1970s, it remained miniscule restricted to a few chromosomal disorders, selected multiple malformation rare dysmorphic syndromes, and common monogenic (single-gene Mendelian) diseases. The concept of polygenic multifactorial diseases was appreciated with the mathematical models of heritability and linkage disequilibrium. The practice of genetic counseling found its firm base with the development of genetics in medicine. This period witnessed

rapid advances in the genetic laboratory diagnosis from the early days of cytogenetics to molecular cytogenetics, notably the fluorescence *in situ* hybridization. The introduction of techniques of molecular DNA analysis allowed the focus on DNA fragments using the restriction enzymes and the recombinant DNA methods.

Several different types of DNA laboratory techniques were developed and applied in clinically useful family linkage studies, gene mapping by positional cloning, genetic risk analysis, prenatal diagnosis, and predictive genetic testing. The DNA analysis received the much-needed impetus with the discovery of the polymerase chain reaction. The modern genetic or genomic laboratory is equipped with the sophisticated facilities for the state-of-the-art genomic diagnosis to as low as at around 100 base pairs. The next-generation sequencing is now available targeted at single gene, multiple gene panel, small and large reads, RNA sequencing, the mitochondrial genome, and epigenome. The microarray chromosome analysis (array comparative genomic hybridization), targeted clinical exome sequencing, whole-exome sequencing, and whole genome sequencing are now available at progressively lower costs. However, new challenges are emerging with huge genome sequencing data, variants of unknown significance, interpretation of the population specific genome sequences, and the relevance of evolutionary conserved genome polymorphisms. New related disciplines are emerging, specifically clinical bioinformatics, computational systems, functional genomics, and many more.

Every clinician, practicing any system of medicine, aims for precision and personalized care to all patients, and if necessary, for the family. Although the clinical evaluation remains the most essential part of medicine, the outcome is closely related to the efficacy and accuracy of diagnostic methods used, whether biochemical, immunological, histopathological, or radio imaging. Most of these lack the much-needed high-order sensitivity and specificity. This gap is now narrowed down to extremely small level with the rapid incorporation of next-generation and emerging future genome technologies. The clinician can now confidently offer precision and personalized care with the added options of predictive and preventive, the 4Ps of modern medicine, now expanded to include preemptive and participatory elements (6Ps Medicine). Several new therapeutic and prophylactic modalities are now possible managing different common and rare diseases. Genomics remain central to the new modern medicine with the acceptance of genomic health care as the preferred choice. However, inclusion of other life sciences is important denoted with OMICS, such as transcriptomics, proteomics, metabolomics, phenomics, microbiomics, glycomics, and lipidomics. There is a strong drive for the modern genomics-led multi-OMICS medicine with the focus on multidisciplinary integrated health care.

The future of genomics led critical, and the specialist care is undoubtedly bright with the prospects of precision and personalized health care. This is continually improved with the development and availability of novel highly sensitive diagnosis options and new drugs and vaccines. Clearly, this would need to modify and modernize the medical and health-care education and training for developing highly skilled and competent workforce. There would be a constant need for adequately funded basic and clinically applied translational research and development (R and D) infrastructure and carefully regulated outcomes. Clinicians, genomic medicine practitioners, and related health-care providers would need to give due care and attention to the ethical, legal, and social issues embedded in the core of the genomic health care.

Finally, this special issue would not have been possible without the contributions of many colleagues and supporters, who worked as the team to write, develop, and deliver in a very short time frame. Many other colleagues worked extremely hard to ensure quality and elegantly produced the special issue of the Apollo Medicine. The Apollo Genomics Institutes across India dedicate this issue to many of our patients and families for the courage and perseverance fighting and/or living with common and rare genetic diseases. They need to be reassured about the bright future led by new advances in genomics and multi-OMICs.

Author's contribution

Author wholly contributed to this Editorial.

Address for correspondence: Prof. Dhavendra Kumar,
Apollo Genomics Institutes, Indraprastha Apollo Hospitals, Sarita Vihar, Delhi, India.
E-mail: drdhavendra_k@apollohospitalsdelhi.com
William Harvey Research Institute, Queen Mary University of London, London, UK.
E-mail: d.kumar@qmul.ac.uk

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DOI: 10.4103/am.am_64_23

Submitted: 07-Mar-2023
Accepted: 14-Mar-2023 **Published:** ***

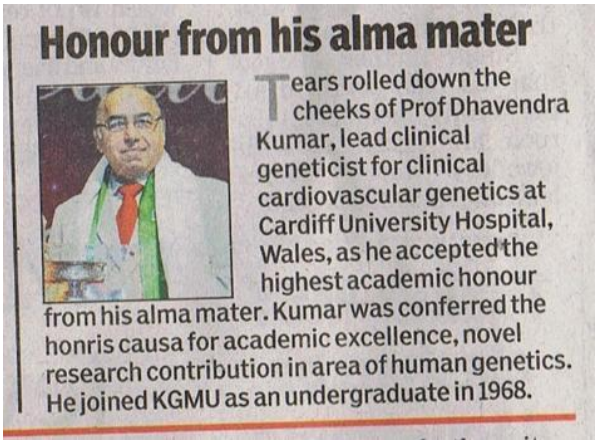
How to cite this article: Kumar D. The genomic health care in modern medicine. Apollo Med 2023:XX:XX-XX.

2.Professional profile- January 2022

Professor Dhavendra Kumar, MBBS, MD, DCH (RCPSI), MMedSci, FRCPI, FRCP, FRCPCH, FACMG, DSc.(Hon) The William Harvey Research Institute, Bart's and The London School of Medicine & Dentistry, Queen Mary University of London, UK.

An alumnus (1968 batch) of the King George's Medical College (now University) with MD in Paediatrics (1977). Highly acclaimed, globally acknowledged genetic and genomic clinician with special interests in clinical genetics and genomic medicine. He is credited with landmark contributions and achievements in genetic-inherited diseases of children, hereditary familial conditions of heart and blood vessels, applications of novel genomic principles and technology in genomic-precision medicine and public and population health genomics.

He is honoured with ***Doctor of Science, Honoris Causa*** by the alma mater, KGMU Lucknow, ***Hind Rattan*** International NRI Award, the ***GAPIO-Siemens Medical Innovation Award*** and the ***Life Time Achievement Award*** of the King George's Medical University Alumni UK. He is widely applauded for his sincere and persistent efforts for medical genetics as the integral part of medical teaching and practice across India and in other developing nations.



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A **B**

A) Prof. Kumar and Mrs. Anju Kumar with the Hind Rattan award

B) Newspaper clip from the Times of India reporting on DSc (Honaris Causa) conferred at the 2015 Convocation of the alma mater King George's Medical University, Lucknow, UP.

Notable services, achievements, contributions and awards include-

- Author/Editor of several peer reviewed research papers, articles and books. Main book titles include ***Genetic Disorders of the Indian Subcontinent; Genomics and Clinical Medicine***; ***Principles and Practice of Genomic Medicine***; ***Cardiovascular***

Genetics & Genomics- Principles and Clinical Practice; Oxford Specialist Handbook Inherited Cardiac Disease; ***Medical & Health Genomics; Genomics and Society; Clinical Molecular Medicine-Principles & Practice***; ***Genomic and Molecular Medicine e-book series and Advances in Genetics series.***

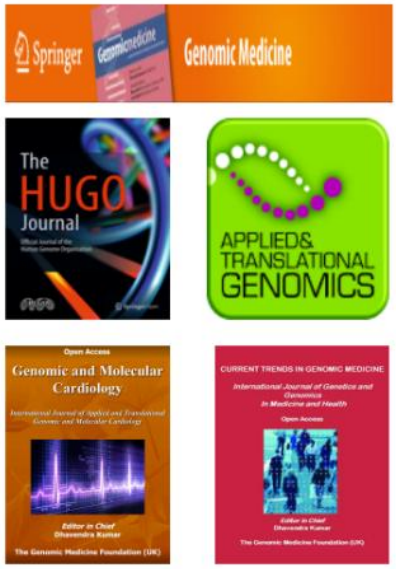
Selected books authored/ edited by Prof. Kumar

Presentation of 'Genomics and Clinical Medicine' to Dr. A.P.J. Abdul Kalam The President of India at the International Clinical Genomics Conference held In New Delhi, India: In picture from left- Prof. Dhavendra Kumar; Dr. Steven Shearer(Canada);Prof. Ed Liu (HUGO President); Dr. Doron Lancet (Israel); Prof. Aravinda Chakravarty (USA) and Prof. Samir Brahmachari (Director General CSIR, India)

*Presentation of the book '**Genomics and Clinical Medicine'** to the Late Former President of India, Bharat Ratna Dr. Abdul Kalam*

- The '***Medical and Health Genomics'*** book was 'Highly Commended' at the British Medical Association Annual Medical Book Awards (see Photo with Mrs. Kumar and Prof. Stylianos Antonarakis, Co-Auhtor, Geneva, Swtizerland

- Founding Editor in Chief of bio-medical journals- ***Genomic Medicine (Kluwer-Springer); Applied and Translational Genomics (Elsevier); Genomic and Molecular Cardiology (GMF-UK) and Current Trends in Genomic Medicine (GMF-UK)***

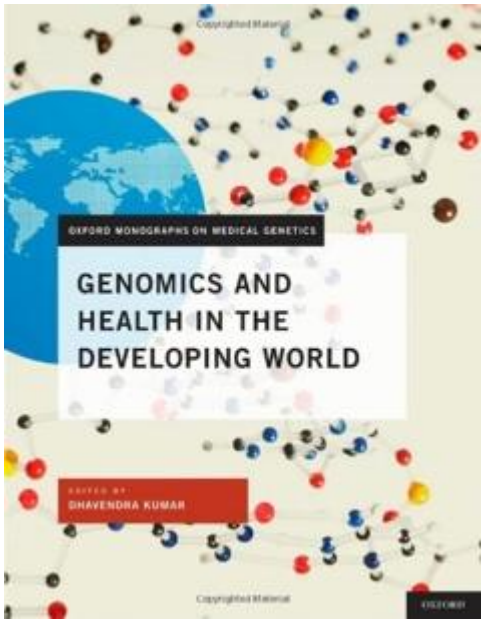


DHAVENDRA KUMAR: BIO-MEDICAL JOURNALS FOUNDER/ EDITOR IN CHIEF

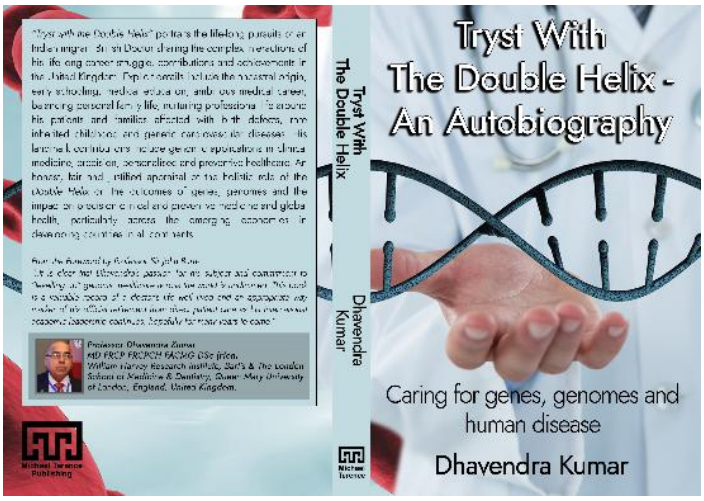
- Founded/ lead the ***Indo-UK Genetic Education Forum*** committed to enhancing the knowledge and clinical skills base for diagnosis & management of wide ranging genetic-inherited diseases.
- Founded-Lead the ***UK India Genomic Medicine Alliance*** (UKIGMA) to promote and enhance mutually beneficial collaboration-partnership in the fast-emerging field of genomic medicine and healthcare. The alliance is closely involved with the ***Genome India*** project through the Department of Science and Technology.

- Established close links with India's leading medical scientific academic institutions through the ***Memorandum of Understanding*** with KGMU-Lucknow and the JSS Higher Education Research Academy, Mysore, Karnataka. Main focus of MOU is to enhance and strengthen genomic and molecular elements in higher medical education and research. Similar links are under development with PGI, Chandigarh; AIIMS, Jodhpur and CMC, Vellore.
- Holds honorary Professorial titles and academic links for higher genomic education and research in the Capital Medical University, Beijing; Shri Mata Vashno Devi University-Jammu Kashmir, PGI- Chandigarh, AIIMS-New Delhi, CMC-Vellore, SGPGI-Lucknow, KGMU-Lucknow, Chettinad University-Chennai, Kasturba University-Manipal and JSS Higher Education and Research Academy-Mysore.
- Steered and contributed for establishing the ***KGMU Advance Centre of Research***, leading research and professional development for precision medicine and healthcare.
- Established the '***The Professor Dhavendra Kumar Young Investigator Gold Medal'*** to enhance research & academic contributions of the junior Faculty of KGMU, Lucknow.
- Established and leads the new ***KGMU Alumni International Seminars*** series sponsored by the Genomic Medicine Foundation on behalf of the KGMU Alumni UK.
- Continue and expand links with the India through active participation in collaborative projects, mainly the *Genome India, UK-India Health Data and Bio-informatics Joint Centre, and served as a panelist in the PM Hon. Narinder Modi's Global Summit of Indian Overseas Researchers and Academicians (**Vai**shvik **Bh**artiya **V**aigyanik **'VAIBHAV' Summit 202***
- *Leading ambassador for harnessing the genetic and genomic advances for improved healthcare in developing nations. Author-editor of the Oxford reference book*

***'Genomics and Health in Developing World'**, a unique resource for genetic-genomic status across all major developing nations.*



- Published memoirs December 2020: '**Tryst with the Double Helix'**



Detailed portrait of the life long struggle, resilience and perseverance in the United Kingdom for developing a successful and rewarding career in genetic and genomic medicine. An inspiring professional account and honest personal appraisal of learning and practising clinical and preventive medicine in and around the *Double Helix*. The book might inspire and help young bio-medical science & bio-technology graduates and Doctors for developing a career in genetics, genomics and related scientific disciplines.
UK: https://www.amazon.co.uk/dp/B08QH3NT6F;
USA: https://www/amazon.com/dp/B08QH3NT6F
India: http/B08QH3NT6F

3.Selected recent academic and professional conferences

1. **'Genomics- From disease prevention to treatment: Population, Medicine and Society', 2-5 October 2018, Haifa, Israel.**

Plenary Session: 'Socio-Economic and Cultural Aspects"
Key note lecture: 'Socio-cultural aspects of genetic testing'

1/23/25

PLENARY SESSION: 'SOCIO-ECONOMIC AND CULTURAL ASPECTS'

SOCIO-CULTURAL ASPECTS OF GENETIC TESTING

Professor Dhavendra Kumar
Institute of Medical Genetics
Cardiff University School of Medicine;
Genomic Policy Unit,
University of South Wales, UK

University of South Wales Prifysgol De Cymru

CARDIFF UNIVERSITY PRIFYSGOL CAERDYDD

1

Disclaimer & Acknowledgements

- Use of multiple sources in preparation of the presentation
- Advance apologies for any misuse of misrepresentation of factual information
- Not an expert- clinical geneticist with special interest in genomic medicine
- Acknowledge input and assistance for developing my insights on socio-cultural aspects of genetics and genomics

2

Regional and Continental population emphasis on socio-cultural and religious aspects of genetics and genomics in the context of illness and healthcare

3

ACKNOWLEDGEMENTS

CO-EDITOR PROF. RUTH CHADWICK

CONTRIBUTORS OF MANY CHAPTERS

4

Dynamics of Medicine & Society

- Socio-Cultural variation in health
- Variation in perception of illness
- Role of 'Sin' or ' Bad Karma' in causation
- 'Bad influence' or 'Wrongful contact'
- 'Bad food' as a causative factor
- Reluctance for new diagnosis
- Suspicion for new tests
- Rejection or delayed acceptance of new treatment

5

Socio-Cultural Views on Genes and Science of Genetics

- Sharing family characteristics
- Physical features and intelligence related to parents
- Few diseases linked to mother's lineage, for example increased bleeding risk following circumcision in the son and other males relatives
- Parent specific factors passed in sperm and ovum

6

1/23/25

7

8

Community awareness of Genetic Disease

- Gradually increasing
- Association of genetic diseases in cousin marriage
- Gender specific diseases, for example Duchenne Muscular Dystrophy & Hemophilia
- Familial late onset diseases- diabetes, dementia and others
- Cancer risks running in the family
- Need and importance of antenatal screening and testing
- New genetic tests based on genome sequencing
- Opportunities for new methods of treatment

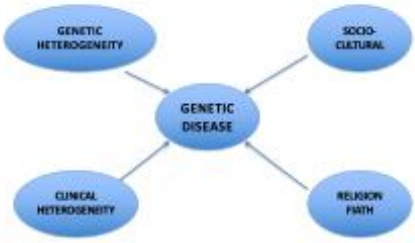
9

Socio-Cultural adaptation to human genetic disease

- Gradually getting better with the help of available information around
- Support from religious leaders
- Awareness of increased risks in cousin marriage
- Opportunity for pre-conception discussion/ counselling on common genetic testing
- Carrier testing for selected conditions
- Acceptance of assisted fertility
- Acceptance of antenatal screening/ testing
- Acceptance of new born screening/ testing

10

HETEROGENEITY



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Consanguinity- Mirror and Window for Human Genetic Disease

- Centuries old accepted socio-cultural custom
- Socio-economic benefits
- Possible safe guards/ protection of female relatives in closely linked families
- Increased infant mortality compensated by high birth rate
- Increasing concern due to small family size
- Awareness of serious genetic diseases in cousin marriages

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Levels of Genetic Testing

- Pre-conception
- Pre-implantation
- Antenatal
- Fetal
- Newborn
- Childhood & Adolescent
- Adult and later

13

Specific Issues in Carrier Testing

Vallence H1, Ford J. 'Carrier testing for autosomal-recessive disorders. Crit Rev Clin Lab Sci. 2003 Aug;40(4):473-97.'

- (1) test selection based on disease severity and test accuracy
- (2) funding for testing and genetic counselling
- (3) definition of the target population to be screened
- (4) development of a public and professional education program
- (5) informed consent for screening
- (6) awareness of community needs.

14

Social approval for Targeted Genetic (Carrier) Testing

- Ashkenazi Jewish population is at increased risk for several recessively inherited disorders- Tay-Sachs disease
  Cystic fibrosis
  Canavan disease
  Gaucher disease
  Familial Dysautonomia
  Niemann-Pick disease
  Fanconi anemia
  Bloom syndrome).

15

Preconception

- Most socio-cultural ethnic groups unaware
- Some awareness in the West
- Awareness in few 'high risk' communities (European; Jewish; Cyprus; Iran; West Africa)
- Most limited to 'talking to family adviser'
- Desire to know the carrier status (Tay Sachs; CF; Beta Thal; Sickle cell)
- Selective partnership; spouse choice?

16

Preimplantation genetic screening and targeted genetic testing

- For most socio-cultural ethnic groups 'Science Fiction'
- Most unable to distinguish 'screening' vs. 'testing'
- Testing mandatory 'gene targeted'
- Probably useful as 'option' in genetic counselling
- Screening 'high risk woman targeted'
- Ethical and socio-economic constraints

17

Prenatal and Fetal Genetic Testing

- Most socio-cultural groups are aware
- Huge variation in concept of this approach
- Many expect or anticipate therapeutic benefits
- Family/ community misconception hurdles
- Lack of adequate and informed genetic counselling
- Issue of Consent- Who is Incharge?
- Lack of uniform statutory guidelines/ regulations

18

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Newborn screening

- Established in Western and Developed nations
- Developing/ Emerging nations moving for this
- No provision in less developed nations
- Lack of quality/ audit data due to 'patchy' availability
- Few countries rely on expensive 'not relevant' metabolic diseases testing on commercial basis
- Huge gap from newborn NGS gene panel & genome sequencing in USA to None in Others!
- Alarmingly almost total lack for around two third global population

19

Childhood and Adolescents

- Major concerns for this age group
- Developing and less developed Nations face increasing numbers with possible genetic disease as primary healthcare expanding
- Often missed as newborn and later identified as symptomatic or possibly affected
- Clinicians and families would expect confirmation by appropriate genetic testing
- Provision of genetic counselling on interpretation, implications and options
- Specialist follow up with targeted intervetion and support

20

Adult and Later

- Most people, irrespective of socio-cultural background would disagree on genetic testing in this category.
- Medical decision making- lack of specialist skills
- Lack of Clinical Genetics/ GC input
- Possibly no local or regional genetic laboratory
- Selection and interpretation of genetic test
- Necessary medical or surgical intervention in 'affected positive'
- Reproductive choices
- Advice / GC to other family members

21

Asymptomatic & Predictive Genetic Testing

- Socio-cultural barriers are getting thin
- More and more people demand from affected 'families' or communities with 'affected families'
- Lack of proper medical documentation
- Lack of proper and effective genetic counselling
- Lack of provision or protocol for 'tested positive' family members

22

Availability and Access to Genetic Testing

- Problematic and Challenging in most developed and less developed nations
- Commonly 'none' around
- 'Out sourcing' by clinicians and local/ regional hospitals
- 'Direct to Consumer' genetic testing
- Usually prohibitive costs- unaffordable
- Lack of 'what next' medical surveillance and support healthcare

23

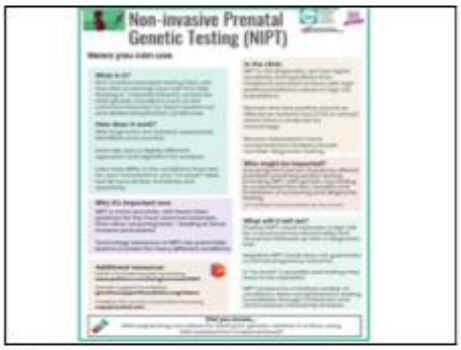
Direct to Consumer
GENETIC TESTING

Direct-to-Consumer (DTC)
Genetic Testing Companies

23andMe
DNA TRIBES
Navigenics
IDENTIGENE
HOMEDNA

24

1/23/25



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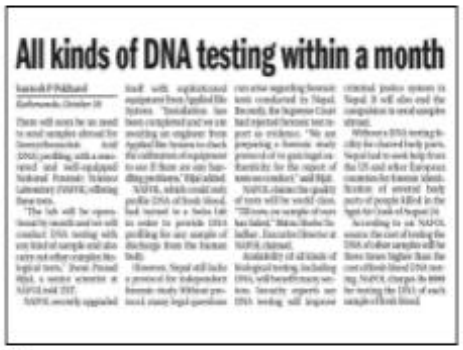

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Social approval for Targeted Genetic (Carrier) Testing- Hemoglobinopathies

- Approximately 5% of the world's population carries a mutation affecting the globin chains of the hemoglobin molecule.
- Among the most common of these disorders are the thalassemias.
- The global birth rate of affected infants is at least 2 per 1000 (in unscreened populations)
- High incidence in Southeast Asian, Indian, Mediterranean, and Middle Eastern ethnic groups.
- Carriers are detected by evaluation of red cell indices and morphology, followed by more sophisticated hematological testing and molecular genetic analyses.

27

Socio-Economic aspects of Genetic Testing

- Not well known due to very patchy and low key practice
- Mostly 'medical' driven and thus seen as part of the overall healthcare costs
- Usually not 'state funded' in most developing/ less developed nations
- Huge 'rich and poor' divide for accessing genetic testing
- Risks of 'Direct to Consumer' genetic testing- wasteful and potential malpractice

28

Ethical standards

- Western style 'bio/medical ethics' principles are possibly not relevant
- Most ethnic and minority socio-cultural groups have their own ancient ethical/ moral codes
- More 'harm than good' by genetic testing unless supervised and managed for medical purposes only
- Risk of 'Geneticisation' or 'Genomicisation'
- Risk for apparent discrimination, disqualification, unfit spouse or doubteful biological fitness

29

Ethical Issues for Genetic Testing

- **Clinical issues including the education of doctors and other health-service providers, people identified with genetic conditions, and the general public; and implementation of standards and quality-control measures.**
- How should health professionals be prepared for the new genetics?
- How can the public be educated to make informed choices?
- How will genetic tests be evaluated and regulated for accuracy, reliability, and usefulness?
- How does society balance current scientific limitations and social risk with long-term benefits?

30

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Legal aspects & Regulation

- Eligibility for 'Consent'
- Safeguarding 'confidentiality'
- Responsibility of 'DNA storage'
- Database maintenance and sharing of information
- Protection from 'Gender discrimination'
- Protection of education, career prospects, employment etc. for those tested positive

31

Media and Genetic Testing

- Continuous challenge for the Profession
- Often too negative
- Could be full of hype or out of proportion importance
- Few are very constructive or informative
- Google and other online resources- Good
- Opportunity for people, patients to view and ponder
- Often more harm than good by inappropriate interpretation of 'direct to consumer' genetic testing

32

Education and Information

- Not available
- Inconsistent and Inappropriate
- Could be misleading in some cases
- Dangerous for 'less is more' situation
- Too much information available 'more in less'
- Need for concise and factually correct information on 'genetic testing' and 'targeted therapy

33

Duties of Genetics and Genomics

- Generous release of research data, pertinent to minority/ ethnic socio-cultural population groups
- Process and protocols for pathogenic vs. non-pathogenic genetic/ genomic variation
- Robust evidence focussed on clinical utility
- Proactive engagement/ partnerships with medical and genetic counselling workforce
- Open doors to People and Community Leaders

34

Summary- Major issues

- Most people from minority/ ethnic population groups are now aware of 'Genetic Test'
- Lack of awareness and perception of 'genetic or inherited disease'
- Lack of adequate and classified information on scope and limitations of genetic testing
- Provision of funding support to avoid inequitable availability of genetic testing
- Provision for dedicated medical input and genetic counselling

35

Thank you
Garcia
Messy
Shukran

36

2. **HUGO/ Human Genome Meeting 2019, Seoul, South Korea**
   Workshop- "Genomic education and Training for Healthcare"

3. **"Global Genomic education and Training- Chellanges and Opportunity"**
   March of Dimes Birth Defects Conference/ WHO South East Asia Region Office
   Colombo, February 2020

The Genomic Medicine Foundation (UK)

The Global Consortium for Genomic Education (GC4GE) invites you to participate in a multi-disciplinary workshop and contribute to genetic and genomic education and training for application and translation of genomic advances and new developments in clinical medicine and healthcare.
Title: "Development of targeted genomic education"
Date: 23rd February 2020 Time: 10am to 4pm
Venue: Colombo, Sri Lanka (Details to follow)
Convenors: Professor Dhavendra Kumar (Cardiff/London, UK)
Professor Vajira Dissanayake (Colombo, Sri Lanka)

1/23/25

GLOBAL GENOMIC EDUCATION AND TRAINING- CHALLENGE AND OPPORTUNITY

DHAVENDRA KUMAR
WILLIAM HARVEY RESEARCH INSTITUTE
QUEEN MARY UNIVERSITY OF LONDON, UK

1

THE GENOMIC MEDICINE FOUNDATION (UK)

FELLOWSHIP, SCHOLARSHIP, AND PROMOTION OF GENOMICS IN MEDICINE, HEALTHCARE AND SOCIO-ECONOMIC PROGRESS

2

THE GENOMIC MEDICINE FOUNDATION (UK)

www.genomicmedicine.org

Independent organization promoting application and translation of ***Genomics*** and other ***OMICS*** sciences in the current and future practice of clinical medicine, personalized healthcare & socio-economic progress

3

THE GENOMIC MEDICINE FOUNDATION (UK)

- Genomic and Precision Medicine- Seminars, Books & Journal
- Cardiovascular Genomic Medicine- Conferences, Books and Journal
- Genomic and Clinical Molecular Medicine- Seminars & Books
- Genomic teaching and training- Postgraduate Seminars & Courses
- Global Consortium for Genomic Education (GC4GE)
- Global Familial Heart Challenge (GFHC)
- Genomics and Society- Books & Seminars
- Genomics and Health in Developing World- Books & Seminars
- Indo-UK Genetic Education Forum- Seminars and Workshops
- UK-India Genomic Medicine Alliance (UKIGMA)

4

Genomic Medicine and Healthcare

- Effective and efficient delivery of the genomic led precision healthcare
- Skills and competencies of genomic healthcare professionals
- Technical specifications and regulation of diagnostic genomic testing
- Genomic led therapeutic applications
- Consumer driven genomic healthcare

5

What needs to be done?

- Setting evidence-based standards for genomic healthcare
- Development of the multi-disciplinary skilled workforce
- Governance- infrastructure and monitoring
- Educational and training approaches- targeted and specific

6

1/23/25

How could we develop skilled genomic healthcare workforce?

- Organize and lead structured program for genomic education and training
- Introduce regulatory/ statutory mechanisms to incorporate genomic education as a prerequisite for genomic led healthcare
- Provision of adequate resources for curriculum design and development of foundation courses tailored for specific needs
- Provision for continued professional development of existing healthcare workforce
- Setting up the database (National/Sub-Continent/International) of skilled genomic healthcare professionals

7

8

UK GENOMIC WORKSFORCE

- Clinical Geneticist- 4 year program; DOH funded; National selection; designated centres; CST with exit examination (KBE); GMC Specialist Register mandatory for Consultant position.
- Medical specialist with Clinical Genetics- Fetal Medicine; Neurology; Oncology & Cardiology; post CST Fellowship
- Genetic Counsellor- 2 years MSc with vocational training; new courses led by Health Education England; GC Board Registration
- Clinical Laboratory Scientist- 3 years program based in one of 6 NHS Genomic Laboratory hubs

9

USA/ Canada Genomic Workforce

- American Board of Medical Genetics & Genomics- 2 years program followed by Certification examination (DABMGG) in Clinical Genetics and Genomics; Clinical Cytogenetics and Genomics, Molecular Genetics and Genomics; Laboratory Genetics and Genomics & Clinical Biochemical Genetics.
- Canadian College of Medical Genetics & Genomics- as above with examination (FCCMGG).
- American / Canadian Board of Genetic Counsellors- Master level courses with vocational training; Certification examination
- Non-accredited/ certified scientists and allied healthcare professionals with specific areas of interest supporting genomic medicine/ healthcare

10

Aim

'To promote genetics and genomics awareness and applications in Medicine and Healthcare and Socio-Economic progress for the people of the Indian subcontinent'

11

12

1/23/25

Mission/ Outcomes

- Promote genetic & genomic education for health professionals in the Indian subcontinent through educational seminars, symposia and exchange programm
- Support and contribute to the development of genetic and genomic infrastructure for the improvement of healthcare in all countries of the Indian subcontinent
- Encourage, advice and supervise collaborative genetic and genomic research between UK and leading genetic/ genomic Institutions and Hospitals in the Indian subcontinent
- Strengthen and encourage patient support groups in the UK and Indian subcontinent through engaging in patient/ family education and welfare related to genetic/ hereditary conditions
- Educate and inform health benefits of genetics/genomics to lay people of the Indian subcontinent including migrant ethnic groups resident in the UK

13

INDO UK GENETIC EDUCATION FORUM

14

UK India Genomic Medicine Alliance [UKGMIA]

"TO ORGANISE AND LEAD A PROFESSIONAL GROUP FOR PROMOTING AND SUPPORTING THE GENOMIC APPLICATIONS AND TRANSLATIONS IN MEDICINE AND HEALTHCARE ACROSS THE INDIAN SUBCONTINENT"

15

UKGMIA- Objectives

- Identify and recruit organisations and institutions engaged in scientific and applied research in genomics relevant to medicine and healthcare
- Encourage collaboration with individual clinicians, scientists, and other professionals in anthropology, population genetics, bio-ethics, social sciences and bio-economics
- Develop a programme for training and skills development through series of structured courses, workshops and webinars in the key areas of applied and translational genomic medicine
- Plan and carry out specific audit on the outcomes of investments in Institutions and Laboratories as part of the current strategy for capital and infrastructure scientific developments
- Develop and steer through individual or group research projects on related to utilization and the delivery of genomics led medical and healthcare

16

Fields of Interest

- Genetic and Genomic Education
- Birth defects (Congenital Anomalies)
- Rare genetic diseases
- Cancer genetics and genomics
- Cardiovascular genetics and genomics
- Genomic and Precision Medicine

17

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1/23/25

Memorandum of Understanding

- Support and collaboration for genomic education and training
- Development of novel educational/ training approaches, for example Digital & IT methods
- Support and guidance for Research governance
- Collaborations and support for targeted higher degree programs in genomic medicine/ healthcare
- Support and guidance for ethical, legal and social issues in the genomic healthcare

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UKIGMA- Memorandum of Understanding

1. Post Graduate Institute of Medical Education & Research CHANDIGARH- PUNJAB/HARYANA
2. King George's Medical University LUCKNOW- UTTAR PRADESH
3. All India Institute of Medical Sciences- JODHPUR- RAJASTHAN
4. The University of GUWAHATI- ASSAM
5. JSS Higher Education Academy MYSORE- KARNATAKA
6. Christian Medical College, VELLORE- TAMILNADU
7. The University of COLOMBO- SRI LANKA

20

The Global Consortium for Genomic Education (GC4GE)
AIM

"To organize, coordinate and steer a global consortium for the integrated genomic education and training program"

21

Objectives

- To identify and engage with Professionals, Institutions and Organizations involved with genetic/genomic education and training.
- To develop the core framework for the consortium in collaboration with participating groups.
- To develop a network for the consortium working on the 'hub and spoke' model.
- To develop the bespoke integrated genomic education and training program incorporating major components of genome science and technology.
- To develop mechanisms for delivering the integrated genomic education program on regional and country basis.

22

The Global Consortium for Genomic Education

23

Process plan

- Website/ online presence: www.genomicmedicine.org/GC4GE
- Invitations to major genome science & bio-technology groups, institutions, organizations, industrial and charitable societies etc.
- 'Memorandum of Understanding'
- No contractual requirement or legal constraints
- Maintain 'Independent' and 'Administrative' arrangement
- Nominal enrolment and continuation annual subscription
- Develop 'working groups' on specific areas of genomic education
- Hold regular international/ regional seminars/ meetings
- Proceeds and reports on freely accessible public domains

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1/23/25

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4. **5th International Conference of Birth Defects, 21-23 November 2022, JSS Higher Education Academy, Mysore, India.**

5. **The IX International Conference of Cardiovascular Genomic Medicine Royal College of Surgeons, Edinburgh, Scotland 23-24 October 2023**

THE GENOMIC MEDICINE FOUNDATION (UK)
FELLOWSHIP, SCHOLARSHIP, EDUCATION AND PROMOTION OF GENOMIC APPLICATIONS IN MEDICINE, HEALTHCARE AND SOCIO-ECONOMIC PROGRESS

The IX International Conference of Cardiovascular Genomic Medicine
Royal College of Surgeons, Edinburgh, Scotland
23-24 October 2023

The next (9th) **Biennial International Cardiovascular genomics conference** is held on 23-24 October 2023. The main theme of this conference is '***Precision Cardiovascular Medicine'***. The scientific programme, delivered by leading global experts, includes the ***Third William Harvey Oration***, plenary/ key-note lectures, and scientific oral & poster sessions.

Organising Committee

Prof. Dhavendra Kumar (Chair)
Dr. Wayne Lam
Ms. Sam Moss
Mr. Nick Miles

Scientific Committee

Prof. Sir Munir Pirmohamed (Univ. Liverpool, UK/ GMF-UK, Chair)
Prof. Dhavendra Kumar (Genomic Medicine Foundation UK/ CEO)
Prof. Arthur Wilde (Univ. Amsterdam, NL)
Prof. Perry Elliott (Univ. College Hospital & Bart's Hospital, London, UK)
Prof. Mary Porteous (Univ. of Edinburgh, Scotland, UK)
Prof. Martin Denvir (Univ. of Edinburgh, Scotland, UK)
Prof. Zaheer Yousef (Cardiff University, Wales, UK)
Prof. Ajay Bahl (PGIMER, Chandigarh, India)
Dr. Wayne Lam (Western General Hospital, Edinburgh, Scotland, UK)
Dr. Catherine Mercer (Southampton Univ. Hospitals, Southampton, UK)
Prof. Bart Loeys (Univ. Antwerp, Belgium)
Dr. John Dean (Royal Infirmary, Aberdeen, Scotland, UK)
Prof. Robert Hamilton (Sick Kids, Toronto, Canada)
Prof. Dan Arking (Johns Hopkins, Baltimore, MD, USA)
Prof. Patricia Munroe (William Harvey Institute, QMUL, London, UK)
Dr. Yasmine Aquib (Sir Magdi Yaquib Heart Hospital, Aswan, Egypt)
Prof. Bill Newman (Centre for Genomic Medicine, Univ. Manchester, UK)
Prof. Christopher Semsarian (University of Sydney, Australia)

Programme

Theme: "PRECISION CARDIOVASCULAR MEDICINE"

Day 1 Monday 23rd October 2023

0800 **Reception/ Registration**

0900 **Welcome/ Introduction**
Professor Dhavendra Kumar, William Harvey Research Centre, Bart's Medical School, QMUL, UK

0915- 1115 **Session I: Diagnostic cardiovascular genomics**
Chair- Professor Mary Porteous, Clinical Geneticist, Edinburgh, Scotland

1. Dr. Lorenza Monserrat, La Coruna, Spain
'Genomic evolution of diagnostic cardiology'

2. Prof. James Ware, Imperial, London
'Phenotype-genotype' in Inherited cardiovascular conditions'

1115 ***Coffee break***

1130-1330 **Session II: Genotype-Phenotype ontology in cardiovascular genomics**
Chair: Dr. John Dean, Clinical Geneticist, Aberdeen, Scotland

3. Dr. Farrah Khawaja, Deputy Director of Genomics Quality Assessment (GenQA), Royal Infirmary of Edinburgh, Scotland, UK.
'Challenges of genome diagnosis in clinical cardiology'

4. Dr. Verity Harthill, Leeds Institute of Medical Research, University of Leeds, St James University Hospital, Beckett Street, Leeds, UK
'Understanding the genetic basis of congenital heart disease; whole genome sequencing opens new avenues for investigation, but significant challenges remain'

1330- 1430 ***LUNCH***

1430- 1500 **Session III: Posters viewing**

1500-1600 **Session IV: 'Multi-OMICS Cardiovascular Medicine'**
Chair- Prof. Martin Denvir, Cardiologist, Edinburgh, Scotland

5. Prof. Seema Mittal, Hospital for Sick Children, Toronto, Canada
'Digital approaches to multi-OMICS clinical cardiology'

6. Dr. Anna Maria Choy, Cardiologist, Univ. Dundee, Scotland
' Multi-disciplinary management of arrhythmia syndromes'

1600-1630 ***TEA***

1630-1730 **Session V: Cardiovascular genomic precision medicine- back to the future'**
Key Note Lecture: Chair- Prof. James Ware, Imperial College, London.

7. Prof. Perry Elliott, UCL, London, UK
'Emerging novel treatment prospects for cardiomyopathies'

1730 **Panel discussion- Reflections of the Day**
CLOSE OF DAY 1

1930 ***Scottish Reception/ Welcome***
2000 ***Conference Dinner (Dress- Black tie/ Traditional/ National)***

Day 2 Tuesday 24th October 2023

0830-0930 **Reception/ Registration**

0930-1015 **Key note lecture, Chair:**
8. Prof. Sir Munir Pirmohamed, Universtity of Liverpool, UK
'Pharmacotherapy cardiovascular genomic medicine'

1015-1115 **Session VI: 'Oral Award presentations (10 minutes each; 10 minutes Q/A & Discussion)**
Chairs: Dr. Caroline Coats, Cardiologist, Glasgow & Dr. Ruth McGowan, Clinical Geneticist, Glasgow, Scotland.

Judges: Dr. Wayne Lam, Edinburgh, Scotland; Dr. Catherine Mercer, Southampton, England; Prof. Seema Mittal, Toronto, Canada

1. **'Double Trouble in the hypertrophic heart'**
A.Kissopoulou, Department of Cardiology, County Hospital-Ryhov, Jönköping, 55185, Sweden

2. **'One test, a lifetime of precision familial hypercholesterolemia reports',** Aditi Babel, Imperial College Healthcare NHS Trust, London, UK

3. 'Distinct signaling events from the overexpression of the PRKAG2 R302Q variant of AMPK lead to Hypertrophic phenotype'
Vanya Vaidya, Department of Cardiology, PGIMER, Chandigarh, India

4. 'WGS analysis reveals an Alu retrotransposon element insertion in the *NEXN* gene confirming a diagnosis of paediatric onset autosomal recessive dilated cardiomyopathy (AR DCM) in a family'
Mary Gable, Bristol Genetics Laboratory/South West Genomics Laboratory Hub, Southmead Hospital, Bristol, England, UK

5. 'Prediction of Atrial Fibrillation using Polygenic Risk Scores for Cardiovascular Risk Factors'
Julia Ramirez, Aragon Institute of Engineering Research, University of Zaragoza, Zaragoza, Spain; Centre of Clinical Pharmacology and Precision Medicine, William Harvey Research Institute, Queen Mary University of London, U.K

1115 ***COFFEE***

1145-1330 **Session VII 'Genomic precision cardiovascular medicine**
Chair: Prof. Sandi Deans, University of Edinburgh, Scotland

10. Prof. Nimesh Desai, Cardiovascular Surgery, University Pennsylvania, Philadelphia, USA
'Genotype driven surgical management of aortopathies'

11. Prof. Sandosh Padmanabhan, Glasgow, Scotland, UK
'Genomics and the cardiovascular continuum'

12. Dr. Rob Ainsworth, Pathologist, University of Edinburgh, Scotland
'Sudden cardiac death- the Scottish perspectives'

1330-1430 ***LUNCH***

1430-1600 **Session VIII: Personal genomics in preventive cardiology**
Chair: Prof. Sandosh Padmanabhan, University of Glasgow

13. Prof. Manuel Mayr, Imperial College, London.
' Cardiovascular proteomics of coronary artery disease'

14. Prof. Panagiotis Deloukas, Queen Mary University, London.
'Polygenic scoring systems in preventive cardiology'

1600-1630 ***TEA***

1630-1730 **'The Third William Harvey Oration'**
Facilitator- Professor Sir Munir Pirmohamed

16. Invited speaker- Prof. Arthur A.M. Wilde, University Amsterdam,
'Evolution of channelopathies in clinical cardiology'

Faculty

Professor Dhavendra Kumar

MBBS, MD, DCH(Ire), MMedSci, FRCPI, FRCP, FRCPCH, FACMG, DSc (Hon)
* The William Harvey Research Institute, Queen Mary University of London (d.kumar@qmul.ac.uk)
*Institute of Medical Genetics, University Hospital of Wales, Division of Cardiff University School of Medicine, UK. (kumard1@cf.ac.uk)
*The Genomic Policy Unit, the University of South Wales, Pontypridd, South Wales, UK.(Dhavendra.kumar@southwales.ac.uk)
*Inherited Cardiac Diseases Unit, St. Bart's Hospital, Bart's NHS Foundation Trust, London, UK
*Department of Medicine, The Medical School, Swansea University, UK
* The Genomic Medicine Foundation UK
(www.genomicmedicine.org; md@genomicmedicine.org)

Professor Dhavendra Kumar, Chair Organising/ Scientific Committees

An alumnus (Graduate,MBBS); Postgraduate, MD and Honorary Doctorate in Science, DSc) of the King George's Medical University, Lucknow, UP, India. He holds Fellowship of the Royal Colleges of Physicians (FRCPI & FRCP London) and Paediatric-Child Health (FRCPCH). In addition, he is a Fellow of the American College of Genetics and Genomics (FACMG). He is one of the globally acknowledged genetic and genomic clinician. His special interests in clinical genetics include genetic diseases of children, inherited conditions of heart and blood vessels, genomic medicine and genomic applications in global healthcare.

He has authored/edited many textbooks and monographs in the field of clinical genetics, cardiovascular genetics and genomic medicine & healthcare. Main titles include ***'Genetic Disorders of the Indian Subcontinent'***, '***Principles and Practice of Genomic Medicine'***, '***', 'Genomics and Health in Developing World' and 'Clinical Molecular Medicine-Principles & Practice'***. His books '***Oxford Specialist Handbook Inherited Cardiac Disease'*** and '***Medical & Health Genomics'*** received ***Highly Commended*** award at the British Medical Association Annual Medical Book Awards. Since 2016, he has served is the Serial Editor for '***Advances in Genetics***' and serves on the editorial board of many biomedical journals.

He is passionate for raising awareness and promoting importance of the inherited cardiovascular conditions (ICC) in clinical cardiology and genetic/genomic in modern medicine. He is acknowledged with the benchmark practice of 'multi-disciplinary care for inherited/familial heart disease'. He founded and leads the '***Global Familial Heart Challenge***' project for promotion; early detection, management and prevention of familial/ inherited heart diseases globally. He is an international authority in cardiovascular genomic medicine (CVGM) and leads the Global Network comprising of leading CVGM Centres. Since 2007, he has organized and led the Biennial International Cardiovascular Genetics and Genomics Conferences. He is the Founding Editor in Chief of the new biomedical journal '***Genomic and Molecular Cardiology***' and co-author/co-editor of '***Cardiovascular Genetics & Genomics-Principles and Clinical Practice' and the 'Oxford Specialist Handbook Inherited Cardiac Disease'.***

6. International Genomics Education and Training Summit
Sanger Genome Centre, Hinxton, Cambrdige, UK; 27-28 November 2023

International Genomics Education and Training Summit
27-28 November 2023
Global Genomic Education & Training Initiatives
Human Genome Organization International (HUGO)
Dhavendra Kumar
Chair- HUGO Education Committee

1

HUGO BOARD
EDUCATION
ETHICS, LAW & SOCIETY
HUGO SOCIETY

2

HUGO
Education Committee
Dhavendra Kumar- Chair
Angela Solano- Co Chair
Aim: "Develop, design, and guide the diverse global community for human genomic education and training"
Objectives:
- Develop mechanisms for delivering the integrated and comprehensive genomic education and training programs employing the 'state of the art' digital and artificial intelligence methods.
- Empowering and enhancing skills and competencies required for specific sectors- laboratory genomics, computational genomics, clinical genomics, genetic/ genomic counselling, non-genetic medical & healthcare providers.
- Designing and implementing genomic education teaching and training programs for students/ trainees, non-genetic physicians and healthcare professionals, general public and continuing adult education etc.
- Identify and support human genomic education and training targeted at specific areas and gaps in 'Low and Middle Income Countries- 'LMICs'

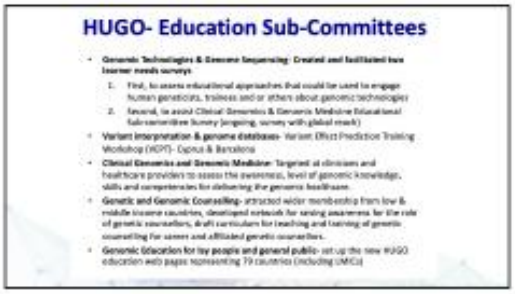
3

HUGO EDUCATION & TRAINING COMMITTEE
HUGO EDUCATION & TRAINING COMMITTEE

4

HUGO- Education Sub-Committees
'Genomic technologies including genome sequencing'
Chair- Charlie Wray, Jackson, USA
'Variant interpretation and genome databases'
Chair- Andreas Laner, Munchen, Germany
'Computational genetics and genomics including bioinformatics'
Chair- Christian Gilissen, Nijmegen, NL
'Clinical genomics and genomic medicine'
Chair- Sheriffa Hamed, Cairo, Egypt
'Genetic/ Genomic Counselling'
Chair- Zilfalil Bin Alwi, Malaysia
'Genomic education for lay people and general public'
Chair- Edward Tobias, Glasgow, Scotland

5


HUGO- Education Sub-Committees
Genomic Technologies & Genome Sequencing: Created and facilitated two learner needs surveys
1. First, to assess educational approaches that could be used to engage human geneticists, trainees and/or others about genomic technologies
2. Second, to assist Clinical Genomics & Genomic Medicine Educational Sub-committee Survey (ongoing, survey with global reach)
Variant Interpretation & genome databases- Variant Effect Prediction Training Workshop (VEPT)- Cyprus & Barcelona
Clinical Genomics and Genomic Medicine- Targeted at clinicians and healthcare providers to assess the awareness, level of genomic knowledge, skills and competencies for delivering the genomic healthcare.
Genetic and Genomic Counselling- attracted wider membership from low & middle income countries, developed outlands for raising awareness for the role of genetic counsellors, draft curriculum for teaching and training of genetic counselling for current and affiliated genetic counsellors.
Genomic Education for lay people and general public- set up the new HUGO education web pages representing 79 countries (including LMICs)

6

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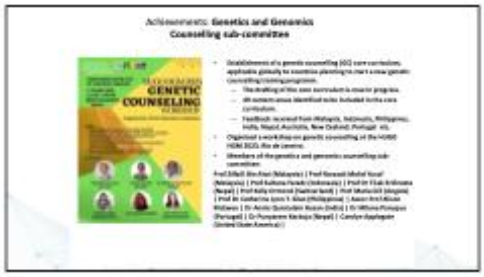

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7. 5th National Symposium 'Genomic Medicine and Healthcare in Clinical Practice' 29th December 2023, Post Graduate Institute of Medical Sciences, University of Health Sciences, Rohtak, Haryana, India

Certificate of Attendance
Certificate of Attendance shall be awarded to the registered attendees during the valedictory session.

Award of Credits
Credits as prescribed may be awarded by the Haryana Medical Council.

Accommodation, hospitality and travel support
No travel support or accommodation will be provided. All outstation attendees need to arrange for their travel, boarding & lodging at their own if they wish to arrive Rohtak a day in advance or wish to stay beyond the duration/day of Symposium. Tea/Coffee, Lunch and Snacks will be served to all the registered delegates during the symposium hours

Important Dates
Registration (for attendance) Opens: 2/12/2023
Registration (for attendance) closes: 24/12/2023

About North India Genomics Consortium (NIGC)
A collaborative venture put forth by Prof. Dhavendra Kumar, a renowned international medical geneticist from London (UK), NIGC is an initiative of human genetic and genomic academic and research scientists, medical and health professionals, genetic counsellors, genetic/genomic laboratory scientists and other related professionals engaged with genetic or genomic developments. The consortium represents human or medical genetic/genomic centers in all north Indian states of Jammu & Kashmir, Punjab, Himanchal Pradesh & Haryana. The consortium was formed in Sept. 2022. The NIGC is currently lead by Prof. AJS Bhanwar.

About the Genomic Medicine Foundation
The Genomic Medicine Foundation is a UK based non-profit organization providing up to date and evidence-based information on genetics/genomics relevant to clinical medicine and healthcare.

About Rohtak & PGIMS
Rohtak is one of the oldest cities in Haryana. It is an educational city located at a distance of 75 km from Delhi and 250 Km from Chandigarh. Spread over 350 acres lush green area, PGIMS is located on NH10. Institute is one of the oldest medical institutes in North India. PGIMS is administered by Pt. B.D. University of Health Sciences Rohtak which was established in 2008 as a state University under Department of Medical Education and Research, Govt. of Haryana.

For any other query or assistance please contact:
Symposium Secretariat
Department of Biotechnology & Molecular Medicine
Contact Person: **Dr. Deepak Kumar** (Mobile) 8901058287

5th
National Symposium
GENOMIC MEDICINE
and
Healthcare
in
Clinical
Practice
DECEMBER 29, 2023
in academic collaboration of
North India Genomics Consortium
&
The Genomic Medicine Foundation(UK)
ORGANIZED BY
Department of
Biotechnology & Molecular Medicine
POST GRADUATE INSTITUTE OF MEDICAL SCIENCES
UNIVERSITY OF HEALTH SCIENCES, ROHTAK
The Department of Biotechnology & Molecular Medicine has been founded at PGIMS Rohtak as a interdisciplinary translational research, training and academic centre for strengthening biomedical research for complementing clinical, therapeutic & surgical efforts in the interest of patient care.

ABOUT THE SYMPOSIUM
Genomic Medicine is a flagship discipline of modern medicine. In last couple of years it has evolved to a level that the knowledge gained from basic research can be utilized to develop newer and improved methods of preventing, diagnosing, or treating diseases. It aims at translating research hypothesis into clinical practice by putting basic genetic and genomic researches to clinical use and utilizing clinical observations to further basic research.

Genomic Medicine is stepping stone to personalized healthcare. Considering the importance of Genomic Medicine, it is imperative to share and discuss various aspects of Genomic medicine-including both the opportunities and the challenges. Organization of this symposium is an effort to provide the students, researchers and teaching faculty a platform to interact with some of the best among the brightest scientists and clinicians, who will present their work on various aspects of medical biotechnology and translational medicine. This one day symposium presents broad spectrum of topics for mixed medical and allied healthcare audience ranging from cardiovascular genomics, rare diseases, fetal medicine, radio-genomics, precision cancer treatment, blood genetic diseases and public health genomics.

This symposium is aimed to provide a glimpse of the latest innovations and applications of Genomic Medicine to all the attendees and particularly to the budding clinicians and basic scientists. The talks to be delivered during various sessions should provide a clear understanding of current translational approaches to find cure for diseases which remain incurable at present. A panel discussion-"*Breaking the barriers of integrating genomic medicine into clinical practice*" has also been planned with aim to find ways to bridge the gap between basic and clinical research and stimulate critical thinking to address issues revolving around responsible use of genomic technologies amongst scientists appropriately qualified and thoroughly trained in these. We are hopeful that deliberations of this symposium will be of immense benefit to further scientific knowhow, expand horizons of analytical thinking, hone genomic competencies and to enhance networking and research connectivity.

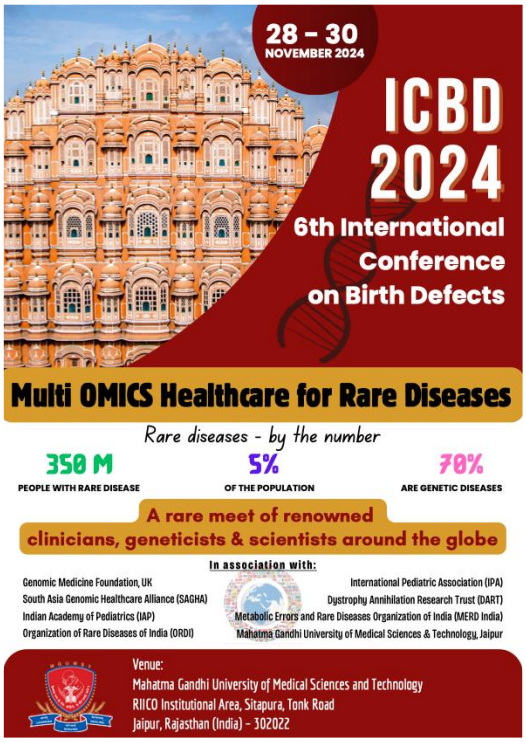
With this note, we cordially invite the scientific fraternity, medical/allied health professionals, research scholars and students to please join us for this academic feast.

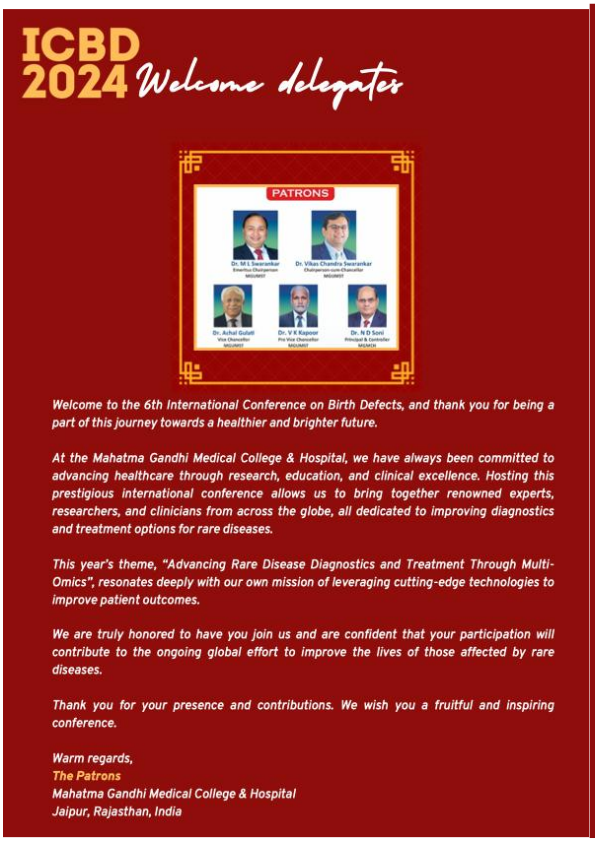
REGISTRATION
For registration, all prospective participants are required to submit a request online through E-mail (BTMM.meetingsandcourses@gmail.com) and fill up the requisite Google form. Google form can be filled by clicking on the link below.
https://docs.google.com/forms/d/e/1FAIpQLSfITdHNkA09pAhR65SgzJW-LJXx3HF4FqKzfkItXEtzqyG4vg/viewform?usp=pp_url

Note: Registration is free but mandatory.

DISTINGUISHED SPEAKERS, CHAIRS & PEANALISTS
Prof. Dhavendra Kumar Prof. L.M. Srivastava Prof. Tej .P. Singh
Prof. A.J.S. Bhanwar Prof. Inusha Panigrahi Prof. Prashant Sharma
Prof. Jitender Saini Dr. Ajay K. Mahto Dr. Eunice Marumudi
Dr. Ambika Gupta Dr. Akshata Sharma Dr. Kriti Menon
Dr. Ashish Fauzdar Dr. Prashant Kumar Dr. Praveen K.S.

8. Sixth International Conference on Birth Defects, 28-30 November 2024





ICBD 2024 Welcome delegates

PATRONS

Dr. M L Swarankar
Emeritus Chairperson
MGUMST

Dr. Vikas Chandra Swarankar
Chairperson-cum-Chancellor
MGUMST

Dr. Achal Gulati
Vice Chancellor
MGUMST

Dr. V K Kapoor
Pro Vice Chancellor
MGUMST

Dr. N D Soni
Principal & Controller
MGMCH

Welcome to the 6th International Conference on Birth Defects, and thank you for being a part of this journey towards a healthier and brighter future.

At the Mahatma Gandhi Medical College & Hospital, we have always been committed to advancing healthcare through research, education, and clinical excellence. Hosting this prestigious international conference allows us to bring together renowned experts, researchers, and clinicians from across the globe, all dedicated to improving diagnostics and treatment options for rare diseases.

This year's theme, "Advancing Rare Disease Diagnostics and Treatment Through Multi-Omics", resonates deeply with our own mission of leveraging cutting-edge technologies to improve patient outcomes.

We are truly honored to have you join us and are confident that your participation will contribute to the ongoing global effort to improve the lives of those affected by rare diseases.

Thank you for your presence and contributions. We wish you a fruitful and inspiring conference.

Warm regards,
The Patrons
Mahatma Gandhi Medical College & Hospital
Jaipur, Rajasthan, India

ICBD 2024 Organisers

Dr Ashok Gupta, India
MD Pediatrics, FIAP
Executive Director: International Neonatology Association Geneva
Fellowships: The University of Illinois, Chicago & American Academy of Paediatrics, USA

Director, Institute of Rare Diseases
Professor & Head, Department of Pediatrics
Mahatma Gandhi Medical College Hospital, Jaipur

Dr Dhavendra Kumar, UK
MD Pediatrics, DSc (Hon), FRCP, FRCPI, FRCPE, FRCPCH, FACMG

Honorary Professor, Queen Mary University London (QMUL), London, UK
Honorary Consultant, Barts Heart Centre, St. Barts Hospital, London, UK
Medical Director/CEO, The Genomic Medicine Foundation, UK
Honorary Professor Medicine, Swansea School of Medicine, Swansea, UK
Consultant Adviser, Apollo Genomics Institutes, Apollo Group, India

Dr Hemant Malhotra, India
MD Medicine, FRCP (London), FRCP (Edinburgh),
FACP (USA), ECMO, FNAMS, FUICC, FICP, FIMSA

Director, Oncology Services, Sri Ram Cancer & Super-specialty Center
Professor & Head, Department of Medical Oncology
Mahatma Gandhi Medical College Hospital, Jaipur

Dr Aditi Singh, India
PhD Genetics, University of Aberdeen, Scotland, UK
MSc Medical Genetics, University of Glasgow, Scotland, UK

Director, Advanced Centre for Medical Genetics, Mahatma Gandhi Hospital, Jaipur

THE GENOMIC MEDICINE FOUNDATION (UK)
FELLOWSHIP, SCHOLARSHIP, EDUCATION AND PROMOTION OF GENOMIC APPLICATIONS IN MEDICINE, HEALTHCARE AND SOCIO-ECONOMIC PROGRESS

MAHATMA GANDHI UNIVERSITY of MEDICAL SCIENCES AND TECHNOLOGY JAIPUR

THE INAUGURAL GREGOR MENDEL ORATION 2024

Delivered by

Professor Reena Das, MD DNB

Professor of Clinical Haematology, Postgraduate Institute of Medical Education & Research, Chandigarh, India

'In recognition of her life time contributions and achievements to Thalassaemias and other inherited Mendelian diseases of the Blood in India and South Asia'

The Sixth International Birth Defects Conference held on **28-30 November 2024**, at Mahatma Gandhi University of Medical Sciences & Technology, Jaipur, India.

Professor Dhavendra Kumar
Chair, The Genomic Medicine Foundation, UK

Dr. Vikas Chandra Swarankar
Chair- Mahatma Gandhi University of Medical Sciences & Technology, Jaipur

आईसीबीडी 2024 : दूसरे दिन यूके के विख्यात जेनेटिक मेडिसिन एक्सपर्ट डॉ. धावेंद्र कुमार ने दी जानकारी

एग्जोम सीक्वेंस से लगा सकते हैं जेनेटिक बीमारी का पता

समाचार जगत न्यूज

जयपुर. डीएनए में आए बदलाव को अलग-अलग करके देख पाना काफी मुश्किल था। इसके लिए अब नई तकनीक एग्जोम सीक्वेंस का इस्तेमाल किया जा रहा है जिससे डीएनए टेस्ट कहीं बेहतर हो गया है और उसमें बदलाव से होने वाली बीमारी का भी पता लगाया जा सकता है। शहर में आयोजित तीन दिवसीय इंटरनेशनल कॉन्फ्रेंस 'आईसीबीडी 2024' का शनिवार को समापन हुआ।

कॉन्फ्रेंस के ऑर्गनाइजिंग चेयरपर्सन डॉ. अशोक गुप्ता ने बताया कि इस कॉन्फ्रेंस का आयोजन महात्मा गांधी यूनिवर्सिटी ऑफ मेडिकल साइंसेज एंड टेक्नोलॉजी ऑफ मेडिकल साइंसेज और द जीनोमिक मेडिसिन फाउंडेशन, यूके की ओर से किया गया। आखिरी दिन पीजीआई चंडीगढ़ से आई डॉ. रीना दास ने द ग्रेगर ओरेशन दिया। इसके अलावा नीदरलैंड्स के प्रो. बर्ट डी ब्रइस ने दुर्लभ बीमारियों को स्क्रीनिंग में आर्टिफिशियल इंटेलिजेंस और फेशियल इमेजिंग, यूके के डॉ. मोहनीश सुरी ने जेनेटिक ब्रेन डिजीज की पहचान के लिए न्यूरोइमेजिंग तकनीक, डॉ. एसके शर्मा ने एंडोक्राइनोलॉजी में दुर्लभ केस, डॉ. अश्विनी दलाल ने एपीजेनेटिक डिसऑर्डर के लेबोरेटरी डायग्नोसिस, डॉ. वैभव उपाध्याय ने इनबॉर्न एरर ऑफ मेटाबॉलिज्म के विषय में अपनी रिसर्च प्रस्तुत की। वहीं बेस्ट पोस्टर बनाने वाले स्टूडेंट्स को पुरस्कृत भी किया गया।

नई तकनीक से डीएनए में से अलग करके देख सकते हैं सक्रिय हिस्सा

प्रो. बर्ट डी ब्रइस ने बताया कि हमारे डीएनए का सिर्फ 2 प्रतिशत हिस्सा ही सक्रिय रहता है और इसी में बदलाव होने या कुछ अनुपस्थित होने पर जेनेटिक बीमारी होती है। इस हिस्से की सटीक जांच के लिए अब एग्जोम सीक्वेंस तकनीक आ गई है जिसकी मदद से जीन के सक्रिय हिस्से को अलग करके देखा जा सकता है। अगर उसमें कोई बदलाव आता है तो उससे किस तरह की जेनेटिक बीमारी हो सकती है यह भी पता लगाया जा सकता है। इसके अलावा पूरे जीन या डीएनए को देखने के लिए भी होल जीनोम सीक्वेंसी तकनीक इजाद की गई है। यह एडवांस टेस्ट है जहां पूरे जीनोम की जांच हो सकती है। अभी यह टेस्ट यूरोपीय देशों में ज्यादा प्रचलन में है।

थैलेसीमिया और सिकल सेल की रोकथाम के लिए कराएं एचपीएलसी टेस्ट

पीजीआई चंडीगढ़ की डॉ. रीना दास ने बताया कि थैलेसीमिया और सिकल सेल बीमारी की रोकथाम के लिए एचपीएलसी टेस्ट कराया जाना चाहिए। इससे मां के शरीर में इन दोनों बीमारियों के वाहक जीन पता लगाए जा सकते हैं। अगर टेस्ट पॉजिटिव होता है तो पिता का टेस्ट भी किया जाता है। टेस्ट नेगेटिव होने पर बच्चे को कोई खतरा नहीं। होता लेकिन पिता भी पॉजिटिव होते हैं तो बच्चे में सिकल सेल या थैलेसीमिया होने की संभावना 25 प्रतिशत तक होती है। इसके अलावा उन्होंने ब्लड दन जीन टेस्ट के बारे में बताया। उन्होंने कहा कि अगर किसी महिला के परिवार में ब्रेस्ट कैंसर का इतिहास है तो उन्हें यह जीन टेस्ट जरूर करवाना चाहिए। इससे उन्हें कैंसर होने की संभावना पता लग सकती है।

9. International Symposium 'Breakthroughs in Genomics and Genetics'
3-4 December 2024, Aligarh Muslim University, Aligarh, India.

Two Days International Symposium
On
BREAKTHROUGHS IN GENOMICS AND GENETICS SHAPING MATERNAL AND FETAL HEALTH

Organized By
AMR-BIC-DBT Centre
Interdisciplinary Biotechnology Unit (I.B.U.), Aligarh Muslim University, Aligarh
Supported By
Dept. Of Biotechnology, Govt. Of India and A.M.U., Aligarh

03-04 DEC, 2024 **09.30 AM**

Chief Guest
PROF. SUDHA BHATTACHARYA
FNA, FNASc, FASc
INSA Senior Scientist
Ashoka University, Haryana

Patron
PROF. NAIMA KHATOON
Hon'ble Vice Chancellor
Aligarh Muslim University, Aligarh

Keynote Speaker
PROF. DHAVENDRA KUMAR
Queen Mary University of London, United Kingdom

Co-Patron
PROF. NAFEES A. KHAN
Dean, Faculty Of Life Sciences
Aligarh Muslim University, Aligarh

Guest Of Honor
PROF. ANNIE HASAN
Director
Board of Genetic Counselling, India

Convener and Coordinator
PROF. ASAD U. KHAN
AMR-BIC-DBT Centre, I.B.U., A.M.U., Aligarh

Coordinator
PROF. HINA YOUNUS
I.B.U., A.M.U., Aligarh

SPEAKERS

Visiting Faculty

1. **Dr. Mariet Elting**, *Consultant Clinical Genetics & Prenatal Genomics, Academic Medical Center, University of Amsterdam, The Netherlands.*
2. **Prof. Pradeep Vasudevan**, *Consultant Clinical Genetics & Head- Dept. of Clinical Genetics, University of Leicester, England, UK.*
3. **Dr. Anita Kaul**, *Director- Apollo Fetal Medicine Institute, Indraprastha Apollo Hospitals, Delhi.*
4. **Dr. Divya Agarwal**, *Consultant Medical Genetics, Apollo Genomics Institute, Apollo Hospital, Delhi.*
5. **Ms. Kriti Menon**, Senior Genetic Counsellor, *Apollo Genomics Institute, Apollo Hospital, Delhi.*

Internal Faculty

1. **Prof. Asad U. Khan**, AMR-BIC-DBT Centre, I.B.U.
2. **Prof. S. Manazir Ali**, *Dept. Of Pediatrics, J.N.M.C.*
3. **Prof. Tamkin Khan**, *Dept. Of Obstetrics and Gynaecology, J.N.M.C., A.M.U., Aligarh*
4. **Dr. Hamid Ashraf**, *Rajiv Gandhi Centre for Diabetes and Endocrinology, J.N.M.C., A.M.U., Aligarh*

REGISTER FOR ORAL AND POSTER PRESENTATION**

Registration Details:
UG/PG/MBBS: Rs. 500/-
Ph.D./MD/MS: Rs. 1500/-
Faculty and Postdoc: Rs. 2000/-

Contact for queries
Dr. Absar Talat
Project Scientist-I
AMR-BIC-DBT Centre
Contact No. +91 7217291459
Email: absartalatm@gmail.com

Register by Scanning the QR

https://forms.gle/JAbBPSnwGB16ETRP8

Last Date Of Abstract Submission: 1st Nov
Last Date for registration: 10th Nov. 24

****BEST POSTER AND ORAL PRESENTATION AWARD**

PROGRAM DETAILS

Day 1: 3rd December 2024

9:30 to 10:30 am	***Inaugural Programme***
10:30 to 11:00 am	***High Tea***
11:00 to 11:30 am	***Keynote Address by Prof. Dhavendra Kumar*** *'Integration of genetics & genomics in Maternal-Fetal Medicine'*
11:30 to 11:55 am	***Plenary Lecture 1- Dr. Anita Kaul*** *'Fetal imaging for genetic/ genomic testing'*
11:55 to 12:20 pm	***Plenary Lecture 2- Dr. Mariet Elting*** *'Prenatal genome sequencing- the Dutch experience'*
12:20 to 12:45 pm	***Plenary Lecture 3- Prof. Pradeep Vasudevan*** *'Prenatal genetics in NHS UK'*
12:45 to 1:45 pm	***Case Presentations & Panel Discussion*** ***Dr. Divya Agarwal; Ms. Kriti Menon; Prof. Annie Hasan; and Prof. Asad U. Khan***
1:45 to 2:30 pm	*LUNCH*
2:30 to 2:50 pm	***Lecture 1 by Dr. Hamid Ashraf*** *'Genetics and Epigenetics: New Insight on Gestational Diabetes Mellitus'*
2:50 to 3:10 pm	***Lecture 2 by Prof. Tamkin Khan*** *'Role of genetic evaluation in unexplained stillbirths'*
3:10 to 3:30 pm	***Lecture 3 by Prof. S. Manazir Ali*** *'Genetic profile of neonates impacting on neonatal health'*
3:30 to 4:00 pm	*Concluding Remarks*
4:00 to 4:30 pm	***High Tea***

Day 2: 4th December 2024

9:30 to 10:30 am	**Poster Presentation**
10:30 to 11:30 am	**Oral Presentation**
11:30 to 12:00 pm	**High Tea**
12:00 to 12:30 pm	**Concluding Session/Award ceremony**

11. Division of Cancer and Genetics Seminar, School of Medicine, Cardiff University, UK Seminar 7th January 2025

"Integrated Genomics and Multi-OMICS for Clinical Diagnosis and Management"

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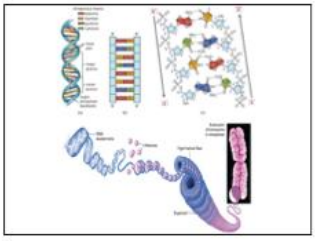

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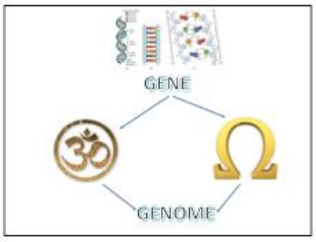

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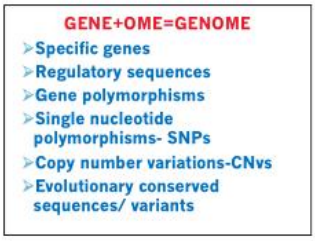

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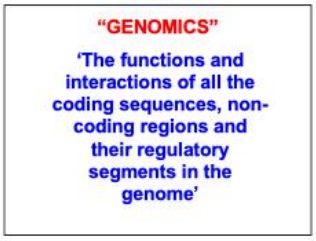

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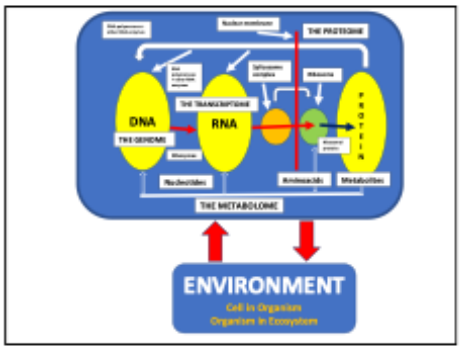

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"OMICS"

The OMICS is an umbrella term to assign specific scientific relevance to a number of life sciences. Genomics is the key field centrally linked to many other fields denoted with the *OMICS* suffix.

Examples- transcriptomics, proteomics, metabolomics, phenomics, epigenomics, lipidomics, glycomics, microbiomics and many more

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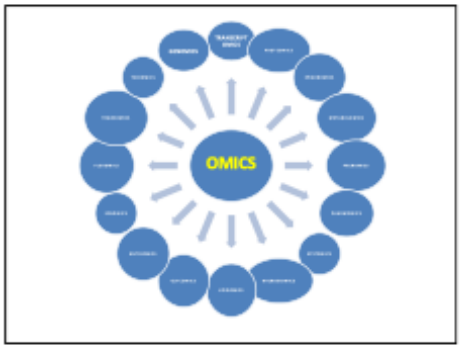

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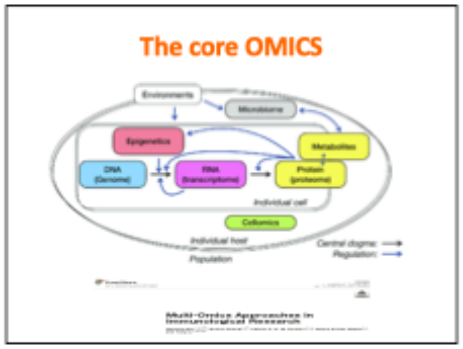

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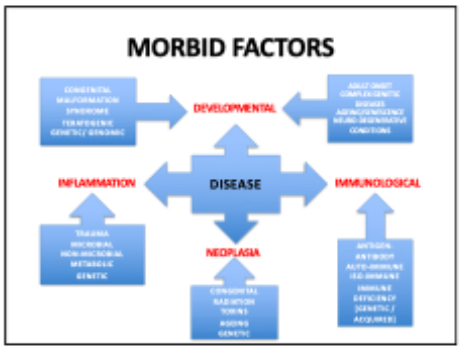

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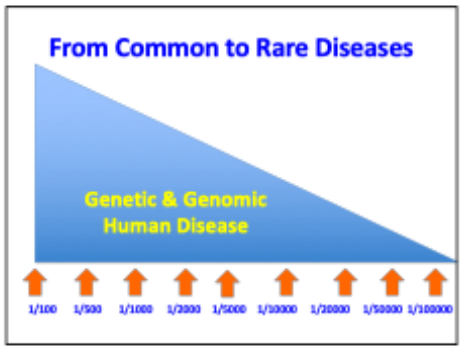

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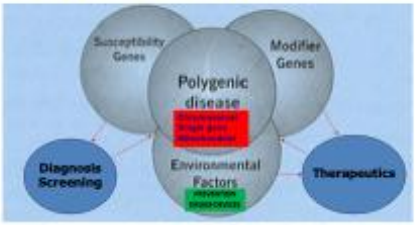
Genetic and Genomic Medicine



Personalised & Precision Medicine

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Spectrum of genetic & genomic pathology in human disease

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Molecular Laboratory Diagnosis

Conventional

- Haematology- Red cell indices; white cell profiling & clotting study
- Lipid & Glycemic profiling
- Inflammatory markers- cytokines, interleukins etc.
- Immunological profiling- antibodies; B-cell & T-cell
- Microbiological studies as appropriate- bacteria; viral; fungus & others
- Proteomics- mass spectrometry rare metabolic diseases

Genetic & Genomic

- Karyotype/ FISH
- Micro-chromosome array/ array CGH
- Single gene sequencing
- Multi-gene panel next generation sequencing
- Whole exome sequencing (WES)- clinical targeted/ whole
- Whole genome sequencing (WGS)- Genes; CNVs; SNPs etc.
- Mitochondrial genome
- Functional genomics- RNA sequencing/ Western blot
- Epigenome

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PHENOMICS
'PHENOTYPE + OMICS'

- Most important component of Multi-OMICS
- Includes the personal and family history
- All possible physical elements-
  - **Clinical**
  - **Imaging**
  - **Pathological**
- Standardisation- 'Human Phenotype Ontology'
- Electronic medical record (EMR

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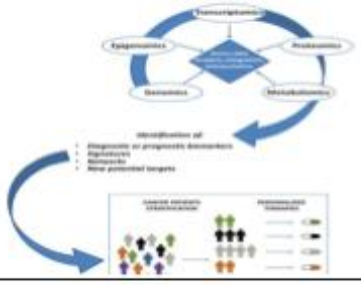
The Multi-OMIC Medicine



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New Paradigms of Clinical Medicine: The P's of Medicine

- *Personalized*
- *Precision*
- *Predictive*
- *Preventive*
- *Preemptive*
- *Participatory*

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Major components of the multi-OMICS Medicine

- Introduction to OMICS life and applied sciences
- Genetics and genomics in medicine and healthcare
- Inclusion of precision and personalised healthcare
- Promotion of integrated multi-disciplinary medicine and healthcare
- Current and future research and development in OMICS
- Ethical, legal and social implications of multi-OMICS medicine and healthcare
- Global health implications of multi-OMICS

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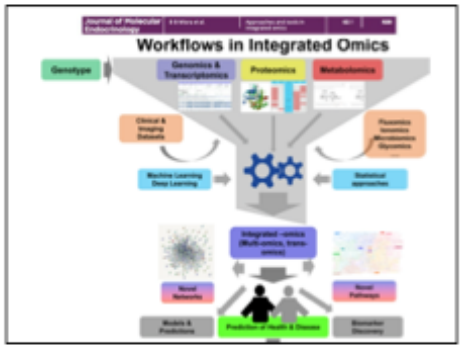

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Why should we know about rare disease?

Management-

- Precision diagnosis
- Personalised treatment
- Multi-disciplinary holistic care
- Explanation and Counselling parents and family
- Reproductive options- planning/ prenatal diagnosis/pre-implantation

In addition-

- Understand the underlying cause
- Insights into molecular biology and pathology
- Correlate with common diseases through molecular mechanisms
- Design and develop novel treatment strategies
- Develop drugs and devices applicable to common disease

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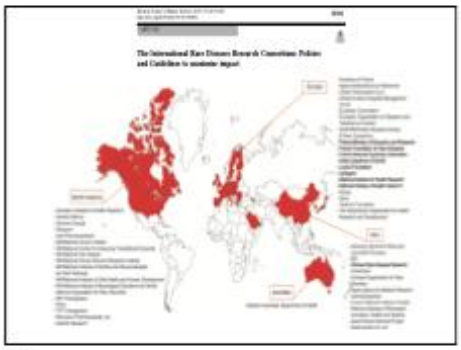

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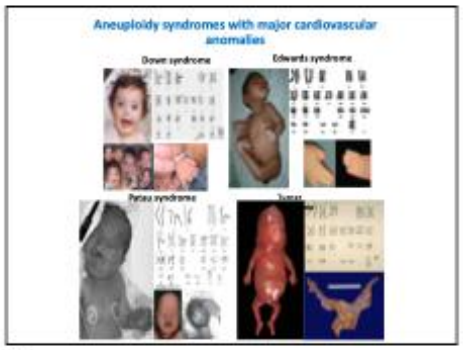

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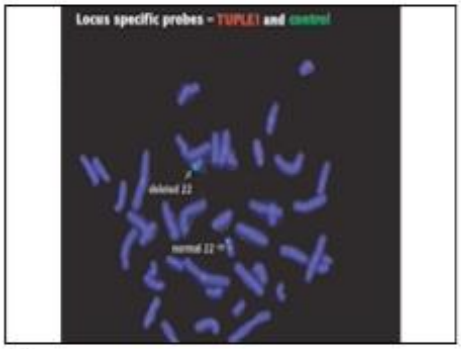

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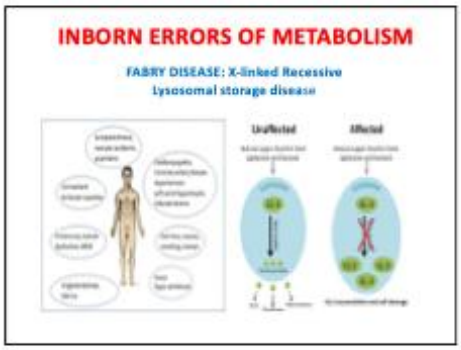

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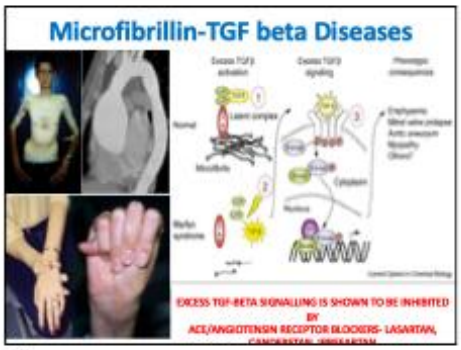

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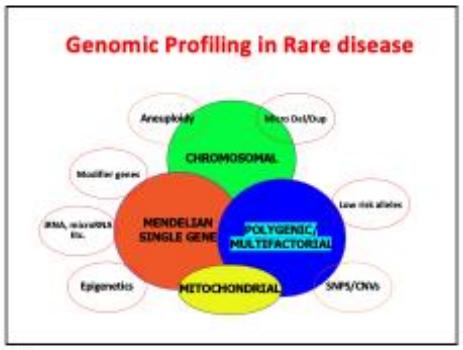

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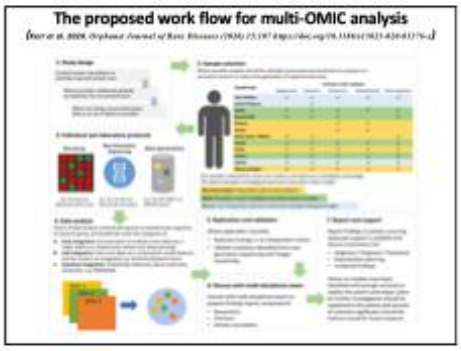

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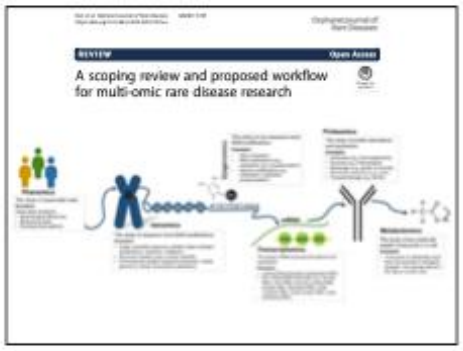

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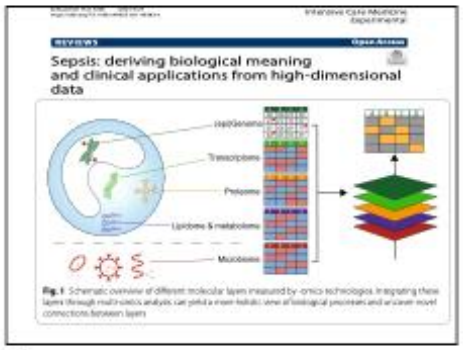

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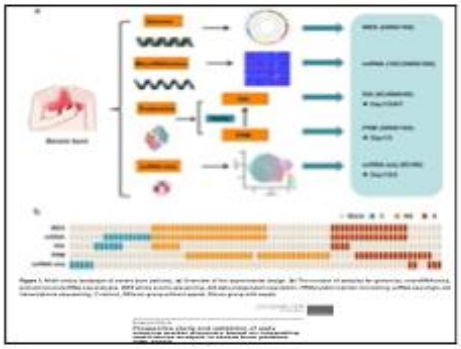

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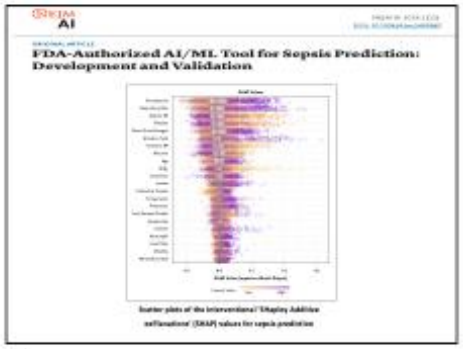

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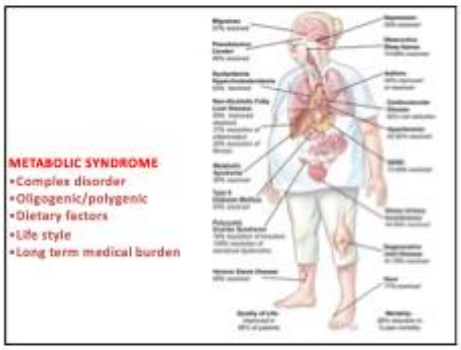

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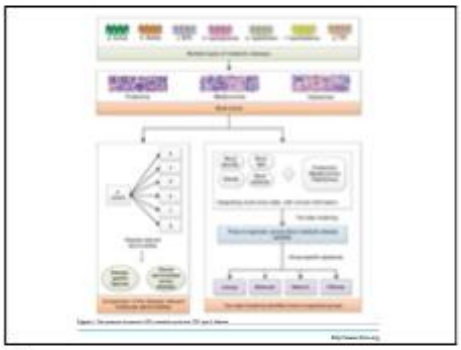

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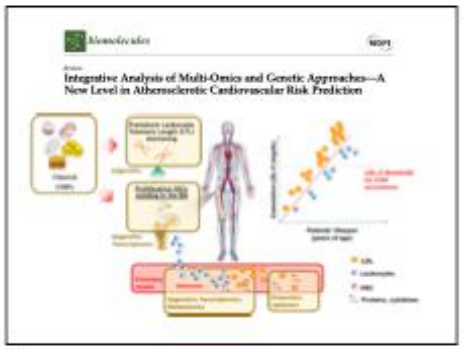

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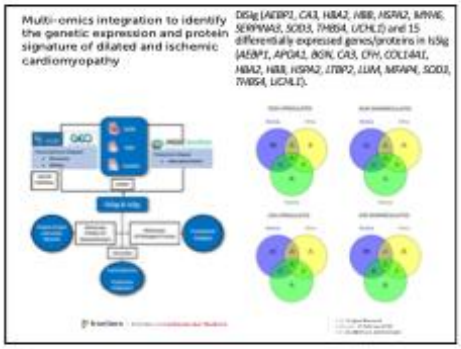

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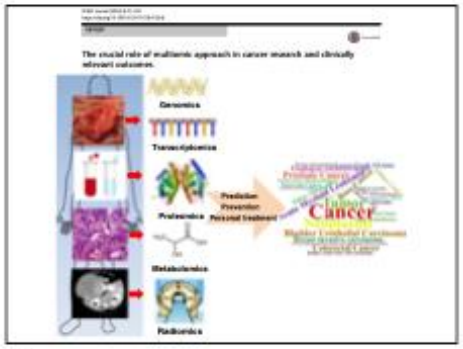

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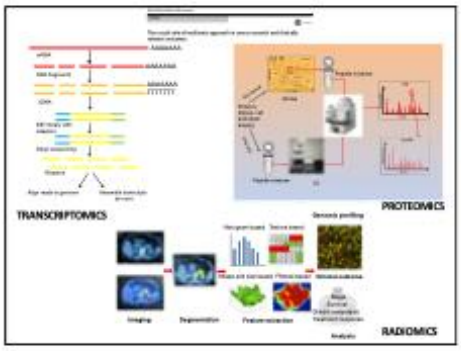

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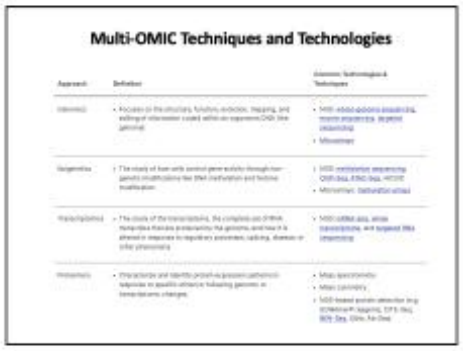

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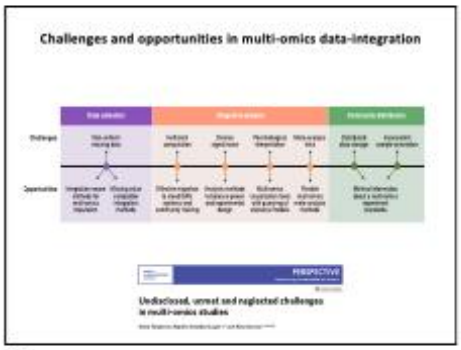

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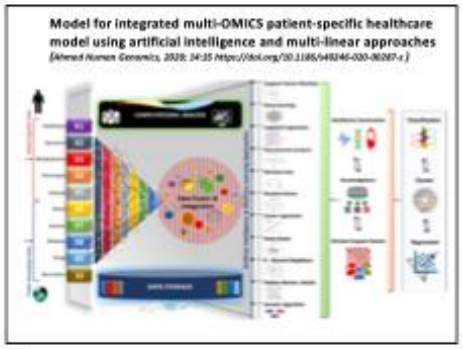

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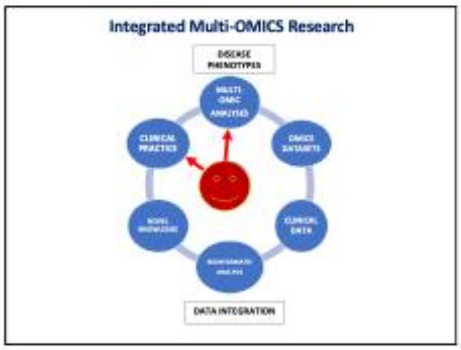

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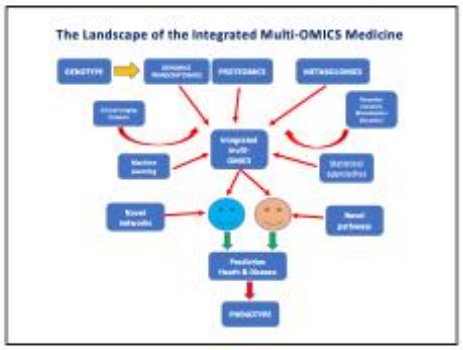

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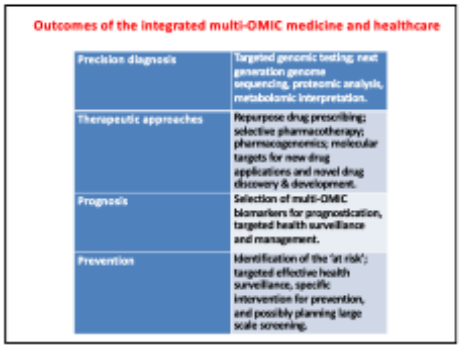

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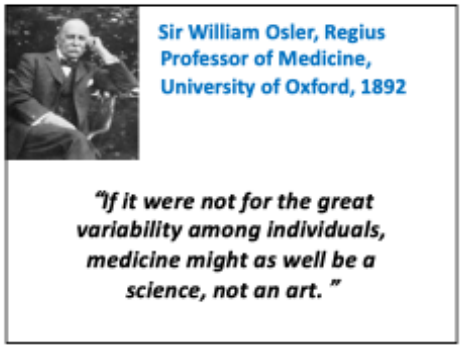

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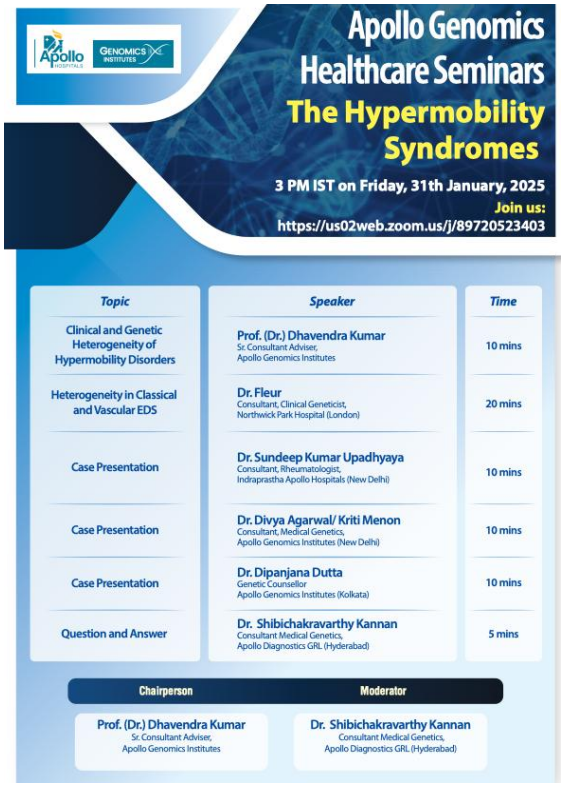
12. Apollo Genomic Healthcare Seminar, 31st January 2025



13. Third International Genomic and Precision Medicine Symposium, 12th February 2025, William Harvey Research Institute, Queen Mary University of London, UK

THE GENOMIC MEDICINE FOUNDATION (UK)

FELLOWSHIP, SCHOLARSHIP, EDUCATION AND PROMOTION OF GENOMIC APPLICATIONS IN MEDICINE, HEALTHCARE AND SOCIO-ECONOMIC PROGRESS

www.genomicmedicine.org

The 3rd Symposium on Genomic & Precision Medicine
12th February 2025

Willoughby Lecture Theatre, Charterhouse Campus, Queen Mary University of London

"Genomics and Multi-OMICS for Precision Healthcare"

You are all invited to participate in the 3rd symposium on genomic precision medicine and healthcare. The symposium aims to discuss and explore importance of emerging novel multi-OMICS approaches for in delivering the precision medicine and healthcare. Renowned global Faculty will deliver the excellent programme including the Professor Sir David Weatherall Oration (2024). The conference is held in person hosted by the William Harvey Research Institute, Queen Mary University of London, England. UK.

Programme

0930	Welcome/ Registration Tea/ Coffee
1000	**Introduction** *Professor Dhavendra Kumar,* *Chair- Programme & Organising Committee*
1015	***Session I: Genomic and OMIC technologies*** ***Chair: Professor Patricia Munroe, WHRI, QMUL, UK*** • **'Genomics and Multi-OMICS testing in NHS Genomic Laboratory'** *Prof Mike Hubank, NHSE North London Genomic Laboratory, UK* • **Pathogen genomics in multi-OMICS healthcare'** *Prof. Tom Connor, Pathogen Genomics Unit, NHS Wales, Cardiff* • **'The importance of artificial intelligence/machine learning in the multi-OMICS medicine'** *Prof. Michael Barnes, WHRI, QMUL, UK*
1130	**Tea/ Coffee**
1150	***Session II:*** ***Chair- Prof. Panos Deloukas, Director, WHRI, QMUL, UK*** • **'Delivering the multi-OMICS Medicine in clinical practice'** *Professor Sir Mark Caulfield, Vice Principal, QMUL* • **'Cardiovascular Multi-OMICS- managing cardiomyopathy'** *Dr. Luis Lopes, University College London, UK* • **'Pharmacogenomics in the Multi-OMICS practice of Medicine'** *Professor Sir Munir Pirmohamed, Univ. of Liverpool, England, UK*

1300	**LUNCH**
1345	***Session III: Organisation and Development of Multi-OMICS Medicine*** ***Chair: Prof. Dame Sue Hill, Chief Advisor, NHSE Genomics Service*** • **'Multi-Disciplinary NHS Wales Service for 'Syndromes without a Name- The SWAN Clinic'** *Dr. Hywel Williams, Senior Lecturer, Cardiff University, Wales, UK* • **'Elements and Challenges for Multi-OMICS Medicine** *Professor Matt Brown, Chief Scientist- Genomics England, UK* • **'Role of Genetic Nurses & Genetic Counsellors in genomic/OMIC healthcare'** *Dr. Tootie Beuser, Director for Nursing & Midwifery, NHS Incisive Health, London, UK*
1500	**Tea/Coffee Break**
1520	**Session III: 'The Professor Sir David Weatherall Oration- 2024"** ***Chair- Professor Sir Munir Pirmohamed, Patron, GMF-UK*** **'DECIPHER- empowering diagnosis and discovery in genomic medicine'** *Delivered by – Professor Helen Firth, Sanger Genome Centre, Hinxton, UK*
1630	***Discussion/ Reflections/ Vote of Thanks- Professor Sir Pirmohamed***
1645	**Close**

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4.Social and Community service

In addition to services to Medicine and Healthcare, Prof. Kumar has also actively engaged with many *social and community welfare* activities with notable achievements and recognition. Some of these roles include-

i) President of the ***Hindu Samaj South Yorkshire District*** and developed a large dedicated ***Indian Community Centre*** along with the traditional temple in the city of Sheffield, South Yorkshire, England, UK. (1994 to 1997)

ii) Founded ***Sheffield Multi-Faith Forum*** that was recognized by the *Archbishop of Canterbury*, the Head of Church of England promoting freedom and place to pray or worship across the UK wide hospitals, educational institutions and professional establishments. (1994-1998).

iii) Founder of the ***India Wales Club*** for secular socio-cultural identity and welfare of the UK Indian diaspora. (August 2020 to date)

iv) Organized and led the ***150th Mahatma Gandhi Birth Anniversary'*** grand event in Cardiff, UK (2nd October 2019)

v) President-elect (2021-22) of the ***Cardiff Rotary Club***, one of the oldest clubs founded in 1917.

Acknowledgements: Grateful and humble thanks to my wife Anju, my children-Nikita & Ashish, my lovely grandchildren- Jaya, Arya, Anya, Krish & Anushka, colleagues, close peers and friends for their affectionate life-long support. Dhavendra Kumar, Cardiff, January 2025