



4th Annual Open Meeting

*Working together to connect and develop the
personalised / precision / stratified medicine community*



30 Euston Square, London

23 March, 2017

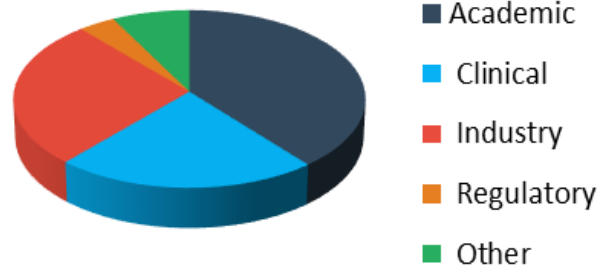
Welcome to the

UK Pharmacogenetics & Stratified Medicine Network

4th Annual Open Meeting

We would like to thank our speakers and sponsors for their contribution to what we are sure will be another successful annual meeting; also thanks to all our delegates for taking the time to attend and contribute to the discussions.

Network membership is approaching 600 representatives from academic, clinical, industrial and regulatory organisations, as well as representatives from patient groups. Membership is free and provides an ideal opportunity to highlight the expertise of your organisation to the wider community.



By linking organisations together we are encouraging multidisciplinary partnerships to move the field of stratified / personalised / precision medicine forward. We are also forging links with the US Pharmacogenetics Research Network and the European Ubiquitous Pharmacogenetics group to help develop a worldwide collaborative network for personalised medicine.

We have partnered with key organisations such as the Academy of Medical Sciences, MHRA, NHS England, and NIHR-CRN to address, and offer solutions to, some of the key challenges of adopting pharmacogenetics and stratified medicine into the clinic. Presentations and reports from these workshops may be viewed on the website.

The Network website www.uk-pgx-stratmed.co.uk attracts global interest as we supply a wealth of information to the wider community. Members regularly visit the website to keep up to date with the progress of personalised medicine and to look for research partners.



Events



Members' Activities



Presentations



Workshops



Education



Funding



Publications



Steering Committee

Today we hope you enjoy the presentations and have the opportunity to make contacts with colleagues from across all sectors.



Professor Sir Munir Pirmohamed, Chair of the UK Pharmacogenetics and Stratified Medicine Network.

Programme Overview - Morning

08.00-09.00 Registration and refreshments

09.00-10.40 **SESSION 1:**

Chair Professor Sir Munir Pirmohamed

09.00-09.10 **Welcome and update on the Pharmacogenetics and Stratified Medicine Network** **Professor Sir Munir Pirmohamed**

09.10-09.40 **100K Genomes project – latest update** **Professor Tim Hubbard**

09.40-10.10 **Mainstreaming personalised medicine in the NHS** **Professor Sue Hill**

10.10-10.40 **The importance of big data for stratified medicine** **Professor Andrew Morris**

10.40-11.20 **Morning Coffee**

11.20-12.20 **SESSION 2:**

Chair Dr Louise Leong

11.20-11.50 **Personalising treatment of diabetes** **Professor Ewan Pearson**

11.50-12.20 **Precision medicine approaches in cystic fibrosis** **Dr Mark Higgins**

Programme Overview - Afternoon

12.20-14.00 Lunch and exhibitors stands

14.00-15.30 **SESSION 3:**

Chair Professor Joanne Hackett

14.00-14.30 **Metabonomics as a tool for stratification** **Professor Elaine Holmes**

14.30-15.00 **Development of an integrated platform for proteomic biomarker discovery** **Professor Antony Whetton**

15.00-15.30 **Does epigenetics have a role in stratified medicine?** **Professor Jonathan Mill**

15.30-16.00 **Afternoon Tea**

16.00-17.10 **SESSION 4:**

Chair Dr Hilary Burton

16.00-16.30 **Health economics of stratified medicine** **Professor Dyfrig Hughes**

16.30-17.00 **A patient perspective of stratified medicine** **Alastair Kent**

17.00-17.10 **Close of conference**

17.10-18.30 **Networking**

Summary of Presentations

Session 1: Chair Professor Sir Munir Pirmohamed

Welcome and update on the Pharmacogenetics & Stratified Medicine Network

Professor Sir Munir Pirmohamed, Chair of the UK Pharmacogenetics and Stratified Medicine Network



Munir will welcome delegates to the event and thank our speakers and sponsors for their contributions. Munir will then give an update on the growth of the Network and how our activities are supporting the promotion of stratified medicine to improve patient outcomes.

100K Genomes project – latest update

Professor Tim Hubbard, Genomics England



The 100,000 genomes project sets out to mainstream whole genome sequencing for treatment into the NHS. Genomics England, set up in 2013 to deliver the project, has established sample handling, sequencing and interpretation pipelines to enable whole genome sequences to be analysed for rare diseases and cancer with individual reports returned to clinicians.

Mainstreaming personalised medicine in the NHS

Professor Sue Hill, NHS England



Professor Hill's talk will cover:

- How the NHS is taking forward a strategic approach to diagnostic testing and increasing diagnostic yield building on the infrastructure from the 100,000 Genomes Project legacy
- The NHS England strategic framework for personalised medicine, including areas for early development
- How this personalisation approach will support future care and innovation and build the UK genomic knowledge base

The importance of big data for stratified medicine

Professor Andrew Morris, University of Edinburgh



Examples will be given from nationwide research and development programmes that integrate electronic patient records with biologic and health system data. Two themes will be explored; specifically:

- How the size of Scotland (5 million residents), allied to a relatively stable population and unified health care structures facilitate the application of health informatics to support nationwide quality-assured provision of diabetes care.

How population-based datasets and disease registries can be integrated with biologic information to facilitate (i) epidemiology; (ii) drug safety studies; (iii) enhanced efficiency of clinical trials through automated follow-up of clinical events and treatment response; and, (iv) the conduct of large-scale genetic, pharmacogenetics, and family-based studies essential for stratified medicine.

Summary of Presentations

Session 2: Chair Dr Louise Leong

Personalising treatment of diabetes

Professor Ewan Pearson, University of Dundee



There are several approaches to the therapy of patients with Type 2 diabetes. One common sense approach is to trial a drug and, as recommended by SIGN and NICE, to stop therapy if a drug is ineffective. However, HbA1c is often quite variable in an individual, and this can make it hard to establish if a diabetes treatment has truly resulted in an improvement in diabetes control – in fact we estimate that we can only say that someone is a ‘responder’ in 25% of patients. This challenges the trial and error approach to personalise care.

An alternative approach is the stratified approach, or even the individualized approach to therapy, as advocated by the joint ADA/EASD guidelines. Yet these guidelines offer no evidence base for how drugs should be individualized. In the MRC-ABPI Mastermind study we show that thiazolidinediones work best in obese patients, yet metformin, another ‘insulin sensitizer’ works best in slimmer patients who are more insulin sensitive with preserved beta-cell function. Thus, BMI, diabetes duration and insulin sensitivity can be used to begin to stratify therapy – identifying clinical characteristics before treatment that increase the likelihood of a good treatment response.

In addition, genetic variation may alter response to or side effects of therapy. This is seen strikingly when we consider the ability to transfer off insulin treatment once monogenic aetiology of diabetes can be established in many cases. Considering drug response, metformin response is variable and heritable suggesting an individual’s genetics will influence response. We have shown that variants at the ATM locus and in SLC2A2 alter metformin response with modest effect sizes; for metformin intolerance, OCT1 genotype, and use of OCT1 interacting drugs have

a large clinically important impact on risk of intolerance to metformin. Other data on the genetics of response to TZDs, DPP4-inhibitors and GLP-1R Agonists will be outlined.

In summary, personalising treatment in common complex disease is challenging. However, as we are beginning to show, with appropriate phenotyping and trial design it is likely that we will be able to stratify treatments to ensure maximal response and minimize side effects of diabetes treatments.

Precision medicine approaches in cystic fibrosis

Dr Mark Higgins, Vertex Pharmaceuticals



This talk will describe the pathway from the discovery of the CF gene in 1989, through the characterization of the specific genetic defects of certain mutations and the development of novel medications designed to address these genetic defects.

The medications are approved for specific CF genotypes and provide an illustration of the ability to use an understanding of genetics, in-vitro data and clinical trials to develop precision medicines to target the underlying defect in CF.

Summary of Presentations

Session 3: Chair Professor Joanne Hackett

Metabolomics as a tool for stratification

Professor Elaine Holmes, Imperial College London



Metabonomic technologies such as NMR spectroscopy and mass spectrometry, coupled with computational modeling strategies can generate metabolic phenotypes from biofluids and tissues that reflect the health or disease status of an individual [1]. Biofluid profiles capture endogenous metabolic processes but can also inform on diet, other ingested xenobiotics and metabolites derived from processing of dietary components by the gut bacteria. Thus the biological profiles (urine, plasma, faeces, tissue biopsies, cell extracts) provide a window for viewing metabolic events that can be used in a diagnostic or even prognostic capacity and which can be used as biomarker panels to monitor response to therapeutic interventions such as drugs or surgery. Additionally the perturbed metabolites can be mapped to biochemical pathways to help understand the mechanisms underpinning disease.

Clinical studies have shown that inter-individual differences in either host or microbial metabolism can impact on patient responses to therapeutics or surgical interventions (pharmacometabonomics) [2] and that these baseline or pretreatment profiles can be used prognostically to predict drug metabolism, efficacy or toxicity. This technology allows the construction of a framework for stratifying patients and improving clinical care with respect to improved clinical outcome and reduced expenditure. The basic technology will be outlined and several clinical exemplars provided.

[1] Nicholson JK, et al *Xenobiotica*. 1999; 29(11):1181-9. PubMed PMID: 10598751.

[2] Clayton TA, et al *Nature* 2006; 440(7087):1073-7 PubMed PMID: 16625200

Development of an integrated platform for proteomic biomarker discovery

Professor Anthony Whetton, University of Manchester, Christie Hospital



Proteins are a key set of biomarkers in healthcare. Recent developments in mass spectrometry (MS) provide opportunities to more effectively and systematically derive information on protein levels in biological fluids and cells. These investigations can include post-translational modification of proteins, such as phosphorylation. The major issue in carrying this forward into clinical proteomics for precision medicine and companion biomarker discovery has been the difficulty in relatively or absolutely quantifying proteins from biofluids in a reasonable time frame. The use of the latest innovations in MS-based technologies offers a high capacity throughput proteomic profiling for clinical biochemistry purposes. Sequential Window Acquisition of all THEoretical fragment-ion spectra MS (SWATH MS) enables the creation of a digitised, quantitative, permanent record of the proteome.

As an example, markers of risk in ovarian cancer have been investigated using a SWATH MS approach. Combined with validation and verification platforms (such as Selected Reaction Monitoring MS or antibody-based methods), this approach offers a platform for discovery and development of novel biomarkers for risk and stratification. Linkage of proteomic data to electronic health records through safe haven health informatics allows the integration of complex molecular phenotyping with endotypic data. The proteomics platform also links to genomic data via an integrated information technology system. By combining discovery, validation and verification platforms with pathology, the time for biomarker discovery, validation, verification and adoption for clinical usage can be reduced for patient benefit.

Does epigenetics have a role in stratified medicine?

Professor Jon Mill, University of Exeter Medical School



Success in the identification of genetic variants that affect complex human phenotypes is one of the major achievements in contemporary biomedical research. Insight into the functional complexity of the genome also draws attention to the probable role of non-sequence-based genomic variation in health and disease. There is growing interest in the role of epigenetic processes that act to developmentally regulate gene expression via modifications to DNA, histone proteins, and chromatin. Although the role of epigenetic mechanisms in some rare developmental syndromes and in cancer is well established, systematic examination of their contribution to common non-malignant disease phenotypes is only just beginning.

I will present on-going work from our group aimed at identifying epigenetic variation associated with a diverse range of neuropsychiatric and neurodegenerative disorders. Novel tools mean that it is now feasible to examine epigenetic variation across the genome in large numbers of samples, and I will give an overview of our recent epigenome-wide association studies (EWAS) of schizophrenia and Alzheimer's disease, integrating findings with those from the recent GWAS analyses. I will also describe the impact of genetic variation on the epigenome, highlighting the utility of taking an integrated genomics approach to understanding disease and the potential utility of these approaches in stratified medicine.

Finally, I will outline some of the issues related to epigenetic epidemiological studies of disease and explore the feasibility of identifying peripheral biomarkers of disease phenotypes manifest in inaccessible tissues such as the brain.

Summary of Presentations

Session 4: Chair Dr Hilary Burton

Health economics of stratified medicine

Professor Dyfrig Hughes, Bangor University



Health economic evaluations are central to decisions on the availability of new treatments and other healthcare interventions in several jurisdictions worldwide. Health technologies are not approved for use in the UK if they are considered to represent poor value for money, that is, if their cost-effectiveness exceeds around £30,000 per quality-adjusted life-year. Personalised medicine, in which treatments are prescribed according to patients' characteristics, holds promise for more favourable health outcomes. However, as pharmaceutical market shares are potentially reduced as a consequence, there is uncertainty as to whether the compensatory price adjustments result in cost-effective treatment strategies. It is necessary, therefore, to conduct stratified cost-effectiveness analyses of treatments based on prognostic factors that reveal populations in which treatments are most likely to be effective or less likely to be harmful.

The cost-effectiveness of pre-prescription genotyping is illustrated using a series of case studies: (i) HLA-B*57:01 testing, which has dramatically reduced the incidence of hypersensitivity reactions to abacavir in patients with HIV; (ii) VKORC1 and CYP2C9 genotyping to guide dose selection with warfarin; (iii) HLA-A*31:01 testing for the reduction in the incidence of carbamazepine-induced cutaneous adverse drug reactions; and (iv) CYP2C19 testing prior to clopidogrel treatment in patients with acute coronary syndrome. With the exception of abacavir, a specific limitation of these analyses, which introduces considerable uncertainty to the estimation of cost-effectiveness, relates to the evidential standards for demonstration of the clinical effectiveness of tests.

A patient perspective of stratified medicine

Alastair Kent, Genetic Alliance



While the rhetoric of personalised medicine is attractive - who would argue with "the right dose for the right patient at the right time" - the present reality is some way from this for most patients. In this talk I will outline how involving patients and their families from the very earliest stages of therapy development will help make this into more of a reality. Patient engagement creates a focus on the things that matter, not just the things that can be counted. It allows for more efficient and more appropriate development programmes and increases the likelihood of patient access when the outcome is successful."

Biographies

Organisational Chair

Professor Sir Munir Pirmohamed



Chair of the UK Pharmacogenetics and Stratified Medicine Network, David Weatherall Chair in Medicine at the University of Liverpool, and a Consultant Physician at the Royal Liverpool University Hospital, Associate Executive Pro Vice Chancellor for Clinical Research for the Faculty of Health and Life Sciences.

Professor Sir Munir Pirmohamed holds the only NHS Chair of Pharmacogenetics in the UK, and is Director of the M.R.C. Centre for Drug Safety Sciences, Director of the Wolfson Centre for Personalised Medicine and Executive Director, Liverpool Health Partners.

Munir was awarded a Knights Bachelor in the Queen's Birthday Honours list in 2015. He is an inaugural NIHR Senior Investigator, a Fellow of the Academy of Medical Sciences in the UK and also a Commissioner on Human Medicines. His research focuses on personalised medicine in order to optimise drug efficacy and minimise toxicity, move discoveries from the lab to the clinic, and from clinic to application. He has authored over 380 peer-reviewed publications, and has an H-index of 78.

Biographies

Session Chairs

Dr Louise Leong



Louise Leong is Director Science Relations in Global Corporate Affairs at AstraZeneca, with focus on Europe /UK. Her career spans the life science sector across research and policy in academia, private foundation, and industry. Before joining AstraZeneca in October 2014, Louise was Director of R&D Policy and on the Senior Leadership Team at the ABPI (Association of the British Pharmaceutical Industry), where she ensured that a leading environment was maintained in the UK for the discovery and development of new innovative medicines, including co-creation of the Life Science Strategy, and initiation of a pan-UK strategy in Stratified Medicine.

Professor Joanne Hackett



Joanne joined the Precision Medicine Catapult in October 2016 to help build a world-leading, UK-based, precision medicine industry. Previously, Joanne has been actively involved in clinical research for over 15 years in Canada, America, Germany, Sweden and the UK. An accomplished entrepreneur, scientist and strategist, she has experience in the execution and management of complex business transactions, as well as broad business development experience in negotiation, execution and management of hundreds of transactions with pharma, biotech, academia and non-profit organisations.

For further information about the Precision Medicine Catapult visit <https://pm.catapult.org.uk/>

Biographies

Session Chairs

Dr Hilary Burton



Dr Hilary Burton is a Fellow of Hughes Hall, Cambridge and one of the founder members of the PHG Foundation, which is a not for profit organisation with a special focus on how genomic and other technologies can provide more effective personalised healthcare and improve population health (www.phgfoundation.org/). Qualified in medicine at Oxford University, Hilary subsequently trained in public health in the Eastern Region and worked as a consultant in Cambridge.

Since 1997 at the PHG Foundation Hilary has focused on the genomics context for population health, and, in particular, has led national work on the implementation of new technologies in mainstream UK health services. As a member of the Joint Committee on Medical Genetics, she was the main author of a report looking at the service implications of introducing genomics across a wide range of clinical specialties. In pursuing this further she is currently chair of a national RCP Steering Group, which aims to promote increased awareness and competence in genomics amongst UK physicians.

Hilary has also written about the importance of genomic technologies in enabling personalised healthcare and prevention. In 2011/2 she sat on the UK Government Human Genomics Strategy Group and is currently a member of the UK Genetic Testing Network Clinical and Scientific Advisory Group and the Joint Committee on Genomic Medicine of the Medical Royal Colleges.

Biographies of Speakers

Session 1

Professor Tim Hubbard



Professor Tim Hubbard is Head of the Department of Medical & Molecular Genetics at King's College London and Director of Bioinformatics for King's Health Partners. He is also Head of Genome Analysis at Genomics England, the company set up by the Department of Health to execute the 100,000 genomes project, which aims to mainstream the use of whole genome sequence analysis for treatment in the UK National Health Service (NHS).

Until 2013 he was Head of Informatics at the Wellcome Trust Sanger Institute where he was one of the organisers of the sequencing of the human genome.

In 1999 he co-founded the Ensembl project to analysis, organise and provide access to the human genome and from 2007 led the GENCODE project to annotate the structure of all human genes. He is also actively involved in efforts to improve data sharing in science and develop open access publishing resources.

He is a member of the cross funding agency Expert Advisory Board on Data Access (EAGDA) and is chair of the Advisory Board of Europe PubMedCentral.

Biographies of Speakers

Session 1

Professor Sue Hill

Chief Scientific Officer for England



Professor Sue Hill OBE PhD DSc CBIol FSB Hon FRCP Hon FRCPath is not only the Chief Scientific Officer for England but is also the head of profession for the 50,000 healthcare science workforce in the NHS and associated bodies – embracing more than 50 separate scientific specialisms. She is a respiratory scientist by background with an international academic and clinical research reputation.

Professor Hill has a broad portfolio of policy responsibilities across NHS England and the wider NHS and provides professional leadership and expert clinical advice across the whole health and care system. In particular, Sue is the Senior Responsible Officer for Genomics in NHS England, leading the establishment and assurance of the NHS Genomic Medicine Centres in delivering the commitment to the 100,000 Genomes Project and planning for the future. Sue is now leading the NHS England approach to Personalised Medicine strategy and also provides clinical leadership to the Health Education England Genomics Education Programme.

A significant part of her role involves working across government, with the Department of Health, with the NHS, Public Health and Health Education England and other external stakeholders to inform policy, influence legislation, deliver strategic change, and to introduce new and innovative ways of working.

Biographies of Speakers

Session 1

Professor Andrew Morris

Chief Scientist, Scottish Government Health Directorate



Andrew Morris took up the position of Professor of Medicine and Director of the Usher Institute at the University of Edinburgh in August 2014, prior to this Andrew was Dean of Medicine at the University of Dundee.

He is seconded as Chief Scientist at the Scottish Government Health Directorate which supports and promotes high quality research aimed at improving the quality and cost-effectiveness of services offered by NHS Scotland and securing lasting improvements to the health of the people of Scotland.

Research interests span informatics and chronic diseases and he is Director of the Farr Institute in Scotland funded by the MRC and nine other funders and Convenor of the UK Health Informatics Research Network, representing a £39M investment in health informatics research.

Andrew was awarded the RD Lawrence Award by Diabetes UK in 2003 and the Arnold Bloom Lecture 2013, the Saltire Society Scottish Science Award in 2005 and is a Fellow of the Royal Society of Edinburgh, Scotland's national academy of science and letters, and Fellow of the Academy of Medical Sciences. In 2007 he co-founded Aridhia Informatics that now employs >70 people in Scotland and uses high performance computing and analytics in health care, with deployments in the UK, Middle East and Australasia.

Andrew is a Governor of the Health Foundation, a leading UK charity that supports quality improvement in healthcare. Andrew also chairs the Informatics Board at UCL Partners, London.

Biographies of Speakers

Session 2

Professor Ewan Pearson

Professor in Diabetic Medicine at the University of Dundee

Honorary Consultant in Diabetes and Endocrinology at Ninewells Hospital and Medical School in Dundee



Professor Pearson obtained his medical degree from the University of Cambridge School of Clinical Medicine, UK. He undertook a Wellcome Trust Clinical Training fellowship with Prof Andrew Hattersley at the University of Exeter Medical School, UK and completed his PhD in the physiology and treatment of monogenic diabetes.

His research interests are the phenotypic and genotypic determinants of drug response and drug side effects, the aetiology of young-onset diabetes and the mechanisms driving progression of diabetes.

He is the academic lead on the €46M IMI-DIRECT project on stratification in Type 2 diabetes and is Strand 2 lead on the £6M MRC funded MASTERMIND project. Professor Pearson's New Investigator Award funding by the Wellcome Trust aims to gain deeper phenotypic, physiological and molecular insights into the mechanism of action of metformin and other diabetes drugs and how patients respond differently and experience different side effects to these agents.

Biographies of Speakers

Session 2

Doctor Mark Higgins

Senior Medical Director, Cystic Fibrosis Vertex Pharmaceuticals



Mark currently works for Vertex Pharmaceuticals. For the last 4 years at Vertex, he has been involved in the clinical development of 2 new drug classes designed to address specific mutations in the Cystic Fibrosis Transmembrane Conductance Protein. These drugs are designed to work on specific genotypes within Cystic Fibrosis and have now been globally approved.

Mark trained in medicine in the UK and worked in the NHS for a number of years before taking on a role in pharmaceutical market research and then joining Novartis to work on competitive intelligence, strategy development and then clinical development of a novel once daily bronchodilator and a dry powder inhaled formulation of tobramycin.

Biographies of Speakers

Session 3

Professor Elaine Holmes

Head of Division of Computational and Systems Medicine, Professor of Chemical Biology, Imperial College London



Professor Holmes' main research area focuses on applying metabolic profiling and computational modelling of biofluids and tissues to understand pathological and physiological processes. She has a broad background in metabolic chemistry, with specific expertise in spectroscopy and in chemometric modelling of spectral data. She began her research career investigating molecular mechanisms of toxicology using spectroscopic methods and then broadened the scope to research clinical pathologies in a range of clinical fields.

Professor Holmes has particular interest in investigating the consequences of modification of the gut microbiota which involves both the development and application of spectroscopic and chemometric methods, and in particular the fusion of metagenomic and metabonomic data to provide a readout of the functionality of the microbiome.

In 2015, Professor Holmes was awarded the Interdisciplinary Prize Medal by the Royal Society of Chemistry and 2016 Analytical Science Power List - Top 50 most influential women. Prof Holmes has an H-index of 87 and is an ISI Highly Cited Researcher (Pharmacology 2014). She has trained over 60 PhD students.

Biographies of Speakers

Session 3

Professor Anthony Whetton

Director, Stoller Centre for Biomarker Discovery

Director, Manchester Precision Medicine Institute

Principal Investigator, Bloodwise Mass Spectrometry programme, Wolfson Molecular Imaging Centre, Christie Hospital



Professor Whetton joined the School of Medicine at Manchester University in 2003 as Professor of Cancer Cell Biology, based at the Christie Hospital. Here he established a state of the art biological mass spectrometry facility for stem cell and cancer research. This platform has been extended into biomarker research for precision medicine in recent years.

In his leukaemia research Tony is currently systematically defining the downstream proteomic and phosphoproteomic effects of the protein tyrosine kinases associated with myeloproliferative disorders and myeloid leukaemias to discover common mechanisms for leukaemic transformation and thus new drug targets. This has led to a new approach to extinguish chronic myeloid leukaemia stem cells. He has built a new £3 million laboratory to house the Stoller Biomarker Discovery Centre which has £25 million of funding to date and opened in June 2016. As Director of the Manchester Precision Medicine Institute Tony Whetton leads on enabling University of Manchester researchers, clinicians and industry to work together for improving clinical outcomes.

Biographies of Speakers

Session 3

Professor Jonathan Mill

Professor of Epigenetics at the University of Exeter Medical School



Jonathan graduated with a degree in Human Sciences from Oxford University, where he took a particular interest in cannibalism, before undertaking his PhD in Psychiatric Genetics at the Institute of Psychiatry.

After spending three years as a Canadian Institutes of Health Research (CIHR) postdoctoral fellow at the University of Toronto, he returned to the Institute of Psychiatry to establish the Psychiatric Epigenetics group in the MRC Social, Genetic and Developmental Psychiatry Centre. He joined the University of Exeter Medical School in 2012.

Jonathan's group studies the role of epigenetic processes in complex disease, with a particular emphasis on neurodegenerative and neuropsychiatric disorders. Current areas of research include: 1) regulatory genomic profiling in post-mortem brain tissue (autism, schizophrenia, depression, and dementia); 2) investigating the role of epigenetic variation in mediating phenotypic/disease discordance between genetically-identical individuals; 3) describing dynamic genomic processes in human brain development and aging; and 4) exploring interactions between the epigenome, environment and DNA sequence variation, with the aim of undertaking an integrated genetic-epigenetic approach to disease. More information on their work can be found at www.epigenomicslab.com.

Biographies of Speakers

Session 4

Professor Dyfrig Hughes

Co-Director of Centre for Health Economics & Medicines Evaluation, Bangor University

Honorary Professor, Dept of Molecular and Clinical Pharmacology, University of Liverpool



Dyfrig graduated in pharmacy before undertaking a PhD in cardiovascular pharmacology. He subsequently re-trained in health economics, and is currently Professor of Pharmacoeconomics and co-director of the Centre for Health Economics and Medicines Evaluation at Bangor University. He is also academic lead for Pharmacy and Medicines Management at the Betsi Cadwaladr University Health Board, and is honorary professor at the Department of Molecular and Clinical Pharmacology, University of Liverpool.

He has led the pharmacoeconomic activities of the All Wales Therapeutics and Toxicology Centre, contributing to over 200 substantive HTA reports. He was inaugural president of the European Society for Patient Adherence, Compliance and Persistence (ESPACOMP) and was elected fellow of: the Learned Society of Wales, the British Pharmacological Society, and the Faculty of the Royal Pharmaceutical Society.

His main research activities, which have led to over 120 publications, concern the economics of medicines and pharmacogenetics, pharmaceutical policy, health technology assessment and medication adherence. He is editorial board member of the journals *Pharmacoeconomics* and *Clinical Pharmacology & Therapeutics*.

Biographies of Speakers

Session 4

Alastair Kent OBE

Director, Genetic Alliance UK



Alastair came to Genetic Alliance UK over 20 years ago because he was excited by the challenge that new knowledge in genetics created - the idea that, for people affected by a genetic condition, yesterday's science fiction is tomorrow's clinical service improvement. Trying to transform these possibilities into positive outcomes whilst reducing the potential for abuse is an incredible challenge, and Alastair feels incredibly privileged to work in this field.

The fact that Genetic Alliance UK is now a respected and authoritative voice for patients and families is something that provides him with a feeling pride, and also a huge sense of responsibility. It is a challenge that excited him on the first day he became aware of the impact of genetic disorders and which continues to excite him today.

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Leicester Precision Medicine Institute



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The Leicester Precision Medicine Institute (LPMI) aims to be the UK Precision Medicine Accelerator from Discovery to Implementation. As a Centre of Excellence, we develop, evaluate and implement treatments and patient care pathways that are based on the characteristics of individuals and subgroups of the population to provide more targeted, effective and safer healthcare that will improve the health outcomes of our diverse population.

Our ambition is to deliver world-class research and enterprise activities in support of diagnostics, targeted drugs and personalised therapy across our portfolio of biological, clinical and health-related disciplines. At Leicester, we deliver Precision Medicine by coalescing and aligning the research missions of the University of Leicester and University Hospitals of Leicester NHS Trust.

We aim to create an aspirational discovery-led culture and discovery-enabling environment that supports people, and encourages and rewards innovation, collaboration and productivity across disciplines. Web: www2.le.ac.uk/institutes/lpmi/leicester-precision-medicine-institute

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- Drug Development
- Biomarkers and Diagnostics
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NIHR-CRN

The NIHR Clinical Research Network Coordinating Centre manages the Clinical Research Network (CRN) on behalf of the Department of Health. The CRN makes it possible for patients and health professionals across England to participate in clinical research studies within the NHS. The CRN provides the infrastructure that allows high-quality clinical research funded by charities, research funders and life-sciences industry to be undertaken throughout the NHS. We work with patients and the public to make sure their needs are placed at the heart of all research, and providing opportunities for patients to gain earlier access to new and better treatments through research participation.



National Institute for Health Research

The NIHR Clinical Research Network Coordinating Centre (CRNCC) is hosted jointly by Guy's and St Thomas' NHS Foundation Trust and the University of Leeds, supported by a wider partnership which also includes King's College London, Imperial College London, Newcastle University, and the University of Liverpool.

The CRNCC enables the CRN to support around 5000 clinical research studies each year. The collection of all studies we support is the CRN Portfolio. The CRN meets the costs of NHS staff that support research and provides specialist training so that patients can be confident that research is being delivered by trained, experienced front-line NHS staff. We also meet the costs of using NHS facilities, such as scanners and x-rays that are needed in the course of a study, so that research is not subsidised with funding that has been provided for patient care. We provide practical help in identifying and recruiting patients for Portfolio studies, so that researchers can be confident of completing the study on time and as planned.

Thank you to our sponsors

The Clinical Research Network is made up of 15 Local Clinical Research Networks that cover the length and breadth of England. The CRN delivers research across 30 clinical specialties at a national and local level. Further details of the CRN can be found at www.nihr.ac.uk

The CRN is working in partnership with the University of Liverpool and the UK Pharmacogenetics and Stratified Medicine Network (UKPSMN) to explore ways to improve the delivery of stratified medicine studies on the CRN Portfolio, and further details of this work is available on the CRN stand at the UKPSMN Annual Meeting.

Northern Ireland Centre for Stratified Medicine



The Centre is based in the Clinical Translational Research and Innovation Centre (C-TRIC) on the Altnagelvin Hospital site in Derry/Londonderry.

The Centre was established in Autumn 2013 following an award of £11.5M (from European Union Regional Development Fund (ERDF) EU Sustainable Competitiveness Programme for Northern Ireland, Invest NI, the Northern Ireland Public Health Agency (HSC R&D), ILEX & Ulster University) to Professor Tony Bjourson (Director). The Centre aims to identify how our genes or patterns in levels and state of molecules within our bodies, or subtle differences in medical images, could be used to create robust clinical decision making tests for a range of degenerative diseases.

This centre brings together academic staff, PhD students and NHS Clinicians affiliated to our Research centre; linking General Practitioners (GPs) and NHS Health Trusts (predominantly from the Western Health & Social care Trust at Altnagelvin Hospital).

Thank you to our sponsors

Tissue Solutions



Tissue Solutions is a leading provider of human biospecimens used in labs throughout the world. We work with more than 120 sources globally to provide high quality, ethically sourced tissues and biofluids for drug discovery, diagnostics development and safety testing. We can provide access to banked human samples and set up prospective collections in the UK, mainland Europe and USA.

Oncology: Tissue, bio-fluids, PBMCs, RNADNA from a wide range of tumour types including breast, pancreas, prostate, uterine, glioblastoma, melanoma, head and neck, bladder, liver, kidney, lung, ovary, thyroid, stomach, lymphoma & leukemias.

Metabolic: Diabetic pancreas, human pancreatic islets, adipose tissue, adipocytes, primary human skeletal muscle cells, human hepatocytes, skeletal muscle (normal/diabetic), diabetic kidney, chronic kidney disease samples.

Autoimmune disorders: MS, Rheumatoid Arthritis (synovium, synovial fluid, cartilage) IBD (ileum, colon), autoimmune disease plasma (available in bulk as well as small volumes).

CNS/Neurodegenerative: Tissue, CSF and plasma/serum from Alzheimer's, Parkinson's, schizophrenia, Huntington's disease depression, brain

tumours. All brain regions are available (e.g. amygdala, BA24, caudate nucleus, entorhinal cortex, cerebral cortex, hippocampus etc. and also spinal cord) with or without tangles, plaque and Lewy bodies.

Inflammation: osteoarthritis, RA (synovial fluid, synovium, cartilage), asthma, COPD, psoriatic skin/blood samples from psoriasis patients, nasal polyps, tonsils, spleen, COPD lung tissue (tissue, blood/serum/plasma, PBMCs, RNA).

Cardiovascular: PAOD, atrial appendage, valves, HUVECs, carotid with atherosclerotic plaque from non-diabetic/diabetic donors, coronary artery (MI donor/control donor).

Blood Disorders: bone marrow, bloods and PBMCs from various leukaemia's and multiple myeloma, polycythemia blood samples.

Thank you to our sponsors

UK Biocentre



The NIHR National Biosample Centre (NIHR-NBC) has been established in Milton Keynes and Oxford to provide a high quality, high capacity service for biomedical researchers engaged in studies that include the collection, processing, storage and analysis of biological samples from their volunteers and patients. This centre of excellence with its high capacity and high quality systems supports both national level and individual Investigator led projects providing a cost-effective, secure and responsive service. Extensive use of automation ensures speed and accuracy of processing, a robust and secure data trail and efficient archiving and retrieval of samples.

NIHR-NBC offers fully automated processing and aliquotting of blood, urine, saliva, solid tissue – up to 2,000 primary samples per day. It has the capacity to store 20 million 1.2ml cryovials in fully automated -80°C and -20°C archives. A recent addition is its ability to support at scale DNA extraction from up to 1,000 samples per day. NIHR-NBC supports the needs of both academic/NHS research as well as those of the commercial sector. NIHR-NBC is a not for profit business investing its revenues in growing its capabilities.

For further details please contact Kris Speckley Commercial Manager
Kristian.Spreckley@ukbiocentre.com

Organisational Blogs

Metabolomics as a Blueprint of Health



METABOLON[®]

Where **knowing** comes to **life**[™]

Precision medicine is at the heart of health care providers' goals to improve health, diagnoses and treatment. The key to advancing precision medicine lies in first creating a blueprint of human health. Metabolon is embracing this challenge.

While genomics is undeniably important in creating the precision medicine blueprint, many initiatives recognize the need to include other types of data in addition to medical records and standard clinical assessment. The last decade of genomics research has revealed higher than anticipated individual genetic variation. In addition, most traits of interest involve a combination of many genes^{1,2} and the majority of mutations reside in non-coding regions of the genome, where we have a poor understanding of function³. Massive amounts of data must be managed before consensus and actionable data can be effectively mined, as illustrated by a recent whole genome sequencing initiative published in JAMA^{5,6}. Elusive influences such as the microbiome⁴ and epigenetics are clearly important also. Thus, many genomics investigators seek additional data types.

Metabolomics is becoming a core element in defining the blueprint of human health. The reason for its inclusion is simple, metabolites are central to the health state, and they reflect the combined impact of factors such as genetics and external influences like diet and lifestyle. The metabolic state offers an intimate assessment of an individual's state of health as it is at the time a sample is provided. Metabolomics measures all of the metabolites within metabolic pathways. This is a critical reason why a growing number of large precision medicine and next-generation sequencing (NGS) initiatives have adopted metabolomics as a cornerstone of their programs to link genetics plus metabolic profiles to phenotypes or health states.

Some of the challenges of genomics are alleviated by metabolomics by identifying genes that are effectively “active” and then creating a functional connection between the gene and the health state. This has been demonstrated for a variety of traits in fairly healthy populations^{7,8} and profoundly illustrated in more severe genetic states^{9,10}. PNAS recently published a study conducted by Metabolon and Baylor College of Medicine, which combined the functional measurement of metabolomics with whole exome sequencing (WES) of individual subjects¹¹. Metabolon’s technology successfully spotted underlying health issues that were previously undetected or not highlighted in the genetic data, illustrating that information derived from metabolomics was more precise than genetic information.

There is growing appreciation that complex illnesses such as diabetes, cancer, cardiovascular and neurological diseases are caused by a combination of genetic and non-genetic factors. Clinicians must take into account the impact of these factors to make an informed diagnosis. Metabolomics reflects the influences of genes, diet, lifestyle, environment and xenobiotics to aid in understanding gene function and how diseases originate. It also provides the biomarkers for health assessment and customized therapy.

Metabolomics has emerged as a powerful technology for precision medicine by dissecting underlying disease processes. This may set the stage for new ways to diagnose, monitor and provide guidance for treatment.

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Organisational Blogs

Lancashire Clinical Research Facility



LANCASHIRE

Clinical Research Facility

Uniquely the facility is a partnership between Lancashire Teaching Hospitals NHS Foundation Trust, Lancashire Care NHS Foundation Trust and Lancaster University which brings together both physical and mental health research expertise. Our aims and key objectives are to provide a dedicated CRF to increase availability of experimental and early phase studies to our local population particularly within with our key priority areas of Oncology, Dementia and Neurosciences.

The facility has a variety of room spaces catering for all types of experimental medicine clinical trials, including an overnight room with a dedicated wet room and ceiling hoist. We have an in house sample processing room and a pharmacy dispensary to facilitate the smooth running of clinical trials and an extensive range of modern medical equipment and technology designed to maintain a high level of patient safety. We employ a team of highly specialised professionals to ensure complex, clinical trials are delivered to a very high standard. We are keen to collaborate and host studies from academia, pharmaceutical partners and other research active organisations.

Please contact us for information. <http://www.lancsteachinghospitals.nhs.uk/lancscrf>

Open Meeting Attendees

First Name	Surname	Organisation	First Name	Surname	Organisation
Brandon	Adams	Metabolon	Clive	Bowman	C4X Discovery Ltd
Tariq	Ahmad	Exeter IBD and PGx Research Group	Alan	Boyd	Faculty of Pharmaceutical Medicine
Lucille	Alexander	Event Sponsor	Katherine	Boylan	MMPATHIC
Yvonne	Alexander	Manchester Metropolitan University	William	Bradlow	University Hospital Birmingham
Anwar	Alhaq	King's College Hospital	Julian	Bradwell	Congenica
Mariam	Ali	MHRA	Elvira	Bramon	UCL
Sharon	Alldrick	Quintiles	Philippa	Brice	PHG Foundation
Nuno	Alves	Stevenage Bioscience Catalyst	Helen	Bulbeck	Brainstrust
Wilma	Anderson	Tissue Solutions	David	Burnett	Micropathology Ltd.
Toby	Athersuch	Imperial College London	Mike	Burrows	GMAHSN
Sarah	Atkinson	NI Centre for Stratified Medicine	Hilary	Burton	Session Chair
Chiara	Bacchelli	Institute of Child Health	Rachel	Butler	All Wales Laboratory Genetics
Sarah	Ball	Micropathology Ltd.	Archie	Campbell	Generation Scotland
Amitava	Banerjee	Farr Institute	Ian	Campbell	Steering Committee
Rodrigo	Barnes	Aridhia Informatics	Dan	Carr	University of Liverpool
Nanette	Bartram	AgPlus Diagnostics	Fiona	Carragher	NHS England
Philip	Beales	Congenica	Tony	Carter	Olink Bioscience
Jane	Beety	NIHR	David	Cavalla	Numedicus Ltd
Mark	Beggs	UK Biocentre	Chris	Chamberlain	Steering Committee
Andreas	Bender	Healz Ltd.	Michael	Chambers	MC Healthcare Evaluation
Michael	Beresford	NIHR CRN	Chris	Chinn	Sanofi
Julie	Bertrand	UCL Genetics Institute	Glen	Clack	University of Sheffield
Claire	Bewshea	Exeter IBD and PGx Research Group	Virginia	Clowes	NHS
Dhiren	Bhatt	myDNA	John	Connolly	Imperial College London
Eddie	Blair	Bristol Myers Squibb Pharma Ltd	Jane	Coppard	Roche
Stephane	Bourgeois	Queen Mary University of London	Sarah	Coupland	University of Liverpool
Janet	Boutell	University of Glasgow	Giles	Courtice	Technologia
Will	Bowen	HRA	Jane	Cowl	NICE

First Name	Surname	Organisation	First Name	Surname	Organisation
Charles	Cox	GlaxoSmithKline	Neil	Goddard	Agena Bioscience
Tim	Cullingford	MRC	Michael	Griffiths	West Midlands Regional Genetics Lab
Julie	Cunningham	CRN SWP	Joanne	Hackett	Session Chair
Alison	Currie	WG Consulting	Audrey	Hamachila	University of Liverpool
Michael	Dalrymple	MRC Technology	Peter	Hamilton	Philips Digital Pathology Hub
Ann	Daly	Steering Committee	Toby	Hampshire	ParaDNA
Robert	Davey	Aridhia Informatics Ltd	Oliver	Hanemann	Plymouth University
Morell	David	Lewis David Consulting	Shahid	Hanif	Steering Committee
Andrea	Davies	University of Liverpool	Shirley	Hannan	NHSA
Mark	Davies	QT Informatics Ltd	Anita	Hanson	Wolfson Centre for Personalised Medicine
Andrew	Davison	RLBUHT	Alison	Hargreaves	Qiagen Applied & Clinical Genomics
Vanessa	Dekou	Tassi & Co. Limited	Jen	Harrison	HRA
Sally	Dews	Pfizer Ltd	Darren	Harvey	Rela8
Liberty	Dixon	Academy of Medical Sciences	Rob	Hastings	Precision Medicine Catapult
Benjamin	Dizier	UCB Biopharma	Oliver	Hatley	Simcyp (Certara)
Paul	Docherty	Tepnel, Hologic Gen-Probe	Marie	Hatton	NIHR CRN
Karla	Duarte	NIHR	Dan	Hawcutt	University of Liverpool
Nicholas	Duggan	Cellesce	Simon	Haworth	Dynasty Bio
Michael	Dunn	Steering Committee	Tanya	Heare	Cooley (UK) LLP
Daryl	Fernandes	Ludger	Kirsty	Henderson	CRUK
Lorraine	Fincham	NIHR CRN	Alexander	Henzing	KTN
Gail	Fitzgerald	RLBUHT	Christopher	Herbert	University of Leeds
Vanessa	Fontana	University of Liverpool	Daniel	Hickmore	Arkivum
Ben	Francis	University of Liverpool	Nick	Hicks	NETSCC
Guoliang	Fu	Genefirst	Mark	Higgins	Speaker
Mike	Furness	DNAnexus	Rebecca	Higgins	University of Liverpool
Helen	Gallagher	University College Dublin	Sue	Hill	Speaker
Ros	Ganderton	University Hospital Southampton	Steve	Hillier	University of Liverpool
Steve	Gardner	Row Analytics	Karen	Hodgson	IoPPN, KCL
Alasdair	Gaw	LPMI	Elaine	Holmes	Speaker
Paul	Gibson	Rela8	Cathy	Holt	University of Manchester
Rose	Gilbert	UCL	Shirley	Hopper	MHRA
Kylie	Glanville	KCL	Martin	Hornshaw	Metabolon

First Name	Surname	Organisation	First Name	Surname	Organisation
Emma	Howard	Liverpool Womens Hospital	Anthony	Marinaki	Purine Research Laboratory, Viapath
Martin	Howell	NHS Blood and Transplant	Sancha	Martin	Wolfson Wohl Cancer Research Centre
Tim	Hubbard	Speaker	Aoibhinn	McDonnell	Pfizer Ltd
Chris	Hudson	Roche Diagnostics	Anne	McDonough	McDonough Clinical Research Ltd
Dyfrig	Hughes	Speaker	Derek	McFerran	Tissue Solutions
Bruce	Humphrey	University of Manchester	John	McKinley	Caldwell Capital Limited
Ed	Hutchinson	Scottish Enterprise	Christine	McNamee	Network Manager
Peter	Jacobs	Clinical Business Development EMEA	Liz	Mear	Innovation Agency
Sean	James	100,000 Genome Project	Ioannis	Melas	UCB
Janusz	Jankowski	UCLAN	Anna	Milan	RLBUHT
Robert	Johnstone	European Patients Forum	Hanna	Milewicz	NIHR
Amy	Jones	Cambridge University Hospital	Jonathan	Mill	Speaker
Stephanie	Jones	Royal Pharmaceutical Society	Iain	Miller	Healthcare Strategies Group
Marika	Kaakinen	Imperial College London	Ken	Mills	CCRCB
Martina	Kaufmann	Martina Kaufmann Strategic Consulting	Alex	Milsom	NHS England
Nick	Kennedy	Institute of Child Health	Mariam	Molokhia	KCL
Janna	Kenny	Institute of Child Health	Catherine	Morlet	CMPM Ltd
Alastair	Kent	Speaker	Andrew	Morris	Speaker
Patrick	Keohane	benevolent.ai	Vikki	Moye	University of Exeter Medical School
James	Knowles	Agena Bioscience	Hussain	Mulla	University Hospitals of Leicester
Felix	Kruger	benevolent.ai	Daniel	Murphy	SASH NHS Trust
Dhavendra	Kumar	University Hospital of Wales	Kay	Murphy	GlaxoSmithKline
Dawn	Lawson	Yorkshire & Humber AHSN	Elaine	Murray	NI Centre for Stratified Medicine
Nadier	Lawson	SJS Awareness	Nisha	Nair	University of Manchester
Andrew	Leary	Regengold	Nic	Namur	Somalogic
Louise	Leong	Session Chair	Stephen	Newhouse	KCL
Cathryn	Lewis	KCL	Clare	Newland	Steering Committee
Julia	Li	Seven Bridges Genomics	Ian	Nickson	NIHR CRN
Margaret	Little	RLBUHT	Nick	Noakes	Global Engage
Sine	Littlewood	NIHR CRN	Brendan	Norman	University of Liverpool
Kath	Mackay	Innovate UK	Anna	Olsson-Brown	University of Liverpool
Cathy	MacLean	UCL	Terry	O'Neill	Steering Committee
Hannah	Mahoney	Terrapinn	Charlie	Orton	Alder Hey Children's Hospital

First Name	Surname	Organisation	First Name	Surname	Organisation
John	Overington	Stratified Medical	Harsh	Sheth	Newcastle University
Sandosh	Padmanabhan	University of Glasgow	Alastair	Smith	Myriad RBM
MariaBeatrice	Panico	MHRA	Catherine	Smith	KCL
Marie-Claire	Parker	SMSIC	Kristian	Speckley	UK Biocentre
Alison	Parry-Jones	Wales Cancer Bank	Charles	Steward	Congenica
Hasi	Patel	Bluebee	Marni	Stott-Miller	GlaxoSmithKline
Colin	Pavelin	Steering Committee	Andrew	Sutton	University of Leeds
Ewan	Pearson	Speaker	Karra	Swinbank	NHS Blood and Transplant
Diana	Pendicheva	Medical University, Pleven	Xavier	Tait	Olink Proteomics
Caroline	Pickstone	NIHR	Euvian	Tan	Profiscio
Jacqui	Pirmohamed	NIHR CRN	Zahid	Tharia	Pistoia Alliance, Inc.
Munir	Pirmohamed	Event Chair	Natasha	Tian	Queen Mary University of London
Richard	Pither	Cytox Ltd	Paul	Townsend	University of Manchester
Vanessa	Poustie	NIHR CRN	Adrian	Towse	Office of Health Economics
Krishna	Prasad	Steering Committee	Laura	Turner	NIHR BRC
Clare	Prince	RLBUHT	Richard	Turner	University of Liverpool
Sudeep	Pushpakom	University of Liverpool	Paula	Underhill	NIHR CRN
Nadeem	Qureshi	University of Nottingham	Mark	Upton	
Shaleenah	Ramjan	MHRA	Ron	Van Schaik	Erasmus University Medical Centre
Anne	Reiman	University of Warwick	Moira	Verbelen	KCL
Diana	Robinson	Independent Cancer Patients' Voice	Gareth	Walker	Exeter IBD and PGx Research Group
Jessica	Robinson	Terrapinn	James	Walters	MRC CNGG
Ana	Rodriguez	University of Liverpool	Andrew	Wardley	NIHR CRUK CRF
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Sam	Rowley	MRC	Simon	Wells	LGC Ltd
Giusy	Russomanno	Imperial College London	Stephen	Weng	University of Nottingham
Gurdeep	Sagoo	University of Leeds	Tony	Whetton	Speaker
Sam	Samaratunga		Doris-Ann	Williams	Steering Committee
Felicity	Sartain	Profiscio	Hywel	Williams	Institute of Child Health
Laura	Sato	HSCIC	John	Williams	Birmingham Health Partners
Andy	Shakeshaft	Innovation Agency	Lindsay	Wilson	MRC
Saad	Shakir	Drug Safety Research Unit	Hakim	Yadi	NHSA
Vishal	Sharma	RLBUHT	Eunice	Zhang	UKPGx Network



Notes



Notes



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Find out more



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Save the date!

Our 5th Annual Open Meeting will take
place in London on March 21st 2018

#UKPGx2018