10th Annual Open Meeting

Working together to deliver personalised/precision medicine

#UKPGx2023

Attendance 6 CPD Credits

Royal College of Physicians, London

21st June 2023

Welcome to the 10th UK Pharmacogenetics & Stratified Medicine Network Annual Open Meeting

We would like to thank all our speakers for kindly taking the time to present their expertise at the meeting. We also thank our sponsors and exhibitors for supporting the event. Finally, we are very pleased to welcome the delegates who are working within academia, industry, healthcare and regulatory sectors to move personalised/precision medicine forward; along with representatives from charities and patient groups supporting research projects. We are privileged to have such a great line up of speakers and hope their presentations will encourage discussion. We are a not-for-profit organisation and all proceeds from the meeting go directly to covering the costs of running our events and maintaining the Network.

Over the last 10 years the Network has steadily grown to over 1,200 members. It provides a great opportunity for different disciplines to come together and develop productive collaborations. You are most welcome to join the Network, membership is free, just contact Christine cjmcn@liverpool.ac.uk.

This last year invited experts from academia, healthcare, regulatory and industry sectors came together to discuss Incorporating Pharmacogenetics into Clinical Decision Support Systems and Pharmacogenetics in Drug Discovery. Presentations from these workshops are available on our website https://www.uk-pgx-stratmed.co.uk/event-presentations. The presentations from all our past open meetings and workshops provide a wealth of information and can be viewed on the website.

Enjoy the day, we hope you are able to network with colleagues from different sectors and develop research collaborations.

Professor Sir Munir Pirmohamed

Programme Overview – Morning

08.00-09.00	Registration and refreshments	
09.00-10.40	SESSION 1: Emerging concepts Chair: Professor Sir Munir Pirmohamed	
09.00-09.10	Welcome	Professor Sir Munir Pirmohamed
09.10-09.40	Mitochondrial genome and precision medicine	Professor Patrick Chinnery
09.40-10.10	Epigenomic profiling in rheumatic diseases	Professor Carl Goodyear
10.10-10.40	Profiling Alzheimer's disease for personalised medicine	Dr Rebecca Sims
10.40-11.20	Morning coffee	
11.20-12.40	SESSION 2: Pharmacogenomics Implementation in the 4 nations	Chair: Professor Ann Daly
11.20-11.40	England	Vicky Chaplin
11.40-12.00	Scotland	Professor Sandosh Padmanabhan
12.00-12.20	Wales	Sian Morgan
12.20-12.40	Northern Ireland	Professor Ian Young
12.40-13.40	Lunch and exhibitor's stands	

Programme Overview – Afternoon

13.40-15.15	SESSION 3: Neuropsychiatric diseases	Chair: Dr Eddie Blaire
13.50-14.00	Standards of care for spinal muscular atrophy: The Patient's Perspective	Portia Thorman
14.00-14.25	Pharmacogenetics for mental health	Professor Elvira Bramon
14.25-14.50	Precision medicine approaches to motor neuron disease	Professor Dame Pamela Shaw
14.50-15.15	Neurofilaments and neurodegeneration	Dr Axel Petzold
15.15-15.40	Afternoon tea	
15.40-17.10	**SESSION 4: Complex Diseases**	**Chair: Professor Mehdi Tavakoli**
15.40-16.10	Health economics of genomic technologies	Professor Sarah Wordsworth
16.10-16.40	Genomics of inflammatory bowel disease	Professor Holm Uhlig
16.40-17.10	Omics approaches in adrenal disease	Professor Wiebke Arlt
17.10	Close of conference	Professor Sir Munir Pirmohamed

Speakers are presenting their own research and opinions

PRESENTATION ABSTRACTS

SESSION 1: Emerging concepts

Mitochondrial genome and precision medicine

Prof Patrick Chinnery

Mitochondria act as metabolic hubs within cells and play a central role in metabolism. They contain their own genome, mtDNA, which codes for 13 essential proteins needed for the efficient production of adenosine triphosphate (ATP), the principal source of energy within cells. Genetic variation of mtDNA can cause rare inherited diseases, with some being precipitated or exacerbated by commonly used drugs. Several of these variants are carried by ~1 in 400 of the population and can be considered risk alleles for drug-toxicity. These observations provide 'proof of principle' that mtDNA is important for pharmacogenomics, but this is an area that has largely been ignored to date.

Epigenomic profiling in rheumatic diseases

Prof Carl Goodyear

Rheumatoid arthritis (RA) is a chronic autoimmune disease with substantial immunopathogenic heterogeneity. It is well established that early diagnosis and initiation of effective therapy is crucial to prevent subsequent disability. Unfortunately, the impact of first-line therapy (i.e., methotrexate) on clinical disease is also heterogeneous, with various treatment trajectories (e.g. response, intermittent response and no-response). Notably, in patients that do respond and are in drug-induced remission, only 50% will have reoccurrence of clinical pathology (i.e., flare) upon discontinued of therapy. We have previously shown that evaluation of the structural epigenome, via determination of chromosome conformation signatures, offers great potential as informative biomarkers that can predict whether early RA patients respond to first-line therapy. We have now expanded this work to evaluate whether chromosome conformation signatures can reveal highly regulated areas of the genome, and define molecular endotypes that correlate with disease trajectories. Finally, characterization of chromosomal architecture prior to withdrawal of effective therapy has defined a "flare" predictive chromosome conformation signature. Take together, our work is providing unique insights into the RA-associated epigenome and how this can be potentially harnessed to inform clinical decisions**.**

Profiling Alzheimer's disease for personalised medicine

Dr Rebecca Sims

Alzheimer's disease (AD) is a debilitating neurodegenerative condition that is the most common cause of dementia. Genes play a strong role in AD with late-onset AD (aged over 65 years) showing heritability of 58-79% and early-onset AD over 90% (aged under 60 years). Genetic association provides a robust platform to build our understanding of the aetiology of the complex, sporadic form of disease. Over 90 loci are now implicated for AD, suggesting that it is a disease comprising multiple components; indeed, pathway analysis implicates immunity, endocytosis, cholesterol transport, ubiquitination, amyloid-β and tau processing. It is estimated that over 50% of AD heritability has been captured, allowing researchers to calculate the accumulation of AD genetic risk through polygenic risk scores. A polygenic risk score predicts disease with up to 90% accuracy and is an exciting tool in our research armoury that could allow selection of those with high polygenic risk scores for clinical trials and precision medicine. It could also allow cellular modelling of the combined risk..

SESSION 2: Pharmacogenomics Implementation in the 4 nations

England Vicky Chaplin

An update on the Accelerating Genomic Medicine in the NHS strategy and important developments and next steps for pharmacogenomics and precision medicine: the session will outline priorities of the Accelerating Genomic Medicine in the NHS strategy, provide an overview of the NHS Genomic Medicine Service and explore how genomic medicine is becoming embedded across the NHS in England in the field of medicines optimisation.

Scotland Prof Sandosh Padmanabhan

I shall discuss the challenges of Pharmacogenomics implementation in Scotland, describe how the Living Laboratory for Precision Medicine is exploring Pharmacogenomics implementation and present how Dundee successfully implemented Pre-emptive Clopidogrel Pharmacogenomics into the Stroke care pathway. I will highlight the Scottish Government's Accelerated National Innovation Adoption Pathway for national adoption of healthcare innovations at pace.

Wales Sian Morgan

In Wales 200,000 new prescriptions could be adjusted based on the genotype. Up to 20%-30% of Adverse Drug Reactions could be prevented by pharmacogenetic testing. The Welsh Government's Genomics for Precision Medicine Strategy published in 2017 noted the anticipated increase in the clinical utility and requirement for pharmacogenetic testing, and advised that services would be prioritised based on clinical need and Welsh expertise. A commitment was made to release funding for genomic investigations through the substitution of more costly investigations, or the cost-avoidance of treatments where these would be ineffective or harmful. In June 2020, Wales became the first in the UK to routinely provide all cancer patients being treated with certain types of chemotherapy DPYD gene screening to identify their risk of severe side effects and help prevent this occurring. In December 2022, Welsh Government published the 'Genomics Delivery Plan for Wales 2022-2025' supporting the ambition to further expand the development of pharmacogenomics services in Wales. The National Pharmacogenomics Group (NPGG) was also established in 2022 following endorsement of a white paper entitled 'Pharmacogenetics in Wales' by the All Wales Medicines Strategy Group (AWMSG) and the Genomics Partnership Wales (GPW) programme board. More recently, in partnership with Health Education and Improvement Wales (HEIW), Bangor University have developed a flexible eLearning module to increase pharmacogenomic understanding for the healthcare workforce in Wales. Pharmacy teams and the wider workforce across all care settings in Wales will play a crucial role in the implementation of pharmacogenomics across the health service.

Northern Ireland Professor Ian Young

Delivery of evidence based genomic medicine services as a component of health and social care is an important overarching principal in the development and implementation of government policy in Northern Ireland. The NI Minister of Health endorsed the overall UK Strategy (Genome UK: the Future of Healthcare) in 2020 and the shared commitments for UK wide implementation published in 2022. As part of the NI Government response to this an NI Genomics Partnership will be established, ensuring that Health and Social Care delivery bodies (including those responsible for public health), industry,

academic partners, and patient representatives can work together to deliver an integrated approach to delivery of a genomic medicine service. Areas of priority for this work are outlined in the NI Rare Diseases Action Plan, Cancer Strategy and UK Pathogen Strategy.

A part of the overall commitment outlined above, delivery of evidence-based pharmacogenomics will be a component. There is an intention to maintain parity of access to appropriate testing with the other countries of the UK, for both patients and clinicians. NI will continue to follow NICE guidance and to consider other emerging evidence and guidelines as appropriate for pharmacogenomics as for other areas of genomic medicine.

To date several areas have been taken forward and others remain under review. There has been a particular focus on cancer treatments, but areas in which routine pharmacogenomic testing has been embedded include cystic fibrosis and muscular dystrophy.

SESSION 3: Neuropsychiatric diseases

Standards of care for spinal muscular atrophy: The Patient's Perspective

Portia Thorman

Just five years ago, children living with SMA type 1 in the UK had an average life expectancy of just two years. Since the advent of treatments, they are now surviving.

SMA type one is essentially a new phenotype with very little clinical evidence to support management pathways. Families are currently the experts and it is essential that clinicians work closely with those living with SMA.

The International Standards of Care for SMA were published in 2017, before treatments were available and need updating. The experiences of families across the country vary hugely. Whether it's access to orthotics, physiotherapy or respiratory management, recommendations and practices are quickly evolving.

Portia will be talking about the experiences of those living within the new landscape of SMA, will describe some of the unanswered questions and how real world evidence can play a part in finding the solutions.

Pharmacogenetics for mental health

Prof Elvira Bramon

Clinical guidelines, FDA or SPC labels recommend drug choices or dose adjustments based on genetic profile for over 100 medications (Bousman et al, 2023; Swen et al, 2023; Beunk et al, 2023). Of those, more than 35 are drugs for the treatment of depression, mania, or psychosis. However, in UK mental health practice we do not use pharmacogenetics and treatment remains empirical.

We are conducting a prospective study of antipsychotic treatment informed by pharmacogenetics compared to treatment as usual with antipsychotics. To date, 220 people with psychosis and 126 clinicians have taken part. The sample is diverse including adults of any sex, ancestry, and age, which ranges from 18 to 91 years. We test a multigene panel selected from evidence-based pharmacogenetic clinical guidelines. We also genotype with arrays with enhanced pharmacogenomics content. Using a 5-gene panel, we find that 97% of patients carry one or more actionable variants. Pharmacogenetic testing shows high acceptability amongst people with psychosis and their clinicians.

To the best of our knowledge, this is the first pharmacogenetics intervention study for mental health in the UK. As genomic medicine advances in the NHS, we will discuss the challenges and opportunities of pharmacogenomics for mental health..

Precision medicine approaches to motor neuron disease

Prof Dame Pamela Shaw

Motor neuron disease (MND) is a neurodegenerative disease affecting the upper and lower motor neurons that is universally fatal but highly heterogenous in clinical course and genetic aeitiology. This heterogeneity has contributed to failures in drug development. The only disease modifying therapies currently approved for use in all MND patients, riluzole and edaravone have very limited effects on disease progression. The targeted SOD1-antisense oligonucleotide therapy, tofersen is approved for use in only the 2% of cases with an SOD1 mutation.

The upstream genetic cause of ALS/MND can be identified in 21-42% patients. This is a good starting point for disease subclassification. There are over 30 monogenic causes of MND. C9ORF72, SOD1, TARDBP, FUS are the commonest genetic variants, but multiple other rarer genetic mutations have also been discovered. For the majority of patients, disease risk and severity are the product of interaction between multiple genetic and environmental risk factors. Complex pathophysiological mechanisms underly motor neuron degeneration in MND that also vary according to the upstream cause. Biomarkers to indicate drug target engagement and further patient stratification are required to support precision medicine approaches.

Through programmes such as the AMBRoSIA (A Multi-Centre Biomarker Resource Strategy In ALS) project funded by the MND Association we are making systematic clinical and biosample observations to link genetics and omics data with the disease course in patients.

The recently completed MIROCALS trial of low dose interleukin 2 showed a substantial increase in life expectancy over 18 months for all forms of MND but there were a range of responses among patients. Transcriptomic analysis of PBMCs identifying baseline inflammatory profiles and baseline CSF neurofilament levels were able to predict treatment response. This information could help to select patients for future clinical trials targeting neuroinflammation.

Neurofilaments and neurodegeneration

Dr Axel Petzold

Neurofilament proteins (Nf) are currently the best validated body fluid biomarker for neurodegenerative pathology in humans. To help separating neurodegeneration of the central from the peripheral nervous system, new data on peripherin (PRPH) will presented to complementing the body of literature on the Nf light (NfL) and Nf heavy (NfH) chains. Mutations in the latter two Nf proteins also cause Amyotrophic Lateral Sclerosis and Charcot-Marie Tooth disease. With focus on this symposium at the interface between pharmacogenetics and stratified medicine, I will select clinical trial relevant Nf biomarker data from the large disease spectrum studied. The presentation will conclude with a discussion of the relevance of proteolytic breakdown products of Nf proteins and considerations for clinical trial design

4: Complex diseases

Health economics of genomic technologies
Prof Sarah Wordsworth

Advanced sequencing (NGS) technologies such as whole genome sequencing (WGS) have resulted in new genomic-based tests that can inform the diagnosis of rare, genetic diseases and guide treatment decisions in cancer. Such tests are now used in several health systems for patients with suspected or known disease, and attention is turning to their use in 'healthy' populations to identify disorders prior to onset. One of the limiting factors in tests being translated from research settings into clinical practice is a lack of health economics evidence demonstrating the value of tests for health care providers relative to alternative testing strategies. This presentation will highlight some of the existing evidence for using sequencing technologies, including health economic analyses of the 100,000 Genomes Project. The presentation will also highlight some of the methodological challenges in evaluating genomic technologies and describe the importance of health economic analyses for initiatives such as newborn screening.

Genomics of inflammatory bowel disease
Prof Holm Uhlig

The genetic basis of inflammatory bowel disease is complex with over 200 common loci impacting on disease susceptibility. Understanding those loci has guided the understanding of pathophysiology of intestinal inflammation. In addition, studies identified variants that affect disease progression, response the medication and identified rare monogenic disorders that can cause intestinal inflammation. Genomic medicine enables the identification of patients with rare or ultra-rare monogenic forms of inflammatory bowel disease (IBD) and supports clinical decision making. Patients with monogenic IBD frequently experience extremely early onset of treatment-refractory disease, with complex extraintestinal disease typical of immunodeficiency. Since more than 100 monogenic disorders can present with IBD, new genetic disorders and variants are being discovered every year, and as phenotypic expression of the gene defects is variable, adaptive genomic technologies are required. Monogenic IBD has become a key area to establish the concept of precision medicine. Clear guidance and standardised, affordable applications of genomic technologies are needed to implement exome or genome sequencing in clinical practice. The British Society of Gastroenterology and British Society of Paediatric Gastroenterology, Hepatology and Nutrition established joint guidelines aiming to ensure that testing resources are appropriately applied to maximise the benefit to patients on a national scale, minimise health-care disparities in accessing genomic technologies, and optimise resource use. Structural requirements were set for genomic medicine as part of a multidisciplinary team approach. We developed a quantitative integrated taxonomy that defines the cellular landscape of monogenic IBD gene expression illustrating cellular networks and defining genotype-phenotype associations (perianal disease and defective anti- microbial activity). This illustrates cellular processes and pathways shared across cellular compartments and phenotypic groups and highlights therapeutic implications.

.

Omics approaches in adrenal disease

Prof Wiebke Arlt

We have developed a novel omics approach, steroid metabolomics, defined as the combination of mass spectrometry-based multi-steroid profiling with machine learning-based data analysis. We initially employed gas chromatography-mass spectrometry for comprehensive steroid metabolome profiling but with the advent of advanced liquid chromatography-tandem mass spectrometry platforms we mostly employ this high-throughput technology. Multi-steroid profiling by tandem mass spectrometry is feasible in multiple biological fluids and matrices and we routinely deploy it for the analysis of urine, serum, and saliva. We use steroid metabolomics in discovery mode to identify mechanisms underlying adrenal disease and I will present two examples, the identification of a novel form of congenital adrenal hyperplasia and new insights into the pathophysiology of primary aldosteronism, the most prevalent form of endocrine hypertension. I will then present two examples for using our approach for biomarker discovery, validation, and diagnostic test development. Firstly, we have developed and prospectively validated a diagnostic test based on urine steroid metabolomics that can detect adrenal cancer in the urine of patients with incidentally discovered adrenal tumours. These so-called adrenal incidentalomas are discovered on 5% of all cross-sectional imaging of abdomen and chest. While most adrenal nodules are harmless, in larger series adrenocortical carcinoma is detected in 5% of referral cases. The second example I provide will be about the use of serum steroid metabolomics for mechanistic discovery and biomarker identification in women with polycystic ovary syndrome (PCOS). PCOS affects 10% of white women and 20% of South Asian women and is a life-long metabolic disorder characterised by androgen excess, insulin resistance and an increased risk of type 2 diabetes, hypertension, fatty liver and cardiovascular disease. I will show recent results illustrating the utility of steroid metabolomics for the development of a biomarker assay for prediction of metabolic risk and therapeutic stratification in PCOS.

..

SPEAKER BIOGRAPHIES

Professor Patrick Chinnery FRCP FRCPath FMedSciProfessor of Neurology and Head of the Department of Clinical Neurosciences at the University of Cambridge and clinical neurologist at Addenbrooke's Hospital. A Wellcome Trust Principal Research Fellow, his research lab is based in the MRC Mitochondrial Biology Unit. He is known for his expertise in rare inherited diseases that affect the nervous system. His lab has been studying the genetic basis of mitochondrial disorders for over two decades, harnessing the power of whole genome sequencing and developing new treatments through experimental medicine and early phase trials. He jointly chairs the NIHR BioResource for Translational Research in Common and Rare diseases, and is Clinical Director of the Medical Research Council.

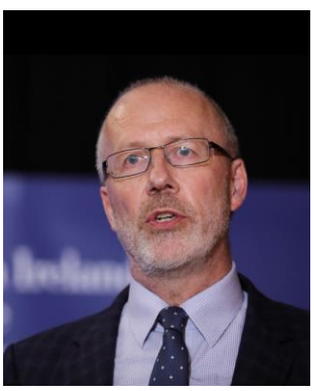
Professor Carl Goodyear PhD, Assistant Vice Principal (Strategy & Resources), Professor of Translational Immunology & Director for Innovation, Engagement & Enterprise in the School of Infection & Immunity, University of Glasgow.Carl undertook his BSc (Hons) in molecular biology at the University of Glasgow and PhD in molecular immunology at Glasgow Caledonian University. He then moved to the US and worked in the Department of Medicine at the University of California at San Diego where he eventually held the position of Assistant Professor. During this period, he was awarded a Cancer Research Institute Postdoctoral Fellowship, became a National Blood Foundation Scholar, and received several awards including the National Blood Foundation David B. Pall Prize for Innovative Research in Transfusion Medicine and an Arthritis Foundation Investigator Award. In 2006 he was awarded a prestigious Arthritis Research UK Fellowship and returned to work in the UK at the Institute of Infection Immunity and Inflammation in the University of Glasgow. His research is currently focused on understanding immunopathogenesis of disease (i.e., Rheumatoid Arthritis, Osteoarthritis & Multiple Myeloma) and translating this knowledge into viable therapeutic agents for patients. He leads a Translational Immunology programme that provides the critical interface between clinical and basic science, with a specific focus on precision medicine. In parallel, he is also the Director of the GLAZgo Discovery Centre and the Glasgow-Lilly Centre, strategic collaborations between the University of Glasgow and AstraZeneca, and Eli-Lilly respectively. Both of which are aimed at driving innovative academic/industry research. Carl has published widely in the areas of immunobiology and rheumatology. He is a Chair/Deputy Chair or member of various Research Advisory committees & grant review Panels.

Dr Rebecca Sims completed a PhD in the genetics of the behavioural symptoms in Alzheimer's disease before undertaking a MSc in genetic epidemiology and bioinformatics. Rebecca was an Alzheimer's Society junior fellow and is now a Senior Research Fellow, based within the Division of Psychological Medicine and Clinical Neuroscience (DPMCN), Cardiff University (CU) and co-investigator in the UK Dementia Research Institute (UKDRI) at Cardiff. Rebecca is the UK lead of the Joint Programme for Neurodegenerative disease (JPND) funded European Alzheimer's disease Biobank (EADB) that has culminated in the largest Genome Wide Association Study in Alzheimer's to date. In addition, Rebecca is a Principal Investigator of the Brains for Dementia Research (BDR) project in Cardiff and is the lead of the Alzheimer' Research UK Wales Network Centre.

Vicky Chaplin is the Pharmacy Genomics Lead for the Genomics Unit at NHS England. She and her team work in collaboration with the NHS GMS Alliances' Pharmacy Leads and other key stakeholders to embed genomic medicine into mainstream care, and enable patients to realise the benefits of medicines optimisation driven by genomic and diagnostic characterisation. This lead role is also part of the Chief Pharmaceutical Officer's Pharmacy Advisory Group ensuring the work is coordinated across pharmacy and medicines developments across the NHS and government. During her career, Vicky has worked across various sectors of pharmacy in the NHS, including primary care, secondary care and community pharmacy as well as in regional and national roles supporting medicines optimisation and the use of medical devices, including digital therapeutics. Her specialist area of interest is diabetes, and she holds postgraduate qualifications in pharmacy, as an independent prescriber, and in health economics. She is a member of the Faculty of Clinical Informatics and has worked in various areas of digital health for many years; she currently supports the Genomics Unit in a Clinical Safety Officer role. She has also worked as a Medical Advisor in the pharmaceutical industry, with a significant part of her role focusing on the intersection of medicines, medical devices and digital tools.

Professor Sandosh Padmanabhan is the Professor of Cardiovascular Genomics and Therapeutics at the University of Glasgow, and an Honorary Consultant Physician at the Queen Elizabeth University Hospital, Glasgow. He is a Clinical Pharmacologist with a research interest in hypertension and pharmacogenomics. His research spans population genetics, epidemiology, real-world evidence, clinical trials, precision medicine and digital health. He is the academic lead of the Pharmacogenomics Informed Medicines Management strand of the UKRI-funded Living Laboratory for Precision Medicine. He is a Fellow of the Royal College of Physicians, the British Pharmacological Society, the British and Irish Hypertension Society and the American Heart Association.

Sian Morgan is currently the All Wales Medical Genomics Service (AWMGS) Laboratory Director. She has extensive experience in the development and delivery of NHS genomic services having started working within the service in 1991. The AWMGS is a tertiary service, hosted by Cardiff and Vale University Health Board and commissioned by the Welsh Health Specialised Services Committee (WHSSC) to deliver Rare Disease, Cancer and Pharmacogenetics services for the population of Wales. She leada a laboratory of over 170 staff. As Laboratory Director she has successfully identified and developed strategic relationships and alliances leading to business, research and wider service developments. Recent laboratory success include the 'first' national DPYD pharmacogenomics UK service launched in June 2020. She is a member and deputy chair of the National Pharmacogenetics Group (NPGG), a multidisciplinary clinical advisory group that was established in 2022. NPGG aims to ensure that there is a multidisciplinary, coordinated national approach with defined clinical input to the development and introduction of pharmacogenetic services within Wales.



Professor Ian Young is Professor of Medicine at Queen's University Belfast, and Deputy Medical Director and Consultant Chemical Pathologist at Belfast Health and Social Care Trust. In addition, he is Chief Scientific Advisor to the Department of Health, Northern Ireland, and Director of Research for Health and Social Care, Northern Ireland. His main clinical and research interests are in nutrition and lipid metabolism, particularly in relation to cardiovascular disease prevention and management of patients with complex lipid disorders. He is author of over 450 published research papers. He is Past-President of the Association for Clinical Biochemistry and Laboratory Medicine, UK, and previous Chair of the Joint Committee for Traceability in Laboratory Medicine (JCTLM). He currently Chair of the UK Government's Scientific Advisory Committee on Nutrition. He is Associate Editor for the journal Clinical Chemistry, and a member of the editorial boards of a number of other international journals.

Portia Thorman Bsc is Advocacy Lead at Spinal Muscular Atrophy (SMA) UK, working to advocate for improved access to treatments, therapies and services for all those living with SMA.

SMA is a rare, genetic neuromuscular condition causing progressive muscle wasting affecting all muscles in the body, including those for breathing and swallowing. Portia is the mother of four children, her youngest son lives with SMA type 1, the most severe form of the condition, and was one of the first children to be treated with Spinraza in the UK in 2017. Due to late diagnosis, he lives with complex needs, giving Portia strong motivation in her work as a member of the UK SMA Newborn Screening Alliance.

Portia is also the UK Delegate for SMA Europe, an umbrella organisation for SMA advocacy groups across Europe, promoting and generating real world evidence to support evidence-based patient advocacy. Portia has a degree in Psychology and before becoming part of the SMA community, worked as a Primary School teacher.

Professor Elvira Bramon is Professor of Neuroscience and Mental Health at University College London, where she heads the Neuroscience Research Department at the UCL Division of Psychiatry. She is interested in the genetics and pharmacogenetics of severe mental disorders. She leads the Psychosis Endophenotypes International Consortium investigating biomarkers for psychosis and their genetic influences.
In collaboration with Genomics England and NHS England, she is contributing to the development of a new pharmacogenomics service within the NHS. Elvira also works as Consultant Psychiatrist at Camden & Islington NHS Foundation Trust. Elvira has published more than 150 scientific papers, some in Nature, Nature Genetics, Biological Psychiatry, Molecular Psychiatry. These international funders support her research: Medical Research Council, Wellcome Trust, NIHR, NARSAD, Mental Health Research UK and EU-Horizon 2020.
More information: https://www.ucl.ac.uk/psychiatry/people/bramon
Twitter: @e_bramon

Professor Dame Pamela Shaw is an academic neurologist and world-leading researcher in motor neuron disease (MND). As Director of the Sheffield Institute for Translational Neuroscience (SITraN) she leads a major multidisciplinary programme investigating the genetic, molecular and neurochemical factors underlying MND to enable disease stratification and develop potential new targeted therapeutics. Undertaking systematic clinical observations and longitudinal bio-sampling in hundreds of patients to understand and subclassify MND, as Director of the NIHR Sheffield Biomedical Research Centre she is working to translate new precision medicine and biomarker supported approaches into early phase experimental medicine trials. She has made significant contributions to:

- Clinical research including the identification and introduction into clinical practice of neuroprotective agent riluzole; Demonstrating non-invasive ventilation as improving the quality of life and prolonging survival of MND patients; Conducting over 22 clinical trials including the evaluation of Biogen's recently FDA approved genetic therapy for SOD1-MND, tofersen (QALSODY) Miller et al 2022 (NEJM).
- Genetic subclassification of MND including the identification of changes in CHMP2B;TARDB;FUS;C9ORF72;TUBA4A;NEK1;Annexin A11;GLT8D1 genes; Characterization of associated clinical phenotype and molecular pathology; Demonstrating the value of offering routine genetic screening for MND patients (Shepheard et al 2021 JNNP).
- Developing a translational pipeline of potential neuroprotective therapies; Using viral vectors to deliver therapeutic cargos to the CNS; demonstrating dramatic therapeutic effects in pre-clinical MND and spinal muscular atrophy models underpinning successful experimental medicine trials; identifying modifiable pathways through transcriptomics including the NRF2-antioxidant response element and SRSF1 nuclear transporter, currently being developed towards MND clinical trials.

Dr Axel Petzold MD PhD FRCP FRCOphth FRCPath, is a consultant neurologist employed by the National Hospital for Neurology and Neurosurgery (UCLH NHNN), Queen Square; Moorfields Eye Hospital (MEH), City Road, London and the Amsterdam University Medical Centre, The Netherlands. He has a clinical and research background in multiple sclerosis, optic neuritis, neurodegeneration and neuro-critical care. His own translational research integrates clinical studies and trials with imaging and biomarker work. Dr Petzold (ORCID ID 0000-0002-0344-9749) has published >310 articles in peer reviewed Journals (>100 first author) with a cumulative impact factor >1600 and a Google Scholar H-Index of 73. He has compiled two books, one monograph and authored 14 book chapters (10 first author). Of the 16 visiting fellows from abroad he trained in protein biomarker research at UCL, 7 now hold a prestigious chair in their home University and one has become an internationally leading figure in the field. He has contributed early to validation and quality control strategies and have over the years matured into frequently cited reporting guidelines. He has been involved in immunoassay development and is delighted that presently neurofilament protein are used around the world by all medical specialities and in experimental studies. For these pioneering activities the Royal College of Physicians in London awarded him with the prestigious Lady Estelle Wolfson Lectureship in translational medicine (2022).

Prof Sarah Wordsworth is a Professor in the Health Economics Research Centre, University of Oxford. She has over 25 years' experience in the evaluation of costs and benefits of health care technologies. She leads a research programme on the economics of genetic and genomic technologies and precision medicine. Of particular interest are the economics of translating genomic high-throughput sequencing technologies from research into clinical practice, in cancer, rare disease and newborn screening. Sarah is lead for the 100,000 Genomes Project, Genomics England Health Economics Clinical Interpretation Partnership and a member of the US National Academies Roundtable on Genomics and Precision Medicine. A lack of evidence on the cost-effectiveness of novel genomic technologies such as whole genome sequencing is a key translational challenge. The genomics research that Sarah has designed and led, has informed key changes in practice, such as producing evidence that gene panels are more cost-effective than single-gene testing. Sarah has co-authored several text books on analysis methods for health economics and genomic research audiences and is Co-Director of the MSc in Precision Cancer Medicine at the University of Oxford.

Professor Holm Uhlig is a Professor of Paediatric Gastroenterology in the Translational Gastroenterology Unit, University of Oxford and Honorary Consultant at the Children's Hospital Oxford. Holm is interested to understand how common and rare genetic variants impact on the immune system. He sees paediatric patients with monogenic forms of IBD, aims to improve diagnostics and to translate the understanding of mechanisms into precision medicine.

Professor Wiebke Arlt is the Director of the Medical Research Council London Institute of Medical Sciences (MRC LMS) as well as Professor of Transdisciplinary Medicine at Imperial College London. At the LMS, Wiebke leads the Steroids & Metabolism research group, which utilizes human-based in vivo, ex vivo and in vivo approaches in conjunction with steroid mass spectrometry and machine learning for mechanistic discovery and the development of precision medicine approaches. She champions the development of integrated multi-disciplinary services for patients with adrenal and reproductive disorders.

Wiebke studied Medicine at the University of Cologne, Germany, followed by integrated clinical and academic training in General Medicine and Endocrinology at the University of Würzburg. This was by a DFG Postdoctoral Fellowship in Molecular Endocrinology at the University of California at San Francisco and a DFG Heisenberg Senior Fellowship, which led her in 2002 to the University of Birmingham. She was subsequently awarded an MRC Senior Clinical Fellowship (2004-2009) and promoted to Professor of Medicine (2006), followed by her appointment to the William Withering Chair of Medicine in 2014. She served as the founding Director of the Institute of Metabolism and Systems Research (IMSR) at the University of Birmingham from 2015-2022

THANKS TO OUR SPONSOR

Big challenges demand big thinkers - those who can unlock the answers and further our understanding of the important issues of our time. Our work encompasses everything from the physical, biological and social sciences, to innovation, engineering, medicine, the environment and the cultural impact of the arts and humanities. In all of these areas, our role is to bring together the people who can innovate and change the world for the better.

We work with the government to invest over £8 billion a year in research and innovation by partnering with academia and industry to make the impossible, possible. Through the UK's nine leading academic and industrial funding councils, we create knowledge with impact.

THANKS TO OUR EXHIBITORS

Agena Bioscience® makes clinical genomics accessible to high-complexity clinical labs by enabling and simplifying genetic test deployment. Our foundational platform, the MassARRAY® System, is a highly sensitive, cost-effective genetic testing system used globally in diverse fields such as pharmacogenetics, hereditary genetics, infectious disease, and cancer profiling for solid tumors and liquid biopsy.

The British Pharmacological Society is a membership charity with a mission to promote and advance all disciplines of pharmacology in the discovery, development and use of medicines. We are an inclusive, nurturing, and professional global community with more than 4,000 members from more than 60 countries. Pharmacology makes a unique contribution to research to develop new drugs, and to improving the use of existing drugs for better patient outcomes. The British Pharmacological Society supports the advancement of pharmacogenomics and, in 2022, published a report in partnership with the Royal College of Physicians: 'Personalised Prescribing – Using pharmacogenomics to improve patient outcomes'. This July, we are hosting the 19th World Congress of Basic and Clinical Pharmacology (WCP2023) on behalf of IUPHAR in Glasgow, Scotland. Pharmacogenomics is a key topic of the meeting, and there will be at least six sessions exploring the subject, including keynote lectures from Professor Sir Munir Pirmohamed of the University of Liverpool and Professor Eran Segal of the Weizmann Institute of Science. Register for WCP2023 now.

FDB (First Databank) is delighted to be supporting the 10th Annual Open Meeting of the UK Pharmacogenetics and Stratified Medicine Network. FDB creates and delivers the world's most powerful medicines knowledge that ignites, inspires, and illuminates critical medication decisions. We collaborate with our partners to help improve patient safety, operational efficiency, and health outcomes.

We now see a growing opportunity to positively impact prescribing for a large percentage of the general population who take many commonly prescribed drugs. However, integration of pharmacogenomics with the software tools used to guide prescribing decisions is fundamentally important if the UK is to harness this opportunity. The enabling technology already exists, it just needs to be joined up in the right way.

As the UK's foremost experts in prescribing decision support - with over four decades of experience working alongside the NHS in multiple care settings – FDB is uniquely positioned to help.

Our drug database, FDB Multilex, is the UK's most widely used and it is currently deployed in over 10,000 healthcare settings around the country. Furthermore, FDB OptimiseRx, our point-of-care medicines optimisation solution, is also the most widely used of its kind and currently in use in over 4,500 GP practices.

While FDB is widely recognised as an authority on medicines knowledge, we also specialise in seamlessly and deeply integrating that knowledge into the clinical systems and prescribing workflows utilised in various care settings. This level of integration results in an unrivalled degree of patient specificity.

As we see it, there is currently a large gap in the implementation and return of actionable pharmacogenetic findings to healthcare professionals and patients in standard clinical practice. As a result, we are now developing a pharmacogenomics decision support solution to support the much-needed shift towards precision prescribing at scale.

Pharmacogenetics-guided drug treatment is not just a concept for the future, but a practical approach that can be employed today. This approach is not only limited to specialised healthcare needs or settings but can be beneficial for a broad range of patients, providing an opportunity to optimise the use of some of the most prescribed drugs. Furthermore, it does not require a significant investment in learning for prescribers, especially if integrated seamlessly and intuitively into existing prescribing workflows.

By collaborating to incorporate pharmacogenomics into clinical practice, we can enhance the quality of care and outcomes for millions of patients. We are actively seeking partners to join us in this initiative, so we'd love to talk to you at or after the upcoming meeting.

For a complete look at our solutions and services, please visit www.fdbhealth.co.uk, or follow us on Twitter, LinkedIn, and YouTube.

Genedrive is a near patient molecular diagnostics company developing and commercialising a rapid, simple-to-use and robust molecular platform for use in patient stratification (genotyping). We are focussed on time critical testing in acute care.

In 2022, Genedrive deployed the world's first point of care genetic test for use in an urgent care setting, the Genedrive® MT-RNR1 ID Kit, to reduce the risk of antibiotic induced hearing loss and avoid lifelong deafness in infants with suspected sepsis. In March 2023, UK NICE recommended the Genedrive MT-RNR1 test for use in the NHS via their new early value assessment programme. Genedrive's point of care test rapidly identifies babies carrying the MT-RNR1 m.1555A>G gene variant via a simple non-invasive cheek swab in under 30 minutes. For those carrying the gene variant, an alternative antibiotic can be prescribed, preserving hearing that would otherwise be lost on exposure to just a single dose of the aminoglycoside, gentamicin.

Following publication of the PALOH Study, Manchester NHS Foundation Trust routinely use the Genedrive MT-RNR1 ID Kit in their neonatal unit, one of the largest neonatal intensive care units in the UK. The test is also being implemented in other neonatal units across the Greater Manchester area for routine clinical use.

The potential clinical usage of pharmacogenetics at the point of care is boundless and enables clinicians to create personalised treatment plans, providing patients the most positive outcome.

As we further develop our portfolio, we have an opportunity to reach millions of people with novel pharmacogenetic tests. Genedrive are currently developing the Genedrive®
CYP2C19 ID Kit to detect specific alleles of the CYP2C19 gene to inform clinicians of an individual's metaboliser status according to CPIC guidelines in treatment strategies using therapeutics that are metabolised by CYP2C19. This test is for use in point of care settings where routine prescribing would take place. This is also part of a NICE diagnostic assessment programme 'Clopidogrel genotype testing after ischaemic stroke or transient ischaemic attack.' Up to one in five patients are unable to convert clopidogrel into its active form, rendering it ineffective.

The Genedrive point of care test for CYP2C19 is due for launch later in 2023.

Ultimately, our goal is to change lives through rapid, near patient access to the benefits of molecular diagnostics in time critical situations. The value of pharmacogenetics in personalised medicine is indisputable. Removing the cost of ineffective prescriptions and reducing the burden of avoidable illness and adverse drug reactions could present a substantial cost-saving opportunity, in addition to optimising the efficacy and safety of the care received by each individual patient.

Health in Code is pioneer in the field of clinical and healthcare genomics and in the application of massive sequencing (NGS, “Next Generation Sequencing”). We are an international leader in cardiovascular genetics and one of the largest providers in Europe of diagnostic products and services for other medical specialties where genomics adds value: oncology, neurology, pharmacogenetics, and other rare diseases. At Health in Code we are constantly innovating, working on new technologies and services such as liquid biopsy and whole genome sequencing.

The Health in Code clinical team, which is formed by cardiologists, neurologists, immunologists, geneticists, pharmacists, and biologists specialized in medical genetics, systematically reviews, and evaluates published clinical bibliography, especially pharmacogenetic clinical practice guidelines. Our clinical report provides specific therapeutic strategies supported by clinical practice guidelines to increase the patients’ quality of life.

We are committed to the management of knowledge acquired with our own databases to provide pre- and post-test counselling that allows professionals in the health sector to improve the prognosis of genetic diseases and decision-making related to their prevention and treatment.

Our focus is on people and our mission is to generate a positive social impact through personalized medicine and the improvement of clinical decision-making based on genomic data, thus increasing the quality of life of people suffering from genetic diseases and the of their families and contributing to the efficient and sustainable development of the health system.

Inagene Diagnostics is an international pharmacogenomics company, providing pharmacogenomic testing and a clinical decision support tool. The parent company is based in Toronto and has over 4 years experience of providing pharmacogenomic tests. Inagene Diagnostics UK Ltd was registered in January 2023, and has been working in partnership with NHS teams in the West Midlands for over 2 years. Our test accurately interrogates genes which have been carefully selected, based on peer reviewed publications with high levels of evidence supporting gene-drug relationships. The results are combined with advanced data analysis software to provide clinical reports which facilitate healthcare providers to select the safest and most effective medicines for their patients. Working in partnership with healthcare providers, Inagene aims to bring the benefits of pharmacogenomic testing into routine clinical practice.

The International Society of Pharmacovigilance (ISoP) is an international non-profit scientific organisation, which aims to foster Pharmacovigilance both scientifically and educationally, and enhance all aspects of the safe and proper use of medicines, in all countries.

LaCAR MDx is a Belgian company developing molecular diagnostic tools for the detection of genetic diseases. We commercialize CE-IVD kits detecting single-nucleotide polymorphisms (SNPs) or specific alleles based on the Loop mediated isothermal AMPlification (LAMP) method.
This technique does not require DNA extraction, which allows to save both time and costs. It works directly on whole blood or dried blood spots, although the kits may also be used with DNA samples. LaCAR MDx kits are related to categories such as genetic thrombosis, pharmacogenetics, food intolerances, autoimmune diseases, etc. It has also taken a first step into the newborn screening with its SMA detection kit. In addition to that, LaCAR MDx has worked closely with another company named to develop GeneFox, a software allowing the automatic interpretation of the results.
More recently, LaCAR has decided to join its forces with ZenTech, a company specialized in newborn screening, becoming then the LaCAR Company. The vision of both companies is to offer a complete and innovative solution for the diagnostics of diseases for every human being, from newborn to adult.

MC Diagnostics Ltd. is an innovative molecular diagnostics company. We have designed, developed, and manufactured an automated low density array platform (ALDAS) which is currently providing proven clinical diagnostic assays in the fields of HLA typing for transplantation and the identification of specific HLA alleles implicated in predisposing patients to adverse drug reactions (ADRs).
Come and talk to us about the new patient profiling product
The PGx Passport

- 5 major healthcare fields in a single test
- 8 genes -36SNPs +structural variants
- HLA ADR associated alleles detected
- CYP2D6 CNVS & whole gene deletions identified
- Same day turnaround
- Fully automated detection

If you have well characterised DNA samples, we would love to talk with you.

PacBio is a premier life science technology company that is designing, developing and manufacturing advanced sequencing solutions to help scientists and clinical researchers resolve genetically complex problems. Our products and technology under development stem from two highly differentiated core technologies focused on accuracy, quality and completeness which include our existing HiFi long read sequencing and our emerging SBB® short read sequencing technologies. Our products address solutions across a broad set of research applications including human germline sequencing, plant and animal sciences, infectious disease and microbiology, oncology, and other emerging applications. For more information, please visit www.pacb.com and follow @PacBio.

Randox Laboratories is a global market leader within the in vitro diagnostics industry, developing solutions for clinical, research and molecular labs. Relatively new to the Randox group is our Genomics Services department. Our established sequencing laboratory has been specifically designed and set up to fulfil a unique range of testing from our specialised laboratory in Northern Ireland. Utilising a multitude of platforms, our sequencing and genotyping facility is suited to a wide range of areas of genome sequencing, where our dedicated scientists and bioinformaticians are on hand to provide customisable sequencing and genotyping services for research, development, validation and running of different genomic tests.

Our Next generation Sequencing (NGS) capabilities include, Whole Exome Sequencing, Human Whole Genome Sequencing, Microbial Whole Genome Sequencing, 16S rNA sequencing as well as Shotgun Sequencing. Randox Genomic Services Department also have target genotyping solutions in multiple areas. Some of our panels include GSA + Custom content and GDA + Enhanced PGx.

Randox have recently become the UK's first commercial partner of Olink® Proximity Extension Assay (PEA) high multiplex technology, offering scientists involved in drug development, clinical, or life science research, the service they need to run large-scale discovery proteomics without compromising data, quality or robustness. We offer our customers access to the entire Olink® protein library, consisting of ~3000 protein assays for exploratory proteomics and multiomics. The Explore 3072 library includes biomarkers that contribute most to key research questions, covering as many biological pathways and functions as possible including organ specific proteins, secreted proteins, exploratory proteins and inflammatory proteins.

MEMBERSHIP

Membership is free please contact Christine cjmcn@liverpool.ac.uk

CPD CREDITS

6 CPD credits are awarded for attending the meeting, contact Christine cjmcn@liverpool.ac.uk for a certificate of attendance.

www.uk-pgx-stratmed.co.uk

@UKPGxStratmed

Find us on LinkedIn