Stratified Medicine Scotland Innovation Centre

“The right treatment, to the right patient, at the right cost........”
## Stratified Medicine Scotland

<table>
<thead>
<tr>
<th><strong>• Challenge</strong></th>
<th><strong>Global &amp; local</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>• Opportunity</strong></td>
<td><strong>Window &amp; technology</strong></td>
</tr>
<tr>
<td><strong>• Partnership</strong></td>
<td><strong>Patient centred &amp; comprehensive</strong></td>
</tr>
<tr>
<td><strong>• Case</strong></td>
<td><strong>Business model</strong></td>
</tr>
<tr>
<td><strong>• Vision</strong></td>
<td><strong>First steps &amp; long game</strong></td>
</tr>
</tbody>
</table>
The Challenge - Global

- Diabetes – affects 366 million
- Chronic respiratory disease – affects >700 million
- Cancer – 22 million cases/year
- Cardiovascular disease – 32 million MIs & CVAs/year

IMPACT ON HEALTHCARE SERVICES:

- Patients with chronic diseases use
  - 60% of hospital bed days
  - 80% of primary care consultations

DEATHS from chronic disease in 2008:

The global economic impact of the five leading chronic diseases -- cancer, diabetes, mental illness, heart disease, and respiratory disease -- could reach $47 trillion over the next 20 years, according to a study by the World Economic Forum.

Reuters
Domains of stratified medicine

Rare disease risk
- Identifying causative genes for Mendelian diseases
- Early prediction of disease
- Pre-conception/PGD screening

Common disease risk
- Risk prediction
- Risk stratification
- Identification of patients to focus on early behaviour change/risk reduction

Pharmacogenomics
- Risk stratification
- Drug efficacy and dosing
- Side effect prediction

Salari K et al. Eur Heart J 2012;33:1564
Our Vision

To transform management of chronic disease globally by accelerating biomedical research, high quality health care provision and economic growth
Given limited ability to predict responders, doctors practice trial-and-error medicine.
Life Technologies acquired Ion Torrent’s robust semiconductor-based technology for $725 million.

- Integrate data-intensive biology with medicine
- Understand clinical & genetic correlations
- Genomics has a network effect to catalyze changes in information technology, medicine, and society
GSK recognises Scotland’s current leadership in electronic Public Health Records ... this IC will provide the opportunity to secure that position through its application to Clinical Trials to stratify patient groups.

*Patrick Vallance, President Pharmaceutical R&D, GSK*
Scotland’s USP

Provider

Informatics

Genetics
Exemplar Programme 1: Oncology

Exemplar Programme 2: Heart disease & diabetes

Exemplar Programme 3: RhA & respiratory

Tissue/Bio-repositories/Datasets

Biomedical Informatics/e Health

Imaging

Genomic/’omic’ medicine

Innovation Centre Business Platform
Drug Trials Get Smarter

OLD

Patients with disease

Clinical Trial agent targets mutation A

Patient sample sent to CRO for genotyping

No Mutation

Rejected (Treatment Delayed)

Enrolled

NEW

NGS Panel

Stratify patients

Enrollment through care-embedded testing (future)

Mutation A

Trial A

Mutation C

Trial C

Mutation B

Trial B

Mutation D

Trial D

Modified from
Genomic profile of tumour

Actionable mutations

EGFR inhibitor responsive

nab-paclitaxel responsive

5-FU responsive

HER2 amplified (ErbB3/4 activation)

Gemcitabine responsive (AKT, IGF1R, ErbB2, c-MET, and ErbB3)

HR defective (Spurin-MHC)

KRAS (G12D)

p16/CDKN2A (loss)

TP53 (V274F)

Genomic profile of tumour

To transform management of chronic disease globally by accelerating biomedical research, high quality health care provision and economic growth.

Modified from ThermoFisher Scientific
Exemplar 1 – Rheumatoid Arthritis

**Involved:**
- Prof Iain McInnes (UoG; PI)
- Dr Duncan Porter (GGHB)
- Prof Paul McKeigue (UoE)
- SMS-IC SMART Lab
- Sistemic
- ThermoFisher
- Aridhia

**Delivers:**
- Pharmacogenomic relationship for response/non response to methotrexate in RhA

**Utility:**
- Allows clinicians to prescribe MTX only in cases where evidence base predicts it will work
- Creates more compelling arguments for use of biological therapy in early RhA
Exemplar 2 – oesophageal cancer

- **Involved:**
  - Prof Zosia Meidzybrodzka (UoA; PI)
  - Dr Russell Petty (NHSGG&C)
  - SMS-IC SMART Lab
  - ThermoFisher
  - Aridhia

- **Delivers:**
  - Pharmacogenomic relationship for response/non response to gefitinib (EGFR TK inhibitor) in OC based on a completed clinical trial

- **Utility:**
  - Would create evidence base for use of gefitinib in OC in pts with appropriate signature
  - May drive future trials (label extensions for gefitinib and/or new EGFRTK agents)
Integrative genomics across data modalities

<table>
<thead>
<tr>
<th>Data modality</th>
<th>Network models</th>
<th>Functional Annotation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic</td>
<td>Genetic variation</td>
<td>OMIM GWAS db Mutation Db</td>
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<tr>
<td>Transcriptional</td>
<td>Regulatory networks</td>
<td>GO KEGG, BBID Biocarta</td>
</tr>
<tr>
<td>Protein</td>
<td>Protein interactions</td>
<td>String InterPro SMART</td>
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<tr>
<td>Metabolic</td>
<td>Metabolic pathways</td>
<td>HMP MatCyc ENZYME</td>
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</tbody>
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Flow of biological information

Endo-phenotype (metabolic, electrical, imaging)

Disease phenotype (e.g. LVH)

modified from Ware et al, Cardiovasc Res 2013;97:623
Permanent home in 2015: South Glasgow University Hospital
Imaging Centre of Excellence (ICE)

Includes UK’s first 7Tesla MRI scanner in a clinical setting
MSc Stratified Medicine and Pharmacological Innovation

• Pan-Scottish Degree, led by University of Glasgow
• Developed with Industry, to meet future needs of Stratified Medicine Industry

• Core Themes:
  • Scientific basis of stratified medicine
  • Commercialisation of Science
  • Application of research and evaluation technologies

• All students have placement with Industry
• First cohort of students will graduate this year
South Glasgow University Hospital
Thank you

www.stratmed.co.uk
Exemplar 3 – Oncology indication - ovarian cancer

• Involved:
  • Prof Charlie Gourley (UoE; PI)
  • Prof Iain McNeish (UoG)
  • NHST HB
  • NHSG HB
  • SMS-IC SMART Lab
  • ThermoFisher
  • Aridhia

• Delivers:
  • Identifies presence/absence of BRAC1/2 mutations in tumours of OC pts currently denied treatment with PARP inhibitors (olaparib).

• Utility:
  • Would create evidence base for use of PARP inhibitors in OC pts with somatic mutations (not just germline mutations)
  • Treatment of 35% more OC pts with PARP inhibitors
Developing a skilled workforce

The Stratified Medicine Scotland consortium has identified the key training needs required to support the exploitation of stratified medicine by Scottish industry.

- Modern apprenticeship
- Further education level

- **Graduate level** (Health science/informatics)
- **Post Graduate** (Health science/informatics) - 50 places shared 10 each between 5 Universities
- Entrepreneurship
- Senior level/industry exchange *(GSK, P Vallance)*
- Industry/Academia mentoring
Exemplar 4 – IBD/COPD indications

- **Involved:**
  - Dr David Bunton (Biopta; PI)
  - Ms Jane Hair (GG&CHB bio-repository)
  - Prof Jack Satsangi (UoE)
  - Prof Colin Palmer (UoD)
  - FIOS Genomics
  - SMS-IC SMART Lab
  - ThermoFisher
  - Aridhia

- **Delivers:**
  - Identifies genetic signature in IBD/COPD tissues predictive of response to positive control agents in in vitro pharmacology organoculture

- **Utility:**
  - Confers a commercial advantage and USP on Biopta – pt samples (blood) could be pre-screened for predicted response ahead of committing to organoculture (contract screening service for pharma/biotech)
SMS-IC and the incubator space
AIM

*Development of a world-class centre of research, innovation & commercialisation in stratified medicine, bringing together excellence in the academic, industrial and NHS communities.*

- Providing a platform for clinical trials, genomic data creation and analysis leading to stratified medicine.
- Delivery of a core facility for genetic sequencing at scale, including both Life Technologies’ Ion Torrent Next Generation Sequencing equipment and Aridhia’s biomedical informatics platform and analytical solutions.
- Integration of EHR based on NHS medical records for the SMS-IC to develop longitudinal data sets for use by its customers.