Stratified, personalised or P4 medicine: a new direction...

Tuesday 12 May 2015
Heartbeat Education Centre, Southampton General Hospital

Session 1

The promise of stratified medicine

#StratMed2015
‘Realising the potential of stratified medicine’

Professor Sir John Tooke PMedSci
President of the Academy of Medical Sciences;
Vice Provost (Health)
and Head of the School of Life & Medical Sciences, UCL
The Academy of Medical Sciences

- Established in 1998 as a new expert body to deal with issues at the interface of medical science and healthcare.

- Part of the national academies group with the Royal Society, British Academy, Royal Academy of Engineering and Royal Society of Edinburgh.

- Core mission: “To promote advances in medical science and ensure these are converted into healthcare benefits for society.”

- The diversity of the Fellows’ talent and expertise ensures we can bring authoritative opinion and practical guidance to complex issues in medical science and healthcare.

New Fellows (2014)
The FORUM programme

- Established in 2003 to recognise the role of industry in medical research and to catalyse connections across industry and academia.
- Brings together researchers, research funders and research users from across the life sciences sector.
- Range of formats including lectures, symposia, roundtables and workshops. All invite-only.
- Provides a platform for promoting partnerships and networks, as well as joint action by key stakeholders.

To discuss how your organisation can become a FORUM member, please speak to one of the members of Academy staff here today.

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Stratified medicine: Our involvement

2007 FORUM symposium:

- ‘Optimizing stratified medicines R&D: addressing scientific and economic issues’
- Meeting organised with Roche and GE Healthcare to explore issues associated with the introduction of stratified medicines.
- Shared perspectives from economists, clinical researchers and policymakers to determine the options for taking forward stratified medicines research and development.
- Identified several challenges for the development and adoption of stratified medicine.

2012 symposium and 2013 report:

- ‘Realising the potential of stratified medicine’
- Focused on finding solutions to the challenges identified, particularly around clinical and research infrastructure, regulation, and pricing and reimbursement.
- Followed by a stakeholder meeting to discuss the implementation of the report’s recommendations.
‘Realising the potential of stratified medicine’

Key conclusions and recommendations:

Regulation

- EU in vitro diagnostic regulation: include risk-based classification, laboratory accreditation, evidence base for diagnostic licensing
- Integration of the scientific advice provided by regulators on therapeutics and partner diagnostics
- ‘Good Genomics Practice’ guidelines

Reimbursement & Pricing

- Flexible pricing based on value
- Flexible approach to the generation of evidence for diagnostics
‘Realising the potential of stratified medicine’

**Infrastructure**

- UK is well placed, but room for improvement
- Integration of the landscape and harmonisation of health and biomedical informatics
- Capacity building – the education and training of professionals
- Engagement with patients and the public

**Collaboration**

- Expand membership of the UK Stratified Medicine Innovation Platform
Where are we in 2015?

**DIAGNOSTIC**
- 100k Genome Project
- MRC-EPSRC molecular pathology nodes

**DRUG**
- MRC Consortia (disease-specific)
- Adaptive licensing
- Early Access to Medicine Scheme
- Capacity building

**TRANSLATION**
- Precision Medicine Catapult
- Knowledge Transfer Partnerships (KTPs) for modelling in the development pipeline

The social contract
Towards more precise medicine for the diagnosis, treatment and prevention of disease – the UK and European perspective

Stephen T Holgate,
University of Southampton, UK
William Osler: the Father of modern medicine 1849-1919

“He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all.”

William Osler

“It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.”

William Osler
William Osler: the Father of modern medicine 1849-1919

“Medicine became a science by combining clinical observation with pathology and function (physiology) and through the application of the chemical, biological and physical sciences”.

“It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.”

William Osler

William Osler at Work in the Blockley Mortuary, Philadelphia General Hospital, 1886
But we now face very serious problems:

• Reductionist models are failing to account for much of the chronic inflammatory and degenerative disease facing society.

• These non-communicable diseases are increasing as we survive longer and as developing nations adopt aspects of the Western lifestyle.

• After years of improvement in public health, lifestyle influences (sedentary, smoking, diet, “recreational” drugs, stress ), especially on the young are creating a health “time-bomb” in NC diseases (e.g. cancer, obesity, diabetes, hypertension, COPD, asthma).

• Unsustainable drug development industry based on “blockbuster, one size fits all” business model.
Drug discovery: A big challenge for addressing both developed and developing world diseases

R&D for a New Medicine: 10+ years, $1 bn+

Pre-Discovery: 3 – 6 Years
Drug Discovery: ~ 5,000 – 10,000 Compounds
Preclinical: 250
Clinical Trials:
- Phase I: 5
- Phase II: 6 – 7 Years
- Phase III: 6 – 7 Years
Number of Patients / Subjects:
- Phase I: 20 – 100
- Phase II: 100 – 500
- Phase III: 1,000 – 5,000
Regulatory Review: 0.5 – 2 Years
Post-Marketing Surveillance: Indefinite
Scale-Up to Manufacture: Indefinite

Set against this is:

- The explosion of new technology to interrogate complex cellular processes – the ‘omics (genomomics, transcriptomics, proteomics, epigenomics, microbiomics, metabolomics) and the exposome.

- New non-hierarchical approaches to phenotyping complex disease (e.g. cluster analyses, machine learning).

- Applications of informatics to interrogate large data-sets from biological collections, clinical trials and linked population-based case records and prescribing practice.
The Changing Focus of Healthcare

**Then**

Information and knowledge → Health practitioner → Patient

**Now**

Information and knowledge → Patient → Health practitioner

Massive cultural change to not just managing stages of diagnosis and treatment but pulling patients through whole pathways.
The emergence and rapid developmental evolution of ‘omics technology platforms.

The ‘omics cascade:

1. What can happen
2. What appears to be happening
3. What makes it happen
4. What has happened & is happening

Next “Genomics”:

- Genome Resequencing
- mRNA Tag Profiling
- Methylation Analysis
- Functional Elements (ChIP-Seq, DNAse-Seq)
- Small RNA Identification
- Transcriptome Sequencing
Stratified Medicine: What are we talking about?

“the tailoring of medical treatment to the individual characteristics of each patient .... involves the use of companion diagnostics to achieve the best outcomes in the management of a patient's disease or disease predisposition. Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not”.

Adapted from: “Priorities for Personalized Medicine” by the US President’s Council of Advisors on Science and Technology (PCAST), 2008

- Personalised Medicine has arrived to an extent:
  - Herceptin®, Gleevec®, Selzentry™, Ziagen®, Vectibix®, Iressa™
Creation of a New Taxonomy first requires an “Information Commons” in which data on large populations of patients become broadly available for research use and a “Knowledge Network” that adds value to these data by highlighting their inter-connectedness and integrating them with evolving knowledge of fundamental biological processes.
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Reclassification of human disease by identifiable causal pathways.
Forward Look on Personalised Medicine

Personalised Medicine “Target”

Medicine will move from a reactive to a proactive discipline over the next decade; one that is predictive, personalised, preventive and participatory - P4 medicine.
MRC Stratified Medicine Initiative

• Set up in 2010/11 and represented a new way of funding from the MRC

• Builds on the MRC/ABPI Inflammation and Immunology (I&I) Initiative

• £60m initiative to develop disease-specific research consortia, involving industry partners

• Consortia exploring predictors of response and mechanisms underpinning disease stratification, where there is evidence that therapeutically relevant strata exist

• Currently supporting nine consortia (three I&I and nine new), bringing together 30 academic and 41 industrial partners
MRC stratified medicine consortia

- **MATURA - Rheumatoid arthritis (£5.0m) led by QMUL and Manchester** Supported with Arthritis Research UK. Industry partners: AbbVie, Pfizer, Amgen, MedImmune, Genentech, Activiomics, BGI-Shenzhen, Jansenn, Qiagen

- **STOP-HCV - Hepatitis C (£4.1m) led by Oxford** Industry partners: GSK, Merck, Jansenn, Actelion, United Therapeutics Europe, Conatus Pharmaceuticals, Okairos, OncImmune, Medivir, Gilead Sciences, Boehringer-Ingelheim

- **GAUCHERITE - Gaucher’s disease (£3.0m) led by Cambridge** Industry partners: Shire, Genzyme, Actelion

- **UK-PBC - Primary biliary cholangitis (£4.8m) led by Newcastle** Industry partners: Jansenn, Inova Diagnostics, Lumena, Intercept Pharmaceuticals, Dr Falk Pharma, Biotie Therapies, Medigene, Biosignatures, NovImmune SA

- **STRATA - Schizophrenia (£3.9m) led by Kings College London** Industry partners: Amgen, Jansenn, Lilly, Roche

- **SORT - Psoriasis (£4.9m) led by Manchester** Industry partners: AbbVie, Becton Dickinson and Company, Celgene, GSK, MedImmune, Novartis, Pfizer, Qiagen
Minister announces £14m investment in stratified medicine
29 Jan 2015:

- **MASTERPLANS (Systemic Lupus Erythematosus)** - PI: Prof Ian Bruce, University of (£4.2m)

- **AIM HY (Hypertension)** - PI: Professor Phil Chowienczyk, King’s College London. Funded by the MRC (£2.4m) and the British Heart Foundation (£1.1m)

- **S-CORT (Colorectal Cancer)** - PI: Professor Tim Maughan, Cancer Research UK and MRC Oxford Institute for Radiation Oncology, University of Oxford (£2.5m)

- **RASP-UK (Asthma)** - PI: Professor Liam Heaney, Queen’s University, Funded by the MRC (£4.8m)

A different type of research involving strong interdisciplinary interactions and a common way of working together for the benefit of the whole
Stratification is not limited to prediction of response.

Grouping patients by diagnosis, prognosis, etc. can also enable greater mechanistic insight and support the assessment of novel stratification hypotheses.

Dementias pose a critical societal challenge and suffer from a paucity of therapeutic options.

To MRC has established the Dementias Platform UK (DPUK) in order to:

- Stage the progression of Neurodegeneration (ND)
- Identify the physiological and molecular drivers of ND progression
- Join up mechanistic understanding across ND in a whole body context
- Translate into therapeutic & public health interventions
Molecular pathology review

• **Path** - Produce clear unified guidance setting out the critical path and required evidence for the discovery, development, approval and evaluation of tests. Address the gaps in the UK’s regulatory, evaluation, adoption and delivery system

• **Proximity** - Establish joint research/clinical service ‘nodes’ aligned with industry and complementing NIHR, TSB and other RC and partner investments

• **People** -
  – Train next generation of research leaders in molecular pathology, potential merit of guaranteed follow through clinical lectureships
  – Further development of UK capacity in statistics, bioinformatics and health economics
  – Undergraduate medical curriculum to include molecular pathology, to aid adoption and interpretation
Initial focus on development of novel molecular pathology approaches

- We anticipate nodes will initially be positioned at discovery/early development boundary working on
  - Validation of biomarkers associated with disease strata
  - Development of novel sensing and analytical technologies for new diagnostic tools
  - Application of mathematical and statistical methodologies for the extraction of information from complex datasets.

- Longer term, we expect nodes to traverse the path to adoption/delivery, as tests under development mature
Utilise population disease risk biomarkers to aid patient stratification and predict individual risks?

Personalized Healthcare
- Patient Stratification and Theranostics

Molecular Epidemiology
- Disease Risk Factors and Prevalence

Models of Individual Variation

Models of Population Variation

BIOLOGICAL METRICS: GENES, PROTEINS, METABOLITES - MICROBIOME AND ENVIRONMENTAL INTERACTIONS

Metabolic phenotyping in clinical and surgical environments
Utilise population disease risk biomarkers to aid Patient stratification and predict individual risks?

BIOLOGICAL METRICS: GENES, PROTEINS, METABOLITES - MICROBIOME AND ENVIRONMENTAL INTERACTIONS

Metabolic phenotyping in clinical and surgical environments
Emergent science drives new disease opportunities and discovery of shared pathways

Where science and unmet need converge

- Core diseases
- Opportunities in “new” diseases featured in the business plan

Key emergent areas of science:
- Lung repair: COPD, fibrotic lung diseases (IPF, ILD, CF)
- Neuronal mechanisms: Rhinitis, asthma, COPD, cough
- Immunomodulation: Asthma, allergic rhinitis
Integrating knowledge for Systems Medicine
Integrating knowledge for Systems Medicine

The “Grand Challenge” is how to combine the different data types for interrogation.
Conclusions

- Many complex diseases can no longer be considered as a single entity with “one size fits all” approaches to diagnosis and treatment.
- Rather, they manifest different subphenotypes arising from complex interplays of diverse pathophysiological processes or “pathways” that vary from patient to patient and within a different patient across the lifecourse.
- Such disease “endotypes” can be identified using “non-hierarchical” statistical approaches applied to validated clinical and laboratory data combined with multiple ‘omic platforms (phenome).
- Effective integration of multiple different types of data and “its intelligent interrogation will identify novel disease pathways.
- Delineation of interacting causal disease pathways linked to companion diagnostics provides the rational for personalised, stratified or P4 medicine in which the right treatment is given to the right patient at the right time.
Leveraging Big Data to advance stratified medicine in Europe

Nathalie Kayadjanian, Ph.D.
Medical Sciences Committee
Science Europe
Science Europe

Brief overview
Science Europe

- Founded in October 2011
- 50 member organisations from 27 countries
- Research funding and research performing organisations
- Represent approximately €30 billion per annum
- Policy organisation – no funding schemes

Foster excellence in EU research and strengthen European Research Area
Science Europe Structure

Working Groups (MOs)
- Cross-border Collaboration
- Open Access to Publications
- Research Data
- Horizon 2020
- Research Integrity
- Research Infrastructures
- Research Careers
- Ex-post Evaluation
- Gender and Diversity

Scientific Committees (Ind.)
- Medical Sciences
- Life, Environmental and Geo-sciences
- Humanities
- Social Sciences
- Engineering Sciences
- Physical, Chemical and Mathematical Sciences

Research and management policy Science-driven policy
MED Committee Activities

**Activities**

**Strategy**
- Fostering the implementation of a health Big Data ecosystem in EU
- Moving forward personalised medicine in EU
- Improving ethical reviews of clinical research in EU
- Improving science quality through implementation of the 3Rs in EU
- Improving translational research in EU

**European regulations & Consultations**
- Data protection regulation
- Clinical trial regulation directive
- Animal use in research
- Embryonic stem cells
- Consultation “Health, demographic change and wellbeing”

**Science Europe**
- ERA consultation
- Consultation “a la carte”
How to transform Big Data into Better Health?:

Fostering the implementation of a health Big Data ecosystem in EU
THE CONTEXT
EU faces Big health challenges

- **Complex diseases**
  multi-factorial, multi-systemic

- **Complex health challenges**
  aging, non-communicable disorders…

- **Inefficient & unsustainable R&D model**
  high attrition rate, lengthy & costly

- Transitioning from “**diagnose and treat**” to “**predict and prevent**”

→ Requires a Big Science approach
FROM BIG DATA TO BIG SCIENCE
Big Data

“Human Health Information System”

Big Data = multi-dimensional & heterogeneous health-related data
The conceptual framework

Data Integration

Knowledge Network

Exposome
Social network
Clinical phenotypes
Microbiome
Epigenome
Metabolome
Proteome
Genome
Other type of data (imaging...)
Individual subjects

Information Commons

Data Interpretation

Public health
Clinical Decision (Personalised Medicine)
Fundamental mechanisms

Data interconnectedness

Creating a Health Big Data Ecosystem

Knowledge Network

Exposome
Social network
Clinical phenotypes
Microbiome
Epigenome
Metabolome
Proteome
Genome
Other type of data (imaging…)
Individual subjects

Information Commons

Infrastructure

Human resources

Funding models

Organisational model

Data sharing
CHALLENGES & RECOMMENDATIONS:

1. Data integration
2. Data interpretation
3. Data-sharing ecosystem
1. Data Integration: challenges

- **Patient data**
  - Health self-monitoring data
  - Wellness
  - Social networks

- **Administrative data**
  - Risk management...

- **Electronic Health records**
  - Patient registries

- **Biological data**
  - Omics data
    - Epigenomics
    - Genomics
    - Proteomics
    - Metabolomics
    - Lipidomics...

- **Imaging data**
  - MRI
  - DTI...

- **Clinical data**
  - Medical records

- **BIOBANKS**
  - Clinical trials

- **INFORMATION COMMONS**

**Data fragmentation, heterogeneity, availability, handling, privacy**
1. Data Integration: Recommendations

1. Integrate –omics data with higher levels of complexity (e.g. lifestyle, environment)

2. Leverage existing national centralised databases (e.g. Scotland, Denmark)

3. Leverage undergoing pilot projects initiative based on disease areas (e.g. HBP, U-BIOPRED, EMIF)

4. Develop best practices to improve data accuracy (e.g. data reproducibility)
2. Data interpretation: Challenges

- Lack of concepts and theory to derive relevant knowledge from data
- Spurious correlations
- Investigator-based approach
2. Data interpretation: Recommendations

1. Develop an integrated approach to biology (i.e. system biology)

2. Implement best research practices to increase proportion of true research findings

3. Foster multi-disciplinary and collaborative expert networks
3. A Data-Sharing Ecosystem: Challenges
The current organisational model

The biomedical R&D chain value: linear & in silos
Inefficient: long, fragmented & disconnected
The current organisational model

Basic Research → Preclinical Development → Clinical Development

Stakeholders/Organisations
- Academia
- CROs/Biotechs
- Regulatory agencies
- Patients
- Industry
- Clinicians

Funding
- Public
- Industry

The DATA chain value: linear & in silos
Inefficient: long, fragmented & disconnected

Death Valley
A data-sharing organisational model

Knowledge Network
- Exposure
- Signs and Symptoms
- Genome
- Epigenome
- Microbiome
- Other Types of Patient Data
- Individual Patients

Information Commons

Mathematics
Preclinical Development

INFRASTRUCTURE

FUNDING

ICT
Basic Research

Clinical Development

Social Sciences
Human resources
A patient-centered model
3. A Data-Sharing Ecosystem: Recommendations

1. INDIVIDUAL
Develop pilot experiments to showcase evidence-based benefits of sharing data for researchers

2. SOCIETAL
Develop transparency practices
Develop patient/citizen-centered model (e.g. health data co-operatives)

3. ORGANISATIONAL
Develop codes of conduct and research practices for data management quality control
Develop funding mechanisms for collaborative research networks
Develop reward and recognition mechanisms for data sharing activities by individual researchers

4. LEGAL
Introduce an appropriate and supportive legal framework (e.g. Data Protection Regulation)
Thank you

nathalie.kayadjanian@scienceeurope.org
100,000 Genomes Project in Rare Disease
Prof Mark Caulfield FMedSci,
Chief Scientist
Academy of Medical Sciences

William Harvey Research Institute
Barts NIHR Cardiovascular Biomedical Research Unit
Queen Mary University of London
Genomics England- mission

• 100,000 whole genome sequences in NHS patients with rare inherited disease, cancers and pathogens from the NHS in England
• Whole Genome Sequencing
• Generate health and wealth
• Legacy of infrastructure, human capacity and capability
• World-leaders in the application of Genomic Medicine for healthcare
Challenges in Rare Disease

• <5% of the population or about 5/10,000 people
• 7000 rare diseases
• Working on 128 phenotypes
• Detailed and genomically primed phenotyping
• Diagnostics- genomic, imaging, pathology
• Human Phenotype Ontology
• Disease progression
• WGS 30X
• Building a Rare Disease Registry

Luke Jostins & Gil McVean Oxford
Over 2000 people with Rare Disease in WGS
The case for WGS coverage of clinical tests at 30X
Augusto Rendon and Matthew Parker

All but two of the 600 genes routinely tested are covered at 95% plus >15x
Two brothers: distal sensory-motor neuropathy

Two brothers with a distal motor neuropathy

Symptoms began in late 40s-early 50s progressed over 20-25 years

Currently aged 79 and 72

Remain ambulatory but with significant difficulties

Whole Genome Sequence
Putative pathogenic mutation: Serine Palmotyltransferase Transporter LC1, First reported stop codon mutation in SPTLC1 c.985C>T, p.R329*

Sanger: Confirmed
Potential for treatment trial with l-serine

Diagnostic odyssey: cost £2905
Father and daughter: focal segmental glomerulosclerosis

- Father presented in late 20s with hypertension and proteinuria
- Dialysis aged 29, renal transplant aged 30.
- Transplant failed aged 55
- Re-transplanted aged 57 last year
- Both his father, brother and uncle died from the same condition
- His daughter is also displaying features of proteinuria.
- She has worried for years her daughter may have inherited this kidney problem

**Pathogenic mutation**: INF2, c.653G>A, p.R218Q

**Sanger**: Confirmed in both affected patients

Previously described pathogenic mutation
Challenges in Cancer
Clinical Lead: Clare Turnbull

• Disease of disordered genomes – over 200 drivers known
• Drugs targets, Tumour heterogeneity, evolution of cancer
• Lung, breast, colon, prostate, ovary and, Leukaemia and
• Rare and Childhood Cancers, unknown primary

• Detailed Phenotyping models- derived from NIHR HIC
• Diagnostics and Imaging, Molecular Pathology (MRC Path Nodes)
• Linked to NHS disease specific cancer registries
• Multi-disciplinary team- Chemo & Radiotherapy & Outcomes

• Sequential biopsy of recurrence/ Stratified medicine- Focus 4
• WGS at 75x somatic and 30x germline

• International Cancer Genomes Consortium
Cancer Programme- extended piloting of SOPs for fresh frozen and cancer in **NIHR BRC/GMC Centres**

Molecular Pathology Lead: Louise Jones

**EXPERIMENTAL WORKSTREAMS**

- **WS 1:** upstream handling
- **WS 2:** tumour processing, fixative, embedding
- **WS 3:** tumour assessment
- **WS 4:** DNA extraction
- **WS 5:** DNA quantification and quality assessment
- **WS 6:** Library preparation and sequencing

**GMC**

Initiation Implementation phase

*SOP development group*

*Led by Prof Louise Jones. Includes molecular pathology leaders from BRC-GMC centres: Schuh, Verrill, Henderson, Flanagan, Gonzalez del Castro, Thomas*

May 2015

September 2015
Genomics England – The main programme

11 Wave 1 NHS Genomic Medicine Centres
Rare diseases, cancers and pathogens
Broad consent, characteristics, molecular pathology and samples

NIHR Biosample Centre
DNA & multi-omics Repository

Sequencing Centre
Wellcome Trust £27m

NIHR Biosample Centre
DNA & multi-omics Repository

Sequencing Centre
Wellcome Trust £27m

MRC £24m Research Data Infrastructure
Sequential builds of pseudonymised data and WGS
Safe haven- users work within 32 GeCIP Domains

Primary Care
Hospital episodes
Cancer Registries
Rare Disease Registries
Infectious Disease
Mortality data
Patient entry

Annotation & QC
Scientists & SMEs
Product comparison

Oxford
Big Data

Refershable identifiable
Clinical Data
Life-course registry
Linked to anonymised
Whole Genome Sequence

Clinicians & Academics

Training
HEE & Funders

Industry
GENE Consortium

Fire wall
Patient data stays in safe haven

Only processed results pass outside
Establishment Phase

Multi-omics in rare disease – plasma and serum sampling
• RNA transcriptomics, micro RNAs
• Epigenetics, Proteomics and metabolomics

• Illumina Partnership

• NHS Sequencing Centre £27m from Wellcome – q4 2015

• MRC Award of £24m for the UK Data Infrastructure for Genomic Medicine – QMUL, UCL, The Farr, Oxford, UK Biobank, Sanger, EBI, Cambridge, Kings, Newcastle

• HEE 700 person years of Masters PhD and short course training - £25m
Genomics England
Clinical Interpretation
Partnership
Why do we need a Clinical Interpretation Partnership?

The standard way

Genomics Research
- Form hypothesis
- Get funds and form collaboration
- Collect, analyse data and validate results

Publication, dissemination, translation
- Publish and disseminate results
- Attempt to translate into healthcare

Healthcare adoption and implementation
- NHS and NICE evaluation and Guidelines
- Education and implementation programme

The GeCIP way

The 100,000 Genomes Project
- Hypothesis – WGS will enhance diagnosis
- Coalition of NHS, academics and trainees
- Work together on WGS within GeCIP domains

Enhanced interpretation linked to implementation
- Validate, publish, educate and translate
- The GeCIP Collaborative accelerates Implementation
- Evaluate therapeutic innovation potential

Earlier Healthcare adoption and implementation
- Accelerated diagnosis and health economic evaluation
- Framework for therapeutic innovation

Securing Patient Benefit
# Genomics England Clinical Interpretation Partnership

**Rare Disease, Cancer and Infection Domains**

<table>
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<tr>
<th>Organised in Disease Domains</th>
<th>Key functions and outputs</th>
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| UK led - steering group                                           | Domain leader & sub-groups  
International collaborators                                         |
| Genomics England Chief Scientist’s Team                          | Oversight, informatics and logistics for the programme                                    |
| Multiple phenotypic sub-groups                                  | Deeper phenotyping & extend programme                                                    |
| Functional characterisation Multi-omics                         | Single cell or model functional studies  
RNA, epigenetics, proteomics                                       |
| Analysts and Bio-informaticians                                 | Novel analytic approaches                                                                |
| Interpretation - NHS and PHE teams and Researchers               | Highest fidelity dynamic reporting system  
Integrated Multi-Disciplinary Team                                 |
| Training - HEE/GECIP trainees                                   | Genomic Medicine Academy                                                                 |
| Precompetitive industry partners                                 | Academic/Industry Collaboration                                                          |
Genomics Priming Therapeutic Innovation

• Genomic information - Protein structure and druggability assessment
• ChEMBL resource - small drug and drug-like molecule interactions with proteins and pharmacological effects
• Identify novel targets repurposing targets in Phase II/III trials

Stratified and adaptive trials

• Embedded Clinical Trials - Reduce patient funnel
• Identify the right genotype and connect clinical teams with trials
• Identify important genetic influences on drug response
• Adaptive designs
GENE Consortium

- 12 pharma/diagnostics/SMEs
- Precompetitive consortia
- Work together on 5000 WGS
- To shape data centre

- Larger consortia
- Individual company interactions

- AbbVie
- Alexion Pharmaceuticals
- AstraZeneca
- Biogen
- Dimension Therapeutics
- GSK
- Helomics
- Roche
- Takeda
- UCB*
- Berg
- Boehringer Ingelheim
Genomics England

- 100,000 WGS on NHS patients and pathogens
- Aware of the challenges
- Working with NHS, academics and industry to drive Genomic Medicine into the NHS
- Support that with education
- Leave a legacy of NGS Centres, sample pipeline and biorepository, large-scale data store that makes this usable by the NHS
- New diagnostics and therapies and opportunities for patients
- By end of 2017
Genomics England – who are we?

- **Officers**: Sir John Chisholm (Executive Chair)
- Mark Caulfield (Chief Scientist), Nick Maltby (Company Secretary), Jim Davies (Informatics), Viv Parry (Outreach), Graham Colbert (COO)
- **Board**: Prof Dame Sally Davies (CMO), Kevin Dean (Cisco), Prof Sir John Bell, Jon Symonds (Audit), Prof Sir Malcom Grant (NHSE)
- **Advisory Committees**:
  - **Science**: Sir John Bell, IT: Kevin Dean and Ethics: Mike Parker
Team members

- **Science** - Tom Fowler, Jeanna Mahon-Pearson, Laura Riley, Nora Wong, Clare Turnbull.

- **Informatics** - Jim Davies, Tim Hubbard, Augusto Rendon, Matthew Parker, Andrew Devereaux, Katherine Smith, Ellie McDonagh, David Brown