3rd International Symposium Genomic & Precision Medicine 2025 1

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

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1300 **LUNCH**

1345 ***Session III: Organisation and Development of Multi-OMICS Medicine***
Chair: Prof. Dame Sue Hill,
Chief Scientific Officer for England & Senior Responsible Officer for Genomics in the NHS

- **'Multi-Disciplinary NHS Wales Service for 'Syndromes without a Name- The SWAN Clinic'**
  Dr. Hywel Williams, Senior Lecturer, Cardiff University, Wales, UK
- **'Genomic and OMIC diagnostics in NHS'**
  Dr. Greg Elgar, Director Sequencing R&D, 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 IV: Selected Posters (Maximum 3; 5 minutes each presenter)**
Chair- Professor Dhavendra Kumar, WHRI/QMUL, London, UK

i) 'Investigating the Relationships between Blood Pressure Polygenic Risk Scores and many disease outcomes within the UK Biobank'
Kulsuma K. Uddin, Centre of Clinical Pharmacology & Precision Medicine, WHRI/QMUL, London, UK

ii) 'Improved diagnosis of adrenal insufficiency in under resourced countries by a step-wise genetic analysis'
Chris J Smith, Centre for Endocrinology, WHRI/ QMUL, London, UK

iii) 'Relationships of circulating plasma metabolites with the QT interval in a large population cohort'
William J. Young, Barts Heart Centre, St. Bartholomew's Hospital, London, UK

1540 **Session V:** **"The Professor Sir David Weatherall Oration- 2024"**

Chair- Professor Sir Munir Pirmohamed, Patron, GMF-UK

- **Legacy of Professor Sir David Weatherall**
  Dhavendra Kumar, Genomic Medicine Foundation UK
- **Oration- 'DECIPHER – Integrating 'Omics' to drive diagnosis and discovery in Genomic medicine'**
  Professor Helen Firth, Hon Professor of Clinical Genomics, University of Cambridge, UK

1640 ***Discussion/ Reflections/ Presentations/ Vote of Thanks***
Professor Sir Pirmohamed

Close- Bon Voyage

To Register: www.genomicmedicine.org/product/genomics2024; For all other enquiries: genomicmedicine@yahoo.co.uk / md@genomicmedicine.org / d.kumar@qmul.ac.uk

Faculty profiles

1. Professor Dhavendra Kumar, Medical Director/ CEO, Genomic Medicine Foundation (d.kumar@qmul.ac.uk; genomicmedicine@yahoo.co.uk)

Professor Dhavendra Kumar, MBBS, MD, DCH (RCPSI), MMedSci, PGCertMedEd, 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

Academic Affiliations:

- *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*

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 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).

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.***

2. Professor Michael Hubank

Dr Mike Hubank

Scientific Director, Clinical Genomics, Royal Marsden Hospital, London
Scientific Director, NHS England North Thames Genomic Laboratory Hub
Professor of Translational Genomics, Institute for Cancer Research, London

Biography
Dr Hubank has worked in Genomics for over 20 years. Following a PhD at UCL, he worked at the University of Sussex and Yale University before returning to the UCL Institute of Child Health in 2000 to found and run *UCL Genomics*. In 2016 he moved into clinical diagnostics at the Royal Marsden Hospital, London, to lead a translational laboratory focused on the development and clinical application of genomic assays for cancer diagnostics. Since 2018 he has been Scientific Director at the NHS England North Thames Genomic Laboratory Hub.

Research Interests
Mike is a joint investigator on several research projects using multiomic profiling for optimising personalised diagnostics and treatments for childhood cancer patients. He has a strong focus on developing and applying genomic assays, and a particular interest in moving circulating biomarkers into standard of care testing.

@generoom Contact: Michael.hubank@icr.ac.uk

3. Professor Thomas Connor, School of Biosciences, Cardiff University

The research that is undertaken in Professor Connor lab seeks to understand pathogen variation in order to answer a range of questions from how pathogens evolve, to how and why they spread in local and global outbreaks. This work has a number of labels, but broadly speaking we use genomic epidemiology, phylogenomics and population genetics approaches to answer our research questions.

Prof. Connor's research is underpinned by whole genome sequencing, using the data from organisms genomes to work out how they are related to, and different from, other organisms of interest. This work is heavily computational with mathematical and computational approaches to analyse and interpret the "Big Biological Data". In a practical sense this work has potential for clinical applications in diagnostic and surveillance services in the NHS in Wales for HIV, TB and other Mycobacteria, C. difficile and Influenza.

The Connor group is part of the recently formed Microbiomes, Microbes and Informatics (MMI) group (webpage underdevelopment). The MMI group currently comprises the research groups of Thomas Connor, Esh Mahenthiralingam, Julian Marchesi and Andrew Weightman, and has over 25 active research staff and postgraduate students.The MMI group are highly research active generating over £3.5 million in grant income between 2010 and 2017, and publishing extensively in top journals (cumulative h index > 150, > 400 publications, and > 25,000 citations; source Scopus.com).

Roles
Module Leader: BI3252 The 'omics revolution (Bioinformatics & Functional Genomics)

Biocomputing Research Hub lead

Member of College of Biomedical and Life Sciences Data Strategy Group

Member of Supercomputing Wales Infrastructure Committee

Member of Cardiff Supercomputing Facility Oversight Group

Wales regional lead and technical lead for the Cloud Infrastructure for Microbial Bioinformatics

Bioinformatics Lead for the Public Health Wales Pathogen Genomics Unit.

4**. Professor Michael Barnes**

Professor Michael Barnes, Professor of Bioinformatics and Director of the Centre for Translational Bioinformatics, William Harvey Research Institute, Queen Mary University of London.
m.r.barnes@qmul.ac.uk

Michael co-leads the Centre for Translational Bioinformatics (C4TB), at Queen Mary University of London and is a Fellow of the Digitial Environment Research Institute, QMUL. His team work across diverse research areas, including genomics, drug discovery, stratified medicine, machine learning and health informatics with a unified objective to drive forward translation into the clinic. He brings an industrial perspective to the C4TB, drawn from 16 years of leadership of bioinformatics teams in the pharmaceutical industry.

Michael is a Fellow of the Alan Turing Institute and an HDR-UK Investigator, and co-leads the Genomics England Stratified medicine genomic interpretation clinical partnership. He has an active portfolio of stratified medicine projects as a co- investigator and data integration lead on several MRC projects, including MRC PSORT (Psoriasis), MRC RA-Map (RA), MRC MATURA (RA), and CLUSTER (Juvenile Arthritis). He also co-leads the NIHR AI-Multiply Consortium which is using AI to investigate the relationship between multiple long-term conditions and polypharmacy. He has served on the MRC Methodology Research Panel and Stratified Medicine panels and also advises on a number of project boards, including the UnitedHealth Group Pharmacogenetics advisory group, the Dutch Heart Foundation, the MRC-eMedLab HPC Cloud facility, the IMI etriks project, and the F1000 faculty.

5. Genomics England Ltd.
a) Prof. Matt Brown, Chief Scientist, Genomics England & King's College, London

Chief Scientific Officer, Genomics England; Professor of Medicine, King's College, London

Professor Matthew Brown, an internationally renowned clinician-scientist, joined Genomics England in 2021.

Prior to joining Genomics England he was Director of the National Institute for Health Research (NIHR) Guy's and St Thomas' Biomedical Research Centre and Professor of Medicine within the Faculty of Life Sciences and Medicine, King's College London.

Professor Brown trained as a clinician-scientist and a rheumatologist in Australia and the UK. Previous positions include Professor of Musculoskeletal Sciences at the University of Oxford; Director of the Australian Translational Genomics Centre, Distinguished Professor, and Director of Genomics at the Queensland University of Technology; and Director of The University of Queensland Diamantina Institute and Professor of Immunogenetics at The University of Queensland.

He has made contributions to the development of gene-mapping approaches in human diseases and genome-wide association study methodology, leading to the discovery of thousands of genetic variants, with a particular interest in ankylosing spondylitis, rheumatoid arthritis, and osteoporosis.

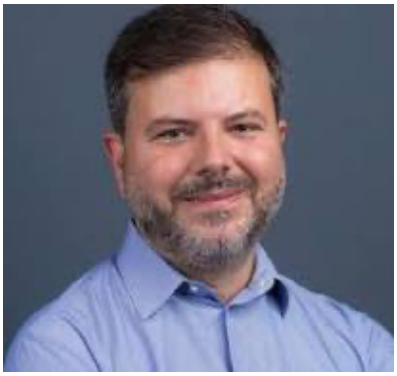
In the genetics of rare human diseases, he has identified genes responsible for monogenic forms of arthritis, ectopic bone development, and skeletal dysplasias. He has also led efforts in Australia to translate research sequencing capability into precision medicine programs for cancer patients.

Professor Brown was elected a Fellow of the Australian Academy of Sciences in recognition for his achievements in genetics research. He still practises medicine, in the specialty of rheumatology, with a particular focus on axial spondyloarthropathies.

b) Dr. Greg Elgar, Director of Sequencing

Dr. Elgar has 40 years' experience in molecular biology, including 30 years in Genomics at Principal Investigator level. He has co-authored over 150 peer reviewed publications and have played lead roles in a number of International genome sequencing projects. His impressive academic career includes positions at the Sanger Campus, QMUL, MRC NIMR and the Crick Institute. He established and leads the R&D lab at Genomics England in 2018 with specific focus on nanopore whole genome sequencing (WGS) with the aim of clinical implementation in both Cancer and Rare Disease. He has coordinated epigenetic, transcriptomic, proteomic and metabolomic programmes of research in Rare Disease.

6. Luis Rocha Lopes, MD, PhD, FESC
Associate Professor, Institute of Cardiovascular Science, University College London
Consultant Cardiologist, Barts Heart Centre, St Bartholomew's Hospital, London
Cardiology Specialty Lead, North Thames Genomic Laboratory Hub, London
Professor Associado de Cardiologia, Faculdade de Medicina da Universidade de Lisboa.

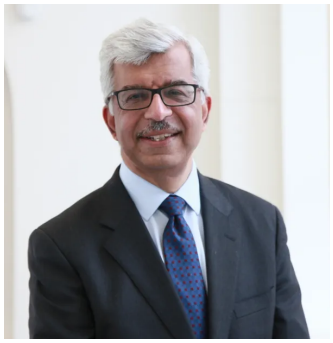


Dr Lopes is a Consultant Cardiologist in the Inherited Cardiovascular Diseases Unit and an Honorary Associate Professor in University College London. He obtained his MD from the University of Lisbon in 2001, finished his Cardiology training in 2009, and achieved his PhD in 2015 at the Institute of Cardiovascular Science, University College London (UCL). Currently, he is a Clinical-Academic Consultant Cardiologist committed to cardiomyopathies, cardiogenetics, and cardiac MRI and an Honorary Senior Lecturer/Assistant Professor at the Centre for Heart Muscle Disease, Institute of Cardiovascular Science, UCL. He is the Cardiology lead for the North Thames Genomic Laboratory Hub (part of the Genomic Medicine Service). His main clinical focus is on genetic cardiomyopathies including hypertrophic cardiomyopathy, dilated cardiomyopathy, and arrhythmogenic cardiomyopathy, metabolic cardiomyopathies including Fabry disease, cardiac involvement in neuromuscular conditions, and mitochondrial cardiomyopathy. Major research interests include the discovery of new genetic causes of cardiomyopathy and the use of advanced imaging in the construction of genotype-phenotype models. His work has been published in several high-impact journals.

7. Professor Sir Munir Pirmohamed, University of Liverpool, UK

Professor- Pharmacology and Therapeutics & Sid David Weatherall Professor of Medicine

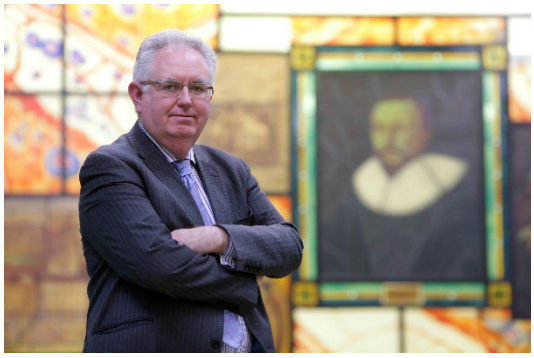
munirp@liverpool.ac.uk



Professor Sir Munir Pirmohamed (MB ChB, PhD, FRCPE, FRCP, FFPM. FRSB, FBPhS, FMedSci) is David Weatherall Chair in Medicine at the University of Liverpool, NHS Chair of Pharmacogenetics, and a Consultant Physician at the Royal Liverpool University Hospital. He is Director of the Centre for Drug Safety Sciences, and Director of the Wolfson Centre for Personalised Medicine. He is also Director of HDR North. He is an inaugural NIHR Senior Investigator, Fellow of the Academy of Medical Sciences in the UK, Commissioner on Human Medicines. He was President of British Pharmacological Society from January 2020-December 2021, and is currently President of the Association of Physicians. He was awarded a Knights Bachelor in the Queen's Birthday Honours in 2015.

His research focuses on personalised medicine, clinical pharmacology and drug safety in a variety of disease areas, including cardiovascular medicine.

8. Professor Sir Mark Caulfield



Professor Sir Mark Caulfield is Professor of Clinical Pharmacology at Queen Mary University of London and the Vice Principal for Health for Queen Mary's Faculty of Medicine and Dentistry.

Professor Caulfield graduated in Medicine in 1984 from the London Hospital Medical College and trained in Clinical Pharmacology at St Bartholomew's Hospital, he developed a research programme in molecular genetics of hypertension and translational clinical research.

At Queen Mary University of London Professor Caulfield has made contributions to the discovery of genes related to blood pressure, cardiovascular health, cancer and rare diseases. His research has changed national and international guidance for high blood pressure.

He has won the Lily Prize of the British Pharmacology Society, the Bjorn Folkow Award of the European Society of Hypertension 2016 and the Franz Volhard Award of the International Society of Hypertension in 2018.

Professor Caulfield was appointed Chief Scientist for Genomics England in 2013, charged with delivery of the 100,000 Genomes Project on whole genome sequencing in rare disease, cancer and infection. He was instrumental in delivering the 100,000 Genomes Project which has delivered life-changing results for many patients. He worked with NHS England to co-create the National Genomic Test Directory, which offers equitable access for 56 million

people to appropriate genomic tests. Professor Caulfield was awarded a knighthood in 2019 for his leadership of the 100,000 Genomes Project.

He is a member of the Barts Health NHS Trust Board, the Barking, Havering and Redbridge University Hospitals NHS Trust, the MedCity Board and is the President Elect of the British Pharmacological Society

9. Dr Hywell Willaims, Senior Lecturer Bioinformatics, Division of Cancer & Genetics, Cardiff University (WilliamsHJ1@cardiff.ac.uk)

Dr. Williams's research is focused on improving our understanding of the biological systems that when dysregulated lead to disease phenotypes in humans. Primarily he is working on rare diseases with an emphasis on neuro-related phenotypes.

One of his main interests is how gene expression is regulated both spatially and temporally during development and throughout life and how DNA variation can influence this. To understand this will require knowledge of how the genome is organised in 3D space, which regions of the genome are in contact to regulate gene expression and the full repertoire of variation each individual possesses within both the coding and non-coding genome.

His aim is to improve our ability to make a diagnosis in the 50-60 % patients with rare disease who currently remain undiagnosed and armed with this knowledge build a better understanding of the functional biology that leads to disease. In turn this will improve our ability to develop new therapeutics to treat patients and in the future may even allow us to prevent these diseases form occurring.

To do this will require the use of techniques such as spatial transcriptomics, Hi-C and whole genome sequencing. The analysis of the Big Data generated will require smart algorithms and informatics to extract the maximum amount of information in a meaningful way. He believes that network analysis techniques will be hugely important in helping us combine

this information so we understand the composition of biological systems in healthy and disease states.

To achieve our goals will require working together as a community to share our data in an open and transparent way.

10. Dr. Tootie Bueser, Chief Nurse, North Thames Genomic Medicine Service; Director of Nursing and Midwifery Southeast GMSA. (tootie.beuser@nhs.net)

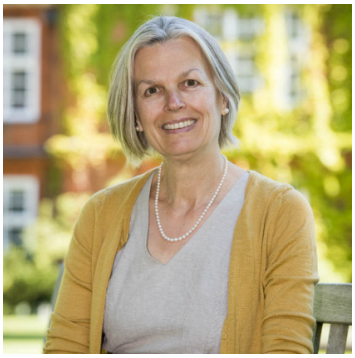
Dr. Tootie Bueser is a Health Education England/National Institute for Health Research Clinical Doctoral Research Fellow at the Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care. Her work is focused on developing a new intervention to improve psychosocial and educational support for patients who have a new diagnosis and/or carrier status for an inherited cardiac condition.

Tootie Bueser is an experienced cardiac nurse and is the lead nurse for the Inherited Cardiac Conditions services at King's College Hospital and Guy's and St Thomas' Hospital.

She is the President of the British Association for Nursing in Cardiovascular Care and is thereby a Council member of the British Cardiovascular Society and the UK representative for the European Society for Cardiology Association of Cardiovascular Nurses and Allied Professionals. She is an active member of the Association for Inherited Cardiac Conditions; and the Cardiovascular and the Ethics & Social Sciences Genomics England Clinical Interpretation Partnership for the 100,000 Genomes Project. Tootie Bueser is on the editorial board of the British Journal of Cardiac Nursing.

Tootie Bueser is a member of the Clinical Expert Advisory Group for Cardiomyopathy UK and volunteers for their patient support line.

11. Prof. Helen Firth, Director, DECIPHER, Sanger Genome Centre, Hinxton, Cambridge, England; Newham College, University of Cambrdige (hvf21@cam.ac.uk)



Professor Helen Firth, DM, FRCP,FMedSci is a Consultant Clinical Geneticist at Cambridge University Hospitals. Her main research interests are in mapping of the clinical genome and the matching of rare genomic variants to empower discovery and diagnosis in rare disease.

Professor Helen Firth DM FRCP FMedSci is a Consultant Clinical Geneticist at Cambridge University Hospitals and Hon Professor of Clinical Genomics at the University of Cambridge. She is an Honorary Faculty Member of the Wellcome Sanger Institute and Bye-Fellow of Newnham College, Cambridge. Her main research interest is mapping the clinical genome by matching rare genomic variants to phenotype to empower diagnosis and discovery in rare disease.

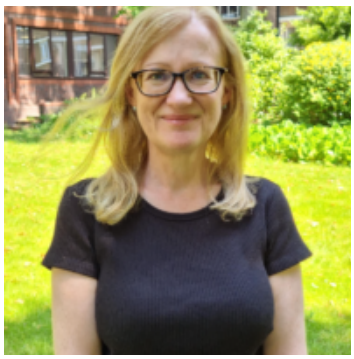
In 2004, she initiated the DECIPHER project (www.deciphergenomics.org) that enables clinicians and scientists around the world to share information about rare genomic variants to facilitate diagnosis and help to elucidate the role of genes and variants whose function is not yet known. DECIPHER is a global project with more than 300 participating projects across six continents, covering the breadth of rare disease at a phenotypic and genotypic level. DECIPHER has been cited by over 3,700 publications.

Since its inception in 2010, Prof Firth has been Clinical Lead for the Deciphering Developmental Disorders study (DDD study) (www.ddduk.org) one of the largest nationwide, genome-wide sequencing projects in rare disease. The DDD study is a partnership project between the UK NHS Genetics Services and Wellcome Sanger Institute that has exome sequenced 33,500 individuals. This has enabled detailed genomic analysis of ~13,500 children with severe developmental disorders & their parents to improve the diagnosis of these conditions and to further understand their genomic architecture and biology. Robust clinico-molecular diagnosis is key to the delivery of high-quality medical care and is the cornerstone of Genomic Medicine as applied to rare disorders.

Prof Firth is joint author of 'Firth HV & Hurst JA Oxford Desk Reference: Clinical Genetics & Genomics (2nd edition OUP 2017 ISBN 978-0-19-955750-9)'.

13. Professor Patricia Munroe, Queen Mary University of London, UK

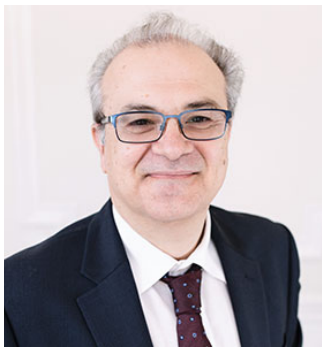
(p.b.munroe@qmul.ac.uk)



Professor Patricia Munroe (Patsy) graduated with a B.Sc. in Biochemistry, and M.Sc. in Biotechnology from the University of Galway, Ireland. She then worked at the Wellcome Trust Research Laboratories for six months before commencing a PhD in cardiovascular genetics at St Bartholomew's Hospital. Patricia was awarded a PhD in Medicine in 1995 and following successful post-doctoral fellowships at University College London (NIH funded), she joined the William Harvey Research Institute as a Lecturer in 1998. In 2007 she was appointed Professor of Molecular Medicine. Prof Munroe's lab investigates the molecular basis of cardiac arrythmia's, hypertension and heart failure. Our research includes genomic studies of cardiovascular risk factors as a route for elucidating disease mechanisms, the development of 'omic biomarkers and clinical models for improved risk prediction, pharmacogenetics and personalised medicine.

She co-leads several international complex genetic disease consortia. Using meta-analysis of genome-wide association studies (GWAS) and large-scale candidate gene studies she has discovered over 1000 genetic loci associated with hypertension. She has also identified hundreds of genetic loci for the electrocardiogram and cardiac magnetic resonance measures of heart structure and function. . As a member of the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium she co-leads projects leading to the discovery of loci for electrocardiogram markers and gene x environment interactions for cardiovascular risk factors. She is the Director of the Genome Centre at FMD and an Adjunct Professor at the Department of Physiology and Pharmacology, The University of Toledo, USA. She was listed as a Highly Cited Researcher by Thomson Reuters in 2015, 2016, 2017 and 2018 (Top 1% in Molecular Biology & Genetics). She was elected as a Fellow of Academy of Medical Sciences in 2021.

14. Professor Panos Deloukas, Director, WHRI, Queen Mary University of London, UK
(p.deloukas@qmul.ac.uk)



Panos Deloukas obtained his BSc in Chemistry from the Aristotelian University of Thessaloniki, Greece and MSc in Microbiology from University Paris 7, France. He received his PhD from the Biozentrum University of Basel, Switzerland in 1991. He joined the Sanger Centre in 1994 where he set up a high-throughput pipeline for radiation hybrid mapping, leading an effort to map 30,000 gene markers, GeneMap98. Panos was an active member of the Human Genome Project coordinating the sequencing and analysis of chromosomes 10 and 20. After the completion of the HGP he joined the International HapMap project constructing SNP maps of the human genome. Since 2005 he is studying the molecular basis of common disease and variable response to drugs in humans through large-scale genetic studies. He joined the William Harvey Research Institute at Queen Mary University London in September 2013 working on the genomics of coronary artery disease and lipid levels. Panos is a member of many consortia including CARDIoGRAMplusC4D, Global Lipids Genetics Consortium, GIANT, the UK Biobank Cardiometabolic Consortium, and the Cardiovascular Genomics England Clinical Interpretation Partnership. He has authored over 400 publications (H-index 121) and is listed by Thomson Reuters among the 1% highly cited researchers in Molecular Biology & Genetics since 2012**.**

15. Professor Dame Sue Hill, Chief Scientific Officer for England & Senior Responsible Officer for Genomics in the NHS .

Professor Dame Sue Hill DBE FMedSci FRSB FRCP(Hon) FRCPath (Hon) FHCS (Hon) is the Chief Scientific Officer (CSO) for England and a respiratory scientist by background.

Throughout her career she has led on large-scale priority programmes across government and in NHS England including as the senior responsible officer for Genomics in the NHS, introducing a world-leading and nationwide Genomic Medicine Service, building on her work in heading up the NHS contribution to the 100,000 Genomes Project.

She has also played a pivotal role in the national COVID-19 programme leading the development and deployment of testing technologies into use for the UK population and co-directing the whole-genome sequencing of SARS-CoV-2 programme.

Abstracts for Poster Presentations

I ‘Investigating the Relationships between Blood Pressure Polygenic Risk Scores and many disease outcomes within the UK Biobank’

Authors: Kulsuma K. Uddin*, Helen R. Warren, Patricia B. Munroe
Centre of Clinical Pharmacology & Precision Medicine, William Harvey Research Institute, London, Barts and The London Faculty of Medicine and Dentistry, QMUL.
Declarations: No conflict of interest ; Funder: British Heart Foundation

Introduction
Hypertension is a leading cause of mortality and morbidity, and genetics is important. Genome-wide association studies (GWAS) have identified >2,000 genetic loci associated with blood pressure (BP). Observational studies assessing risks of BP on other diseases may be biased by confounding factors. Polygenic risk scores (PRS) quantify each individual’s genetic risk profile. This project performs a hypothesis-free Phenome-Wide Association Study (PheWAS) using BP-PRS to investigate the relationships between BP and different health outcomes, to: (i) uncover novel BP-disease associations; (ii) confirm/challenge prior observations.
Methods
A new meta-analysis of BP-GWAS data (N=458,575) for systolic BP (SBP), diastolic BP (DBP), and pulse pressure (PP) was performed and three BP-PRS were generated in the UK Biobank (N=423,657) using the SBayesRC-PRS approach. Three PheWAS analyses of the trait-specific BP-PRS were undertaken, testing associations with~1,000 phenotypes based on ICD9/ICD10 codes linked to electronic health records.
Results
The PheWAS included 387 PheCodes across 14 disease categories (Ncases>200). In total, 100 significant disease associations were identified after Bonferroni correction: 48 for all BP-PRS; 17 for SBP & DBP; 14 for SBP & PP; and 14, 4 and 2 for SBP, DBP, or PP only, respectively.
Future
We will follow-up novel findings, assessing causality using Mendelian randomization.

II ‘Investigating the epigenomics of atrial fibrillation (AF) in a paired left and right human atrial cohort

Adrian Rodriguez* - PhD student, Blizard Institute (Queen Mary University of London)

Stephanie Frost, Diego Fernandez, Jishan Choudhury, Georgios Tikkas, Alison Thomas, Andrew Tinker, Patricia B Munroe, Christopher Bell and Diego Villar.

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia, approximately affecting 2% of individuals worldwide, with cases expected to double over the next two decades. Recent genome-wide association studies (GWAS) have revealed over 150 genetic loci associated to AF interindividual susceptibility, the great majority of which reside within the non-coding portion of the human genome, suggesting they are involved in gene regulation processes. However, the mechanisms linking dysregulated gene expression with AF occurrence remain largely unexplored.

In this work, we aimed to further investigate the mechanistic basis of AF with a particular focus on the regulatory landscape of the adult AF atria. To achieve this, we employed epigenomic approaches across a set of AF patient atrial samples and sinus rhythm controls, comprising paired left and right atrial tissue. Specifically, we profiled H3K27ac histone mark to annotate active promoters and enhancers and DNA methylation levels, which we integrated with matched gene expression profiles. Interestingly, we identified epigenomic regions associating with concordant gene expression and DNAm patterns pointing to candidate disease loci and biological pathways. Lastly, we validated a subset of these using locus-targeted qPCR assays in an independent atrial cohort and defined *bona fide* regulatory regions dysregulated in AF patients.

Funding source: Barts Charity

The use of the samples for research was ethically approved by the East of England-Cambridge Central Research Committee (14/EE/0007).

No conflicts of interest

III **'The role of body mass index in mediating relationship between polygenic scores and age at type 2 diabetes onset across ancestries'**

Authors: Binur Orazumbekova*[1], Julia Zollner[1,2], Sam Hodgkin[1], Margherita Bigossi[1], Genes and Health Research Team[3], David A. van Heel[3], Sarah Finer[1], Rohini Mathur[1], Moneeza Siddiqui[1]

1. Wolfson Institute for Population Health, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK.
2. Institute for Women's Health, Population Health Sciences, University College London, London, UK
3. Centre for Cell Biology and Cutaneous Research, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK.

Background and Aim: Body mass index (BMI) is an imperfect indicator of adiposity. This study examined the relationship between genetic risk for BMI, age at type 2 diabetes (T2D) onset, and BMI's mediating role across ancestries.
Material and Methods: Mediation analysis was conducted with South Asians (n=3,901, Genes & Health) and white Europeans (n=729, UK Biobank) aged 40 years or older, using polygenic score (PGS) for BMI, measured BMI and age at T2D onset. Cox proportional hazard regression models were used to assess the effect of PGS on T2D complications.
Results. South Asians in the highest PGS decile had a BMI at diagnosis 6 points lower than Europeans in the same decile. A one SD increment in PGS for BMI was associated with earlier T2D onset by -0.73 years (95%CI -1.01; -0.45) in South Asians and -0.33 years (95%CI -0.49; -0.16) in Europeans. BMI mediated 100% of the PGS effect in Europeans but only 30% in South Asians. South Asians in the top PGS decile had a higher lifetime risk of diabetic eye disease (HR 1.20, 95%CI 1.08-1.29).
Conclusion: BMI partially mediates the PGS-T2D relationship in South Asians, highlighting the need to explore alternative mechanisms, potentially involving central adiposity.

Ethics. Genes & Health operates under ethical approval (14/LO/1240), from London South East National Research Ethics Committee of the Health Research Authority (September 2014). Analyses in the UK Biobank were conducted under application ID 153692.
Funding. This study was supported by the Wellcome Trust PhD programme - health data in practice: human-centred science (218584/Z/19/Z).
Conflict of interest. Authors declare no conflict of interests.

IV ‘**Improved diagnosis of adrenal insufficiency in under resourced countries by a step-wise genetic analysis’**

Chris J Smith[1*], Mohamed A. Abdullah[2,3], Samar S. Hassan[2], Luqman S Fauzi[1], Younus Qamar[1], Charlotte L Hall[1], Saptarshi Maitra[1], Avinaash V Maharaj[1], Lucia Mariela Marroquin Ramirez[1], Jordan Read[1], Li F Chan[1], Salwa A. Musa[2,4], Louise A Metherell[1]
1. Centre for Endocrinology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom
2. Department of Paediatric Endocrinology and Diabetes, Gaafar Ibn Auf paediatric Tertiary Hospital, Khartoum, Sudan.
3. Department of Paediatrics, Faculty of Medicine, University of Khartoum, Khartoum, Sudan.
4. Department of Paediatrics and Child Health Faculty of Medicine, Al-Neelain University, Khartoum, Sudan.

Genetic studies of Primary Adrenal Insufficiency (PAI) in African children are rare and differential diagnosis is challenging, presentation mimics common childhood diseases and biochemical testing may be restricted. To provide genetic diagnoses to such individuals and

investigate the genomic diversity in Sudan, 48 patients from 43 families (31M:17F) with PAI were included, co-morbidities included white matter changes on MRI, auto-immune features and/or obesity. Sanger, WES and WGS were employed for diagnosis, confirmation and segregation with *in vitro* assays to investigate potential splice defects and CNV analysis to detect deletions. In 23/43 families a genetic aetiology consistent with non-autoimmune PAI was discovered, and in 3 families *AIRE* mutations were found, indicating an autoimmune origin. In Sudan, *ABCD1*/*NNT*/*AIRE* mutations were commonest, including recurrent *NNT* splice and *AIRE* deletion mutations. *Putative causal variants for co-morbidities were concomitantly detected and in two cases discriminated metachromatic leukodystrophy from adrenoleukodystrophy.* In this population WES revealed itself as a useful frontline tool for the differential diagnosis of individuals presenting with adrenal insufficiency and giving plausible gene defects for additional co-morbidities such as obesity. Such genetic diagnoses are crucial to design optimal treatment plans and for genetic counselling, while also reducing the genetic diversity gap of PAI.

The authors confirm they have no conflicts of interest to declare.

V **"Pathway-based genetic risk score analyses identify biological pathways linking together hypertension and brain-MRI traits"**

PRESENTING AUTHOR: Helen Warren (h.r.warren@qmul.ac.uk)

(Senior Lecturer, Clinical Pharmacology & Precision Medicine, WHRI)

Helen R Warren[*1,,2] Osorio Meirelles[3], Claudia P Cabrera[1,2], Zhiguang Li[3], Michael R Barnes[1,2], Ajay K Gupta[1,4], Morris J Brown[1], Patricia B Munroe[1,2], Mark J Caulfield[1,2], Lenore J Launer[3]

AFFILIATIONS

1. Centre of Clinical Pharmacology & Precision Medicine, William Harvey Research Institute, Barts and The London Faculty of Medicine and Dentistry, Queen Mary University of London, London, UK
2. NIHR Cardiovascular Biomedical Research Centre, Barts and The London Faculty of Medicine and Dentistry, Queen Mary University of London, London, UK
3. Intramural Research Program, National Institute on Aging, National Institutes of Health, Baltimore, Maryland, USA
4. Barts Blood Pressure Centre of Excellence, St Bartholomew's & Royal London Hospital, London, UK

ABSTRACT

Elevated blood pressure (BP) increases risks for late-life cognitive impairment and cerebrovascular tissue damage, but underlying mechanisms need elucidation. We aim to identify which BP-related genetically-defined pathways are associated with both BP and brain-MRI traits, as endophenotypes for Dementia.

We split UK-Biobank into training (n=417,839) vs MRI-study testing datasets (n=37,599). Using training dataset BP-GWAS results, we conducted BP pathway analysis, yielding 59 BP-enriched KEGG pathways. Ee constructed three pathway-based genetic risk scores (BPpathGRS) per pathway, for systolic-, diastolic BP and pulse pressure. We tested all 177 BPpathGRS for association with three brain-MRI traits (volumes of grey matter, white matter; white matter hyperintensities (WMH)) within the testing dataset.
We identified 27 pathways with significant associations (FDR<1%) between any BPpathGRS and any brain-MRI trait: 6 pathways for GM; 8 for WM; 22 for WMH. We prioritized 8 of the 22 WMH pathways according to two prioritization criteria, and highlight 2 final pathways: the Cytomegalovirus pathway and Endocrine/calcium pathway. Validation analyses show support for these 8 prioritized pathways. Bioinformatics analyses of prioritized pathways show greatest genetic enrichment for e.g: cardiac morphology; neurovascular disease; cognitive impairment, indicating underlying calcium dysregulation as a core modulator. Our findings provide new insights towards future neurovascular therapeutic targets.

VI **"'Current management of hypertensive disorders of pregnancy – a systematic review of international guidelines"**

PRESENTING AUTHOR: Marianna Danielli (m.danielli@qmul.ac.uk)
Academic Clinical Fellow (ACF) in Clinical Pharmacology and Therapeutics and General Internal Medicine
ALL AUTHORS:
Marianna Danielli [1,2], Thurkga Moothathamby[1], Kate Wiles[1,2], CM, Mohammed Y Khanji[1,2,3], Ajay Gupta[1,2]
AFFILIATIONS:
1 Queen Mary University of London, London, E1 4NS, UK
2 Barts Health NHS Trust, London, E1 1BB, UK
3 Newham University Hospital, Barts Health NHS Trust, London E13 8SL, UK

ABSTRACT:
Background and Objective: Hypertensive disorders of pregnancy (HDP) are a leading cause of adverse maternal and perinatal outcomes worldwide. This systematic review aims to critically analyse international guidelines pertaining specifically to the management of HDP in cases of gestational hypertension and pre-eclampsia. Our objective is to identify best practices and existing discrepancies in the classification, diagnosis and management of treatment approaches, to help improve the quality of care of HDP.

Methods: Published guidelines from January 2010 to April 2024 were searched, utilising databases as MEDLINE and EMBASE; guidelines were only included if not derived from other guidelines and if written in English. All guidelines meeting the criteria were extracted for a

full-text review. Additional databases were explored, including the Emergency Care Research Institute (ECRI) Guidelines Trust, and the Guidelines International Network's website (GIN).

Results: Recommendation from 12 included guidelines were compared. All guidelines were consistent in their definition of gestational hypertension and pre-eclampsia and which antihypertensive agents to avoid but differed in other management-related key aspects. Despite agreement on which antihypertensives to avoid, the recommended blood pressure thresholds for initiation of antihypertensive medication and treatment targets varied. The use of aspirin and calcium were universally recommended, but guidance on non-pharmacological interventions such as obesity, exercise and the role of salt restriction in diet lacked evidence and showed discrepancies among guidelines.

Conclusion: All guidelines acknowledge the significant morbidity associated with HDP and advocate for timely diagnosis and management to reduce associated morbidity and mortality. We highlight areas of consensus that may be of practical value to healthcare professionals in decision-making. More research is needed to understand optimal BP thresholds at which to initiate antihypertensive medication regimens, the choice of antihypertensive, and the efficacy and benefits of non-pharmacological interventions in HDP. These findings exhibit knowledge gaps, and call for new guideline development.

VII **'Relationships of circulating plasma metabolites with the QT interval in a large population cohort'**

*William J. Young PhD[1,2], Mihir M. Sanghvi MRCP[1,2], Julia Ramírez PhD[1,3,4], Michele Orini PhD[5], Stefan van Duijvenboden PhD[1,5,6], Helen R. Warren PhD[1,7], Andrew Tinker PhD[1,7], Pier D. Lambiase MD PhD[2,5], Patricia B. Munroe PhD[1,7]

1.Clinical Pharmacology and Precision Medicine, William Harvey Research Institute, Queen Mary University of London, London, UK. 2.Barts Heart Centre, St Bartholomew's Hospital, Barts Health NHS trust, London, UK. 3.Aragon Institute of Engineering Research, University of Zaragoza, Spain. 4.Centro de Investigación Biomédica en Red – Bioingeniería, Biomateriales y Nanomedicina, Spain. 5.Institute of Cardiovascular Sciences, University of College London, London, UK. 6.Nuffield Department of Population Health, University of Oxford, Oxford, UK. 7.NIHR Barts Biomedical Research Centre, Barts and The London Faculty of Medicine and Dentistry, Queen Mary University of London, London, UK.

Background: There is a higher prevalence of heart-rate corrected QT (QTc) prolongation in patients with diabetes and metabolic syndrome. Despite this, there has been limited study of metabolite concentration relationships with QT intervals.

Methods: In 21,056 UK Biobank participants with same day electrocardiograms and plasma-profiling of 100 metabolites, per-metabolite regression analyses with the QTc were performed. Participants with ischaemic heart disease or heart failure were excluded. Metabolites that replicated ($P<5x10^{-4}$) in an independent UKB sample (N=5,304) underwent LASSO regression to identify top predictors and QTc variance explained. Two-Sample Mendelian randomization and colocalization analyses were performed.

Results: Twenty-two metabolites had QTc associations that replicated including ketone bodies, fatty acids, glycolysis-related molecules and amino acids. Top associations were 3-hydroxybutyrate (8.9ms, highest vs lowest deciles), acetone (7.9ms) and PUFAs (-7.3ms). Addition of metabolites to clinical variables in the LASSO model significantly increased the QTc variance explained (11.2% vs 7.7%, *P*=0.002). There was support for a causal relationship with Linoleic acid to fatty acid ratio and evidence for colocalization for 15 metabolites at 7 QT-loci.

Conclusions: In the largest study of metabolite-QTc relationships, we identify 22 associated metabolites and clinically relevant effect sizes. These metabolites could be risk factors in acquired and congenital LQTS.

Conflicts of interest: None

Funding: William J Young recognises the National Institute for Health and Care Research (NIHR) Integrated Academic Training programme, which supports his Academic Clinical Lectureship post.