THE GENOMIC MEDICINE
FOUNDATION PRESENTS

OXFORD VIRTUAL SYMPOSIUM "CLINICAL GENOMIC AND PRECISION MEDICINE"

11TH NOVEMBER 2020

CONFERENCE PACK

The Oxford Virtual Symposium 'Genomic and Precision Medicine' is brought to to by the Genomic Medicine Foundation

The Genomic Medicine Foundation (UK) is a registered non-profit corporate organization providing up to date and evidence-based information on all aspects of OMICS and Genomics relevant to the contemporary practice in clinical and preventive medicine and healthcare. The Foundation undertakes a number of professional activities including publishing books & journals, organizing dedicated educational conferences, seminars and symposia on genetics & genomics, advise and consultancy on genomic research projects and providing information to the lay public, press and media. The Foundation shares its objectives and works in partnership with several international genomics and biotechnological organisations for improving the global health and enhancing the socio-economic progress in many developing and less developed nations. For more information, please visit:

www.genomicmedicine.org

Our Agenda for Today

0900 Welcome/ Introduction
Dhavendra Kumar, Cardiff & London
0915 Key Note Lecture 1
Status of genomic medicine in NHS
Bill Newman, Manchester
0945 Session I: Genome diagnostics in clinical practice
Chair- Helen Stewart, Consultant Clinical Geneticist, Oxford, UK
0950 Clinical genome sequencing and variant interpretation
Sian Ellard, Exeter
1015 Mitochondrial genomics in clinical practice
Robert Taylor, Newcastle upon Tyne
1040 Whole genome sequencing in rare genetic diseases
Ellen Thomas, Genomics, London, England

Our Agenda for Today

1115 Coffee break
1125 Session II: Stratified and Precision Medicine
Chair: Patricia Munroe, Professor of
Molecular Medicine, QMUL, London,UK
1135 Cancer stratification for targeted molecular therapy
Rebecca Fitzgerald, Cambridge
1200 Pharmacogenetics in clinical practice- way forward
Sir Munir Pirmohamed, Liverpool
1225 Genomics in complex diseases- the model of Rheumatoid arthritis
Costantino Pitzalis, QMUL, London
1250 The 100000 Genomes Project transforming the NHS
Sir Mark Caulfield, QMUL, London
1300 Lunch

Our Agenda for Today

1430 Key note Lecture 2
Viral diagnostics & pathogenomics--lessons learnt from SARS-CoV2
Professor Ekta Gupta, ILBS, New Delhi, India
1430 Session III: Broader issues in genomic & precision medicine
Chair: Tessa Homfray, Consultant Clinical Geneticist, St. George's Hospital, London, UK
1435 Ethical ground rules in genomic and precision medicine
Tara Clancy, Manchester
1450 Harmonization in genomic and precision medicine
Ruth Chadwick, Leeds & Cardiff
1515 A health economic perspective on precision medicine
Sarah Wordsworth, Oxford

Our Agenda for Today

1540 Coffee/ Tea
1550 ‘Sir David Weatherall Oration”
Chair- Professor Doug Higgs, WIMM, University of Oxford
Professor Sir Stephen Patrick O’Rahilly, Cambridge
1650 Discussion/ Reflections/ Vote of Thanks
1700 Close

Speaker Profile

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

Accredited genetic and genomic clinician with special interests in clinical genetics and genomic medicine. Credited with landmark contributions and achievements in genetic-inherited diseases of children, hereditary familial conditions of heart and blood vessels, applications of novel genomic principles and technology in genomic-precision medicine and public and population health genomics. Founder and the Medical Director of The Genomic Medicine Foundation (UK) globally raising awareness and promoting genomic applications in medicine, healthcare and socio-economic benefits.

Speaker Profile

Professor Bill Newman

Bill Newman is a Consultant in Genomic Medicine and Professor of Translational Genomic Medicine at the Manchester Centre for Genomic Medicine, where he is the Clinical Head of Division. His diverse research interests include pharmacogenetics and the use of genomic technologies to identify novel causes of rare inherited disorders.He is the current chair of the NHS England Clinical Reference Group for Clinical Genomics which is tasked with the overall responsibility of ensuring that service specifications and clinical commissioning policies are delivered to a high quality standard.

Speaker Profile

Helen Stewart

HS is a consultant in clinical genetics, Oxford UK. She is currently training and education lead for the Oxford region, with a remit to roll out genomic education. She has expertise in the genetics of rare diseases.

Speaker Profile

Professor Sian Ellard

Sian is Professor of Genomic Medicine at the University of Exeter Medical School, Scientific Director for the South West Genomic Laboratory Hub and a Consultant Clinical Scientist at the Royal Devon and Exeter NHS Foundation Trust where she heads the Genomic Laboratory. She came to Exeter in 1995 to set up a Molecular Genetics Laboratory providing a core facility for integrated research and diagnostic genetic testing. The laboratory receives samples from >75 countries throughout the world and is acclaimed for both its research into monogenic disorders and the translation of its research discoveries into diagnostic service

Speaker Profile

Professor Robert Taylor

Rob Taylor is Professor of Mitochondrial Pathology at the Wellcome Centre for Mitochondrial Research, Newcastle University where he also leads the multidisciplinary NHS Highly Specialised Mitochondrial laboratory. He is Scientific Director of the Yorkshire and North East Genomic Laboratory Hub and co-chairs NHS England's Genomics Test Evaluation Working Group for Rare and Inherited Disease. His research focuses on mitochondrial gene discovery and understanding molecular disease mechanism, translating genomic innovation and discovery into clinical practice through improved diagnosis. His laboratory has contributed to the identification of >30 novel disease genes, publishing over 470 peer-reviewed scientific papers.

Speaker Profile

Ellen Thomas

Ellen Thomas is Clinical Lead for Rare Disease and Clinical Safety Officer at Genomics England, and a Consultant in Clinical Genetics at Guy's and St Thomas' NHS Trust. Her training included a PhD thesis at Imperial College, studying genetic factors contributing to monogenic and complex diseases using high-throughput sequencing. As part of the Genomics England Science Team led by Professor Sir Mark Caulfield, she has worked on delivery of the 100,000 Genomes Project, and now focuses primarily on Genomics England's contributions to the Genomic Medicine Service, as well as supporting the interface between research and clinical care for participants and researchers within the National Genomic Research Library.

Speaker Profile

Professor Sir Munir Pirmohamed (MB ChB, PhD, FRCPE, FRCP, FBPhS, FMedSci)

Professor Sir Munir Pirmohamed (MB ChB, PhD, FRCPE, FRCP, FBPhS, FMedSci) is David Weatherall Chair in Medicine at the University of Liverpool, and a Consultant Physician at the Royal Liverpool University Hospital. He is Director of the MRC Centre for Drug Safety Sciences, and Director of the Wolfson Centre for Personalised Medicine. He is also Director of HDR North. He is an inaugural NIHR Senior Investigator, Fellow of the Academy of Medical Sciences in the UK, Commissioner on Human Medicines and is a non-executive director of NHS England, and has been appointed as President of British Pharmacological Society . He was awarded a Knights Bachelor in the Queen's Birthday Honours in 2015. His research focuses on personalised medicine, clinical pharmacology and drug safety

Speaker Profile

Professor Costantino Pitzalis MD, PhD, FRCP

Costantino Pitzalis is Versus Arthritis (VA) Professor of Rheumatology at the William Harvey Research Institute (WHRI), Barts and The London School of Medicine and Dentistry Queen Mary University of London. His research interests focus on the cellular and molecular mechanisms of inflammation and autoimmunity in chronic rheumatic conditions particularly rheumatoid arthritis (RA). He leads a Research Team of approximately 50 Researchers (Clinicians and Scientists) and has published over 280 peer-reviewed papers in the field of inflammation, immunity and arthritis. He is the Chief Investigator of a comprehensive biopsy-driven stratified-medicine randomised clinical trials (RCTs) programme funded by MRC/VA and NIHR with the ultimate goal of the programme is the delineation of synovial specific signatures able to define a new taxonomy of disease. The aim is to integrate clinical and molecular pathology algorithms to more accurately predict prognosis and treatment response, towards precision medicine.

Speaker Profile

Professor Sir Mark Caulfield MD FRCP FESC
HonPharm FBHS FMedSci

Sir Mark Caulfield graduated in Medicine in 1984 from the London Hospital Medical College and trained in Clinical Pharmacology at St Bartholomew's Hospital where he developed a research programme in molecular genetics of hypertension, which has discovered over 1000 gene loci for blood pressure. He served on the NICE Guideline Group for hypertension and was President of the British Hypertension Society (2009-2011). He was Director of the William Harvey Research Institute between 2002 and 2020 and was elected a Fellow of the Academy of Medical Sciences in 2008. Since 2008 he directs the National Institute for Health Research Cardiovascular Biomedical Research Unit and Centre at Barts. Between 2010 and 2015 he co-led the merger of three hospitals in North London to create the new £400 million Barts Heart Centre. He has won the Lily Prize of the British Pharmacology Society, the Bjorn Folkow Award of the European Society of Hypertension 2016 and the Franz Volhard Award of the International Society of Hypertension in 2018.

Speaker Profile

Professor Ekta Gupta

Dr. Ekta Gupta is Professor and Head, Clinical Virology and nodal officer for WHO collaborative centre on Viral Hepatitis at the Institute of liver and Biliary Sciences. Dr. Ekta Gupta did her ,MBBS from GSVM Medical College, Kanpur in 1993 and MD Microbiology from KGMC Lucknow in 1998, Senior Residency from All India Institute of Medical Sciences (AIIMS), New Delhi and Senior Research Associateship in Clinical Virology from AIIMS, New Delhi. She has more than 22 years of experience in Clinical diagnostic Virology. Have more than 90 scientific publications in indexed National & International Journals and author of 9 chapters in books. She has to her credit several extramural research grants both at National and International level. She has been instrumental in initiation of a unique PDCC course in Hepato-virology and Transplant Virology at ILBS. ILBS Virology lab is NABL accredited and is proud to be first few NABL accredited Government Molecular Virology laboratory In India. She is also the In-charge of COVID-19 testing laboratory for Delhi State Govt, is actively involved in COVID testing since March 2020.

Speaker Profile

Dr Tara Clancy

Dr Tara Clancy is a Consultant Genetic Counsellor and Honorary Senior Lecturer in the Manchester Centre for Genomic Medicine. Her main clinical and research interests are in cancer genetics and ethical, legal and psychosocial issues in genetics. Tara is a member of the Nuffield Council on Bioethics, the British Society for Genetic Medicine's Ethics and Policy Committee and is on the Steering Group of the UK's Genethics Forum. She is also a member of Manchester University NHS Foundation Trust's Clinical Ethics Committee, and previously chaired a University of Manchester's Research Ethics Committee.

Speaker Profile

Professor Ruth Chadwick

Ruth Chadwick is Professor Emerita, Cardiff University and Visiting Professor, University of Leeds. She co-edits the journal Bioethics and has served on numerous bodies including the Council of the Human Genome Organisation. She is Fellow of the Academy of Social Sciences, the Hastings Center, New York, the Royal Society of Arts, the Royal Society of Biology and the Learned Society of Wales.

Speaker Profile

Professor Sarah Wordsworth

Dr. Wordsworth is Professor of Health Economics at the University of Oxford and has over 25 years' experience in evaluating the costs and benefits of health care technologies. Since 2003
she has led a research programme on the economics of genomic technologies and precision medicine. Of particular interest are the economics of translating sequencing technologies from research into clinical practice in rare diseases and cancer. Sarah is lead for the 100,000 Genomes Project, Genomics England Health Economics Clinical Interpretation Partnership. Sarah's work is highly translational and the genomics research she has led, has informed key changes in practice in the NHS. Sarah has co-authored several text books on economic evaluation methods for health economics and genomic research audiences. She is Co-Director of the MSc in Precision Cancer Medicine at the University of Oxford.

Speaker Profile

Professor Douglas Higgs

Douglas Higgs (FRS, DSc, FRCP, FRCPath FMedSci, member of EMBO) qualified in Medicine at King's College Hospital Medical School (University of London) in 1974 and trained as a haematologist. He is currently Emeritus Professor of Molecular Haematology at the University of Oxford, and a Principal Investigator at the MRC Weatherall Institute of Molecular Medicine (WIMM). The main interest of his laboratory is to understand how mammalian genes are normally switched on and off during differentiation and development using haematopoiesis as the experimental model. His laboratory also studies how gene expression is perturbed in human genetic disease.

Speaker Profile

Professor Sir Stephen O'Rahilly

Professor Sir Stephen O'Rahilly MD FRCP FMedSci FRS, is Director of the MRC Metabolic Diseases Unit (MDU) and the Wellcome-MRC Institute of Metabolic Science-Metabolic Research Laboratories, University of Cambridge. On the wider Cambridge Biomedical Campus, he is Scientific Director of the NIHR Biomedical Research Centre and Head of the University Department of Clinical Biochemistry. He was elected FRS in 2003, to the National Academy of Sciences, USA in 2011, has received four honorary doctorates and numerous scientific awards including the 2014 Zülch Prize of the Max Planck Society, the 2014 Baly Medal of the RCP (London) and in 2015 was the first recipient of the EASD/Novo Nordisk Foundation Diabetes Prize for Excellence. In 2013 he was made Knight Bachelor "for services to medical research". His main research area is the aetiology and pathophysiology of human metabolic and endocrine disease and how such information might be used to improve the diagnosis, therapy and prevention of these diseases.

Abstract

Stratification of pre-cancer and cancer to inform therapy

Rebecca Fitzgerald, MD FMedSCi University of Cambridge

Cancer diagnosis and treatment is undergoing a radical shift away from reliance on the histopathological subtype towards a more precise and individualised approach based on the molecular characteristics of the tumour. Furthermore, it is recognised that earlier diagnosis at the pre-cancer stage can radically improve outcomes. Oesophageal adenocarcinoma is an example of a tumour with poor outcomes that is ripe for a more precision approach to diagnosis and therapy. Oesophageal adenocarcinoma develops gradually from the pre-malignant condition Barrett's oesophagus. Molecular evaluation of Barrett's samples over time and space is shedding light on the pathogenesis of this disease and leading to the development of algorithms to predict progression to cancer. Moreover these can be applied to samples obtained from a novel non-endoscopic cell collection device called Cytosponge to facilitate earlier diagnosis. In more advanced cases genome wide studies of the mutational landscape have elucidated molecular subtypes which are informing trials for more tailored treatment regimes.

Abstract

Professor Bill Newman

In this talk I will set out the landscape for current practice of genomic medicine in the NHS and consider how high-quality service delivery is intimately interwoven with outstanding research and education. The NHS has a worldwide reputation for innovation and adoption of new genomic technologies and practices to improve patient outcomes and experience. This talk will share an overview of the developing service specification for clinical genomics to ensure that these innovations are embedded in practice in an equitable manner for all who need them.

Abstract

Pharmacogenomics in Clinical Practice: Way Forward
Munir Pirmohamed, Department of Pharmacology and Therapeutics, University of Liverpool

Pharmacogenetics/genomics has been around for a long time: although this has led to many discoveries, i.e. associations between phenotypes (drug efficacy and safety) and genotypes, translation of these discoveries into clinical practice has generally been slow and fragmented. Worldwide, there is now greater emphasis on implementation, with many different approaches and areas being investigated including pre-emptive genotyping. The latter is being explored in a number of centres of excellence in the US. To date, no healthcare system in the world has implemented pharmacogenomics for the whole population. The 100,000 genomes project and the Genomic Medicine Service in England represent unprecedent opportunities to undertake implementation of pharmacogenomics for the whole population. The availability of 100,000 genomes data represents pre-emptive genotyping and return of pharmacogenomic variants is planned for the participants who have been sequenced. The implementation of pharmacogenomic testing on demand from healthcare professionals in the UK via the genomic medicine service is part of the promise in the NHS long term plan, and work is currently on-going to determine how this can be achieved.

Abstract

Professor Robert Taylor
Mitochondrial genomics in clinical practice Wellcome Centre for Mitochondrial Research, Newcastle University; NHS Highly Specialised Mitochondrial Service, Yorkshire and North East Genomic Laboratory Hub

Mitochondrial disease arises due to defects in either the maternally inherited mitochondrial genome or one of ~1200 proteins of the mitoproteome encoded by nuclear genes, leading to both childhood and adulthood presentations that are characterised by significant clinical heterogeneity and multisystem involvement. Mitochondrial disease has an estimated incidence of 1 in 4,500 but in spite of its common occurrence, its heterogeneous nature offers challenges in accurately defining the molecular aetiology in many families, even with increased access to an array of functional tools and assays to validate candidate pathogenic gene variants identified within whole exome/genome sequencing datasets. There remains no therapeutic cure for the vast majority of mitochondrial disease patients and as such providing an accurate and rapid genetic diagnosis is crucial for genetic counselling, determining recurrence risks and offering reproductive choices. My talk focuses on the current genetic landscape associated with mitochondrial disease illustrating how the advent of high-throughput genomic sequencing has revolutionised a “genetics first” approach to diagnosis, referencing our experience of providing a national, accredited laboratory diagnostic service investigating adults and children and highlighting the outstanding challenges within revised diagnostic algorithms.

Abstract

Prof Costantino Pitzalis MD, PhD, FRCP

Presentation title: “Genomics in complex diseases - the model of Rheumatoid arthritis”.

The treatment rheumatoid arthritis (RA) has been revolutionized through the development of biologic therapies targeting critical pathways involved in disease pathogenesis. Such targeted approach has made a tremendous difference to the life of million of patients. Yet there is still a sizable proportion of patients (30-40%) who do not respond to current medications and remission still remains an elusive goal in the majority of patients. Notably, the mechanisms for response/non-response remain unknow and, currently, we unable to predict which patients would benefit from individual therapeutic modalities leaving a huge unmet clinical need and a massive health-economic burden. Disease tissue heterogeneity is postulated to play a major role in drug response/non-response related to diverse target expression levels and drug pharmacology. The delineation of synovial specific signatures may enable to define a new taxonomy of disease and integrate molecular pathology into clinical algorithms to more accurately predict prognosis and treatment response: towards precision medicine.

Abstract

Professor Sarah Wordsworth

Genomic sequencing technologies such as whole exome and whole genome sequencing have been used in a research setting for over a decade. Clinical evidence suggests that these technologies can improve the diagnosis and care of genetic rare diseases and cancers. However, to determine whether these technologies should be translated from research settings into routine clinical care requires evidence on their cost-effectiveness. However, a lack of economic evidence on sequencing technologies and targeted therapies has been a key translational challenge worldwide. Therefore, initiatives such as the 100,000 Genomes Project have provided important opportunities to generate health economic evidence of the value of genomic sequencing. This presentation provides an overview of the information required to support the financing and reimbursement of precision medicines from a health economic perspective.

Abstract

Professor Ruth Chadwick

Harmonisation in genomic and precision medicine

In considering ethical and social issues in precision medicine, thought needs to be given to patient expectations and to avoiding problems such as have been encountered by the roll-out of ‘Track and Trace’. Prominent among the issues here is the use of language. Previous consideration of the term ‘personalised’ medicine has revealed at least 9 different senses of personalisation’ with associated potential expectations. Harmonisation is desirable. It is a different concept from standardisation, and is an ongoing process. In speaking of ethics, Aristotle made the point that the degree of precision sought should be appropriate to the subject matter. How ‘precision’ is understood, implemented and introduced, gives rise to ethical as well as practical challenges.

Abstract

Ellen Thomas

Whole genome sequencing in rare genetic diseasesOver 35,000 families with a broad range of undiagnosed rare and inherited disorders participated in the 100,000 Genomes Project, and all have been analysed using a complex bioinformatic pipeline. I will discuss the diagnostic outputs of this endeavour across the spectrum of pathogenic genomic variation, the implications for patients, and some of the learning points which are now supporting introduction of whole genome sequencing as a first-line diagnostic test in the NHS.

‘Sir David Weatherall Oration’

Professor Sir Stephen O'Rahilly

The recent increase in the proportion of the population with obesity and/or type 2 diabetes is a matter of great concern for global public health. The rising incidence of these disorders is clearly attributable to changes in the environment that promote caloric consumption and decrease energy expenditure. However we need to understand why some individuals are susceptible to obesogenic influences while others remain resistant. Similarly, it would be helpful to have a better insight into the mechanises whereby some seriously obese people completely avoid the metabolic consequences of over-nutrition while others succumb to the disabling complications of metabolic derangement despite being only modestly obese. In this lecture I will describe how human genetics has helped to enhance our understanding of our susceptibility or resistance to obesity and its adverse metabolic consequences. The findings have broad-ranging implications for the management of individual patients, for drug development and for public health strategies.

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THANK YOU