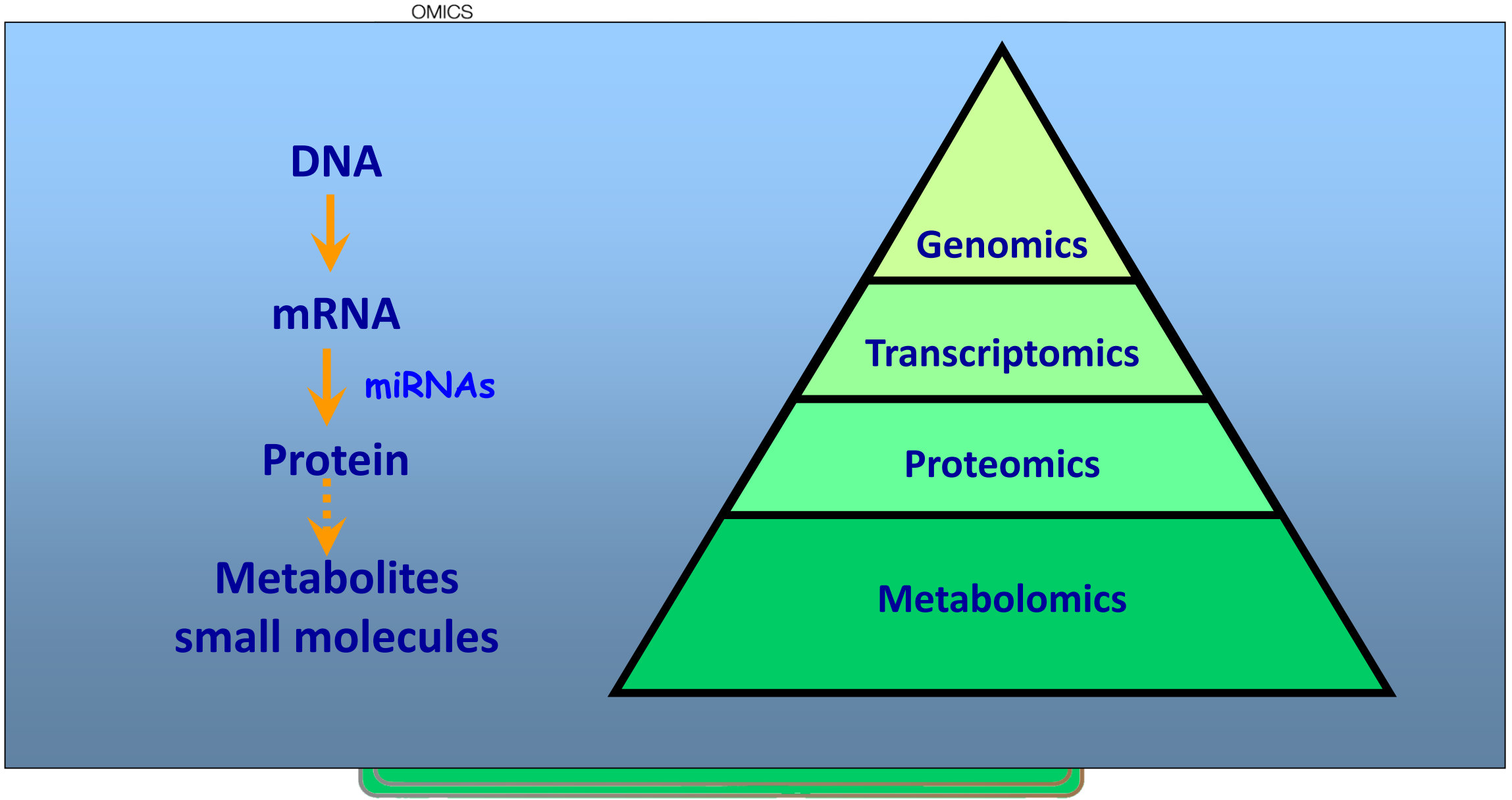
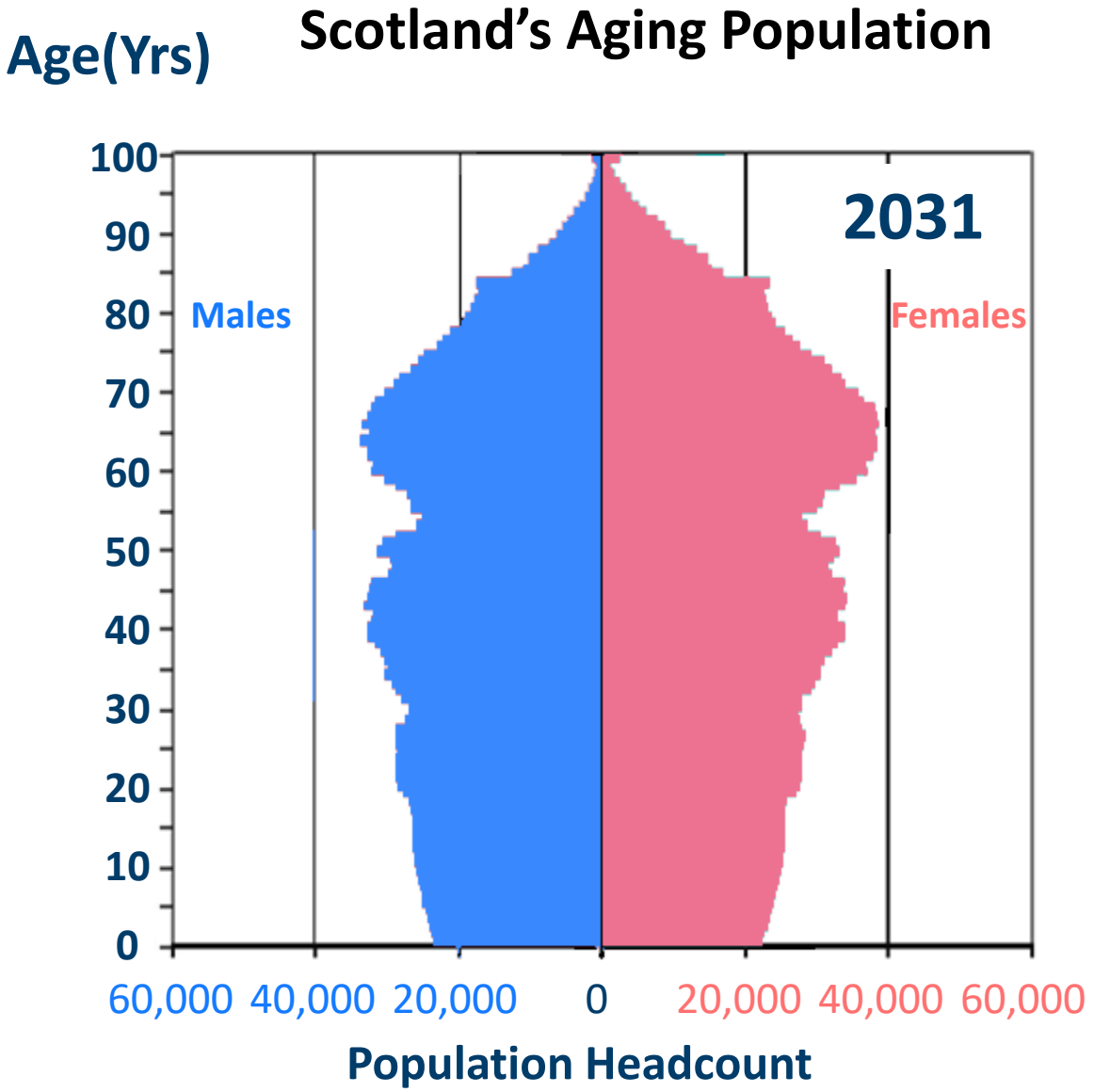

University of Glasgow
Professor Dame Anna Dominiczak
Regius Chair of Medicine
Vice-Principal and Head of College of
Medical, Veterinary & Life Sciences
CELEBRATING 10 YEARS OF LUCID

Genomics and other Omics



Pjanic M et al. Curr Cardiol Rep 2016;18:102

The Perfect Storm

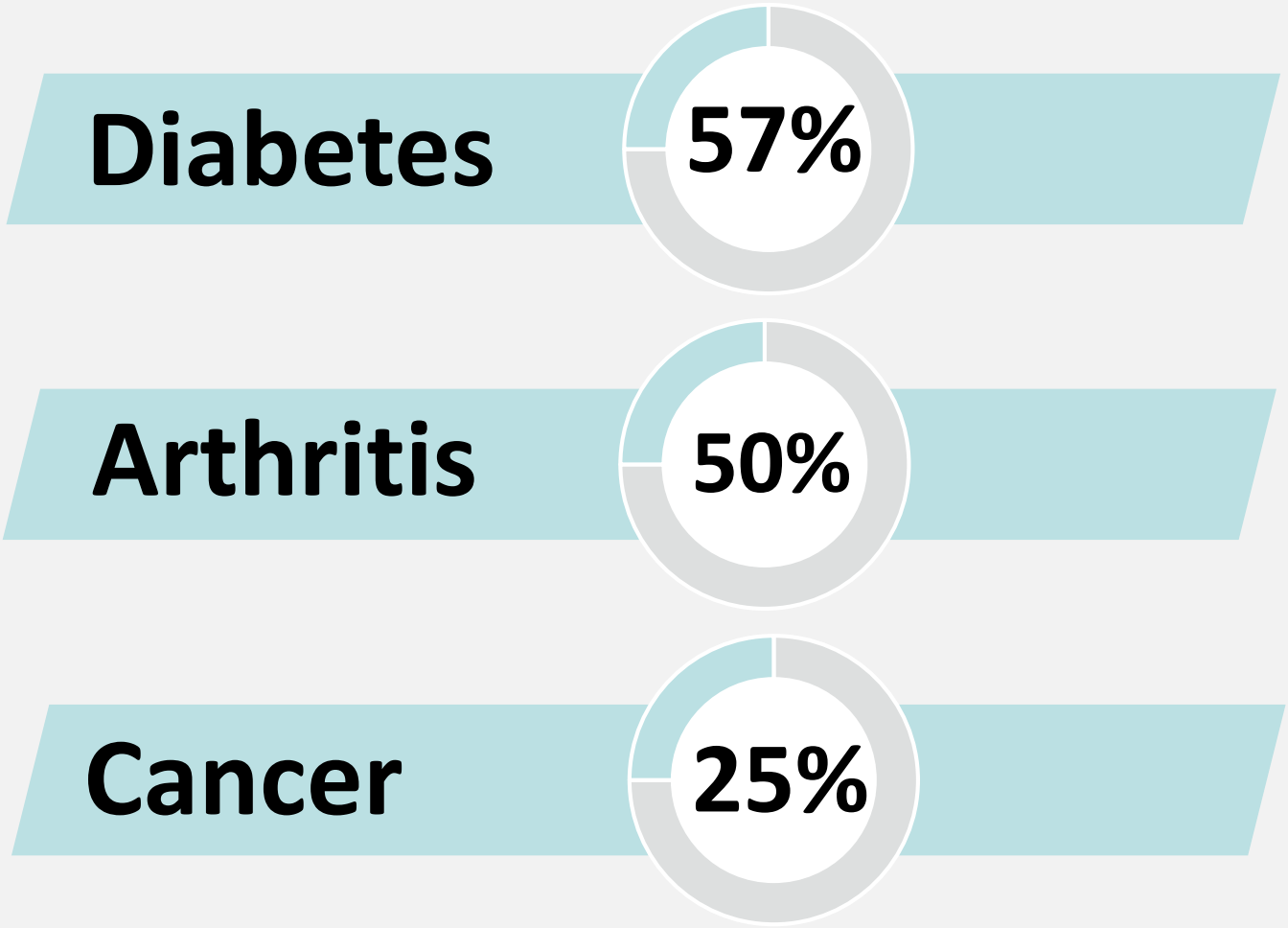


Global economic impact of the chronic diseases -- *cancer, diabetes, mental illness, heart disease, and respiratory disease* -- $47 trillion over the next 20 years.
(World Economic Forum)

Trial & Error Medicine

90% top selling blockbuster medicines only work for 30–50% of patients

% patient population that responds to drug class

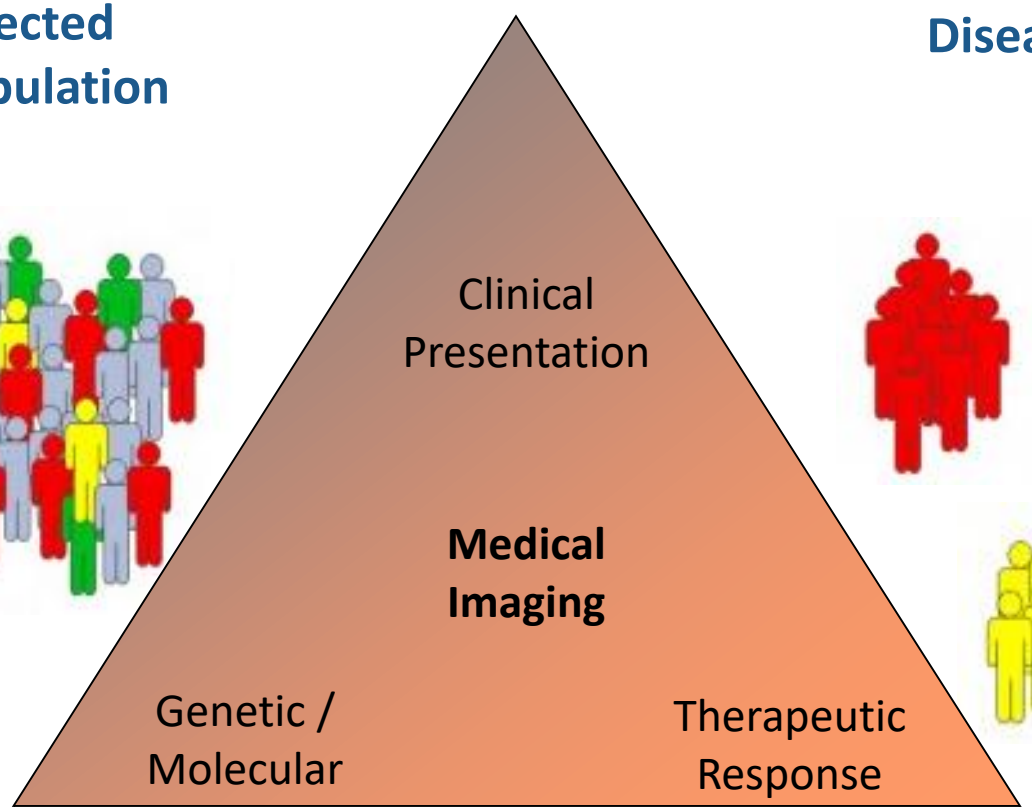


Precision Medicine

Input

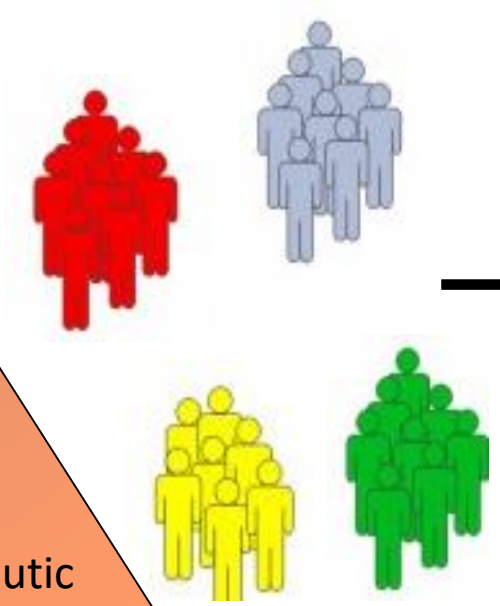
Affected population

Tools



Outputs

Disease Strata

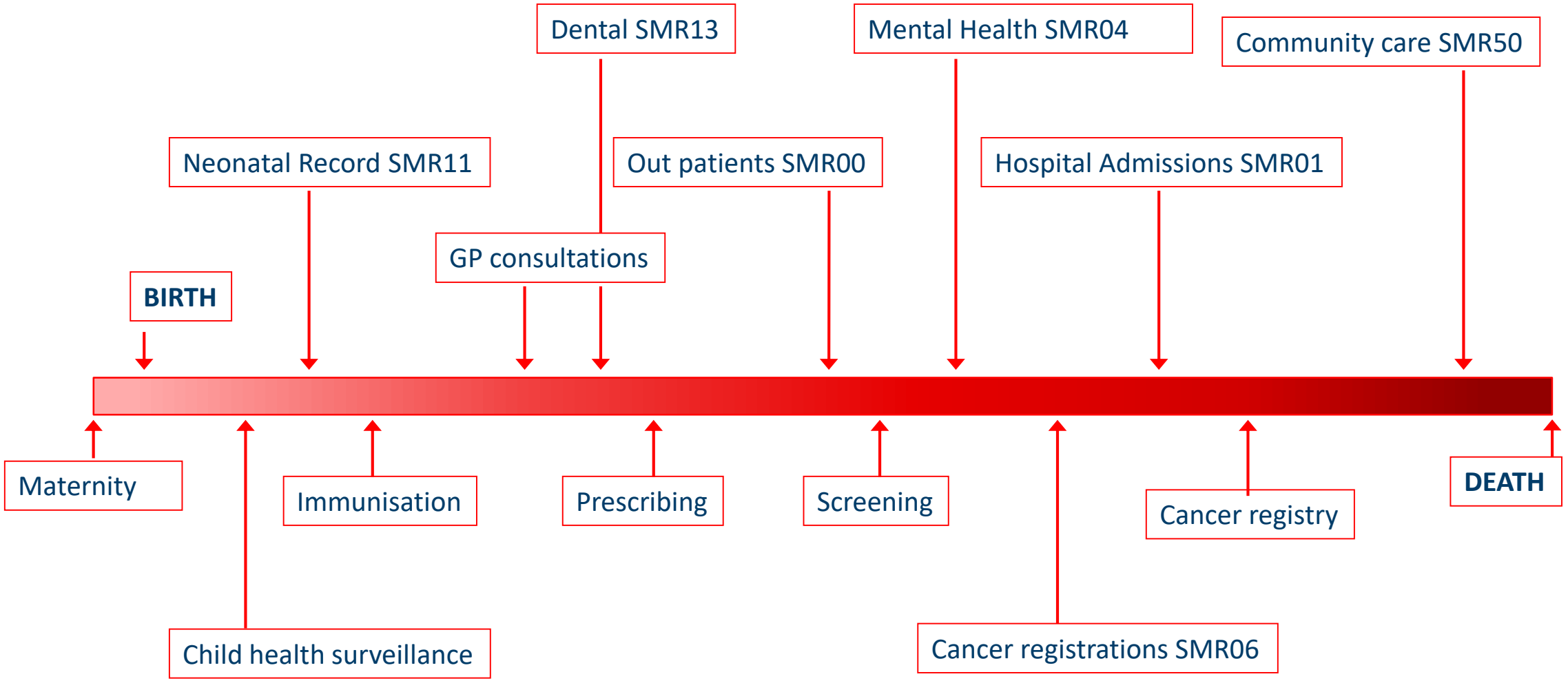


Value

- Diagnostics to better predict disease state, prognosis, response to treatment
- Mechanism of disease leading to new therapies

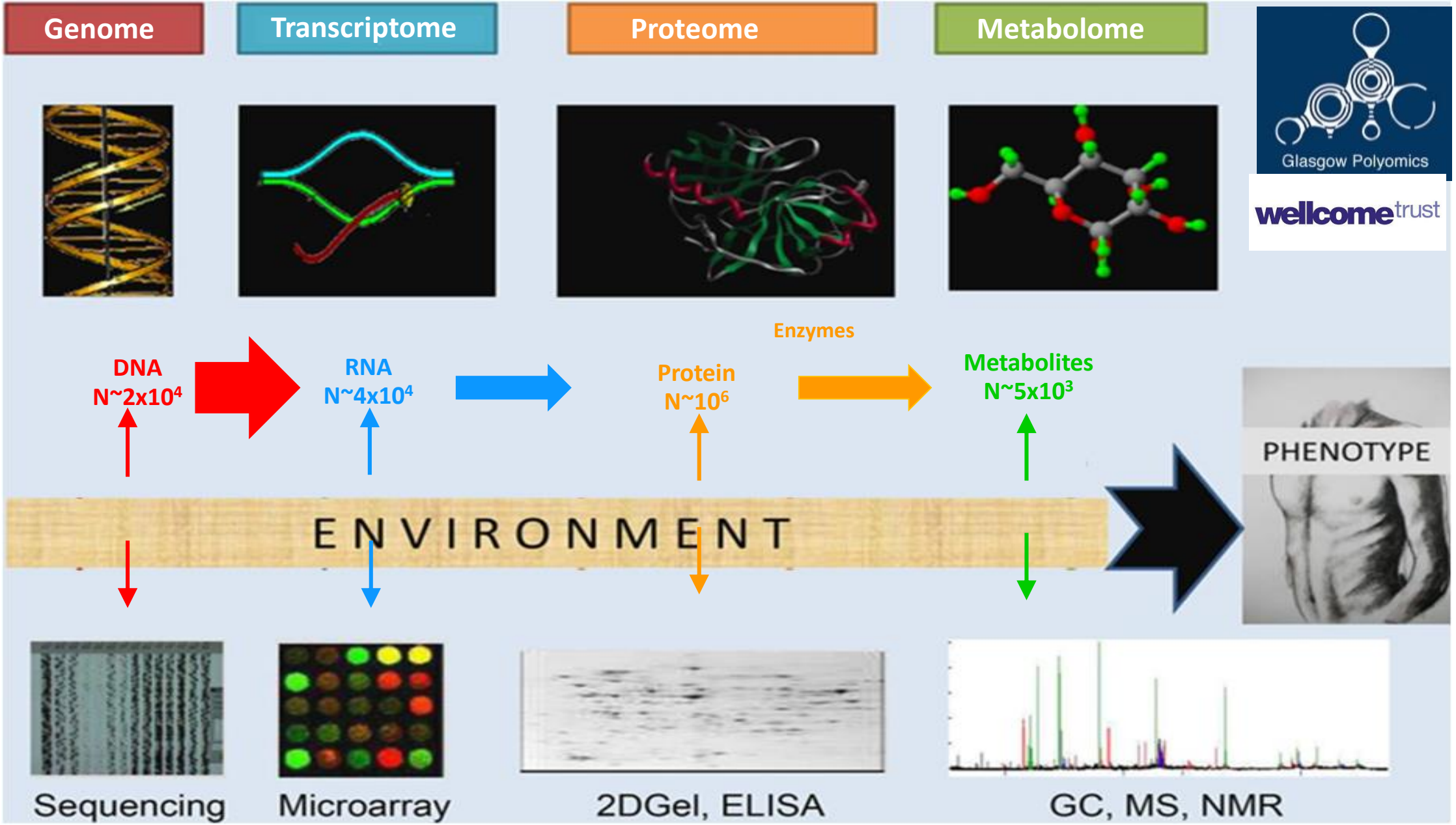
Capturing this potential requires partnership between researchers, industry (BioPharma and Diagnostics) NHS and patients. No one group has all the necessary skills/resources.

Linkage of Scottish Health Records



CHI = Community Health Index

Omics technologies available for integrated analyses



Stratified Medicine Scotland

Scottish Funding Council
Promoting further and higher education

Precision Medicine Scotland – Innovation Centre

6 Exemplars: Ovarian, Oesophageal & Pancreatic Cancers, Rheumatoid Arthritis, Multiple Sclerosis, IBD/COPD

Sistemic

ThermoFisher SCIENTIFIC

aridhia

ARRAYJET

AXIS-SHIELD Innovation for Life

CHIEF SCIENTIST OFFICE

gsk

NOVARTIS

NH DestiNA

Syntropharma

Alere™

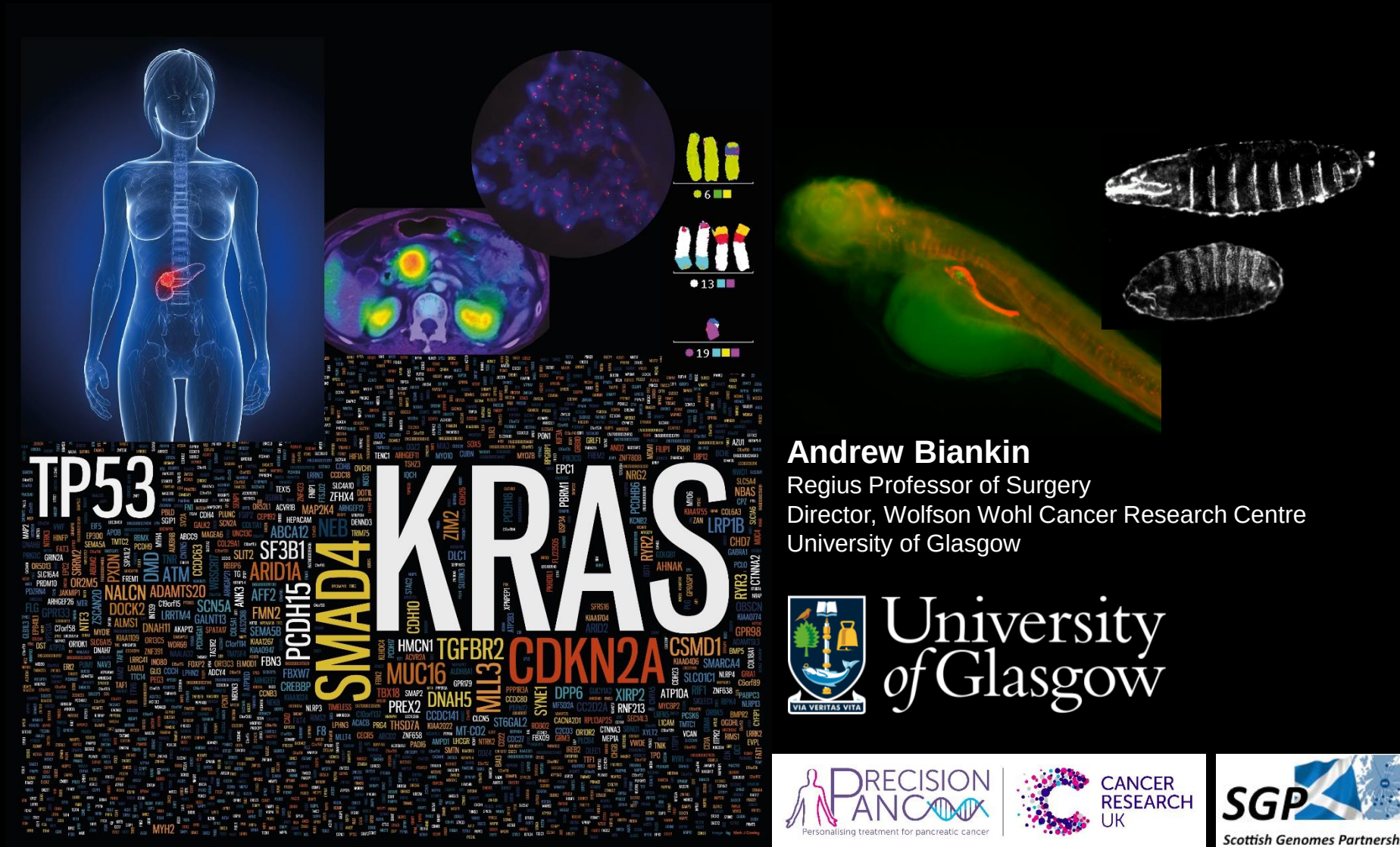
fios GENOMICS

AstraZeneca

QUINTILES

biopta human tissue experts

Precision Oncology Therapeutic Development



Andrew Biankin
Regius Professor of Surgery
Director, Wolfson Wohl Cancer Research Centre
University of Glasgow

University of Glasgow
VIA VERITAS VITA

PRECISION PANCOO
Personalising treatment for pancreatic cancer
CANCER RESEARCH UK

SGP
Scottish Genomes Partnership

wellcome trust

MRC Medical Research Council

PANCREATIC CANCER UK

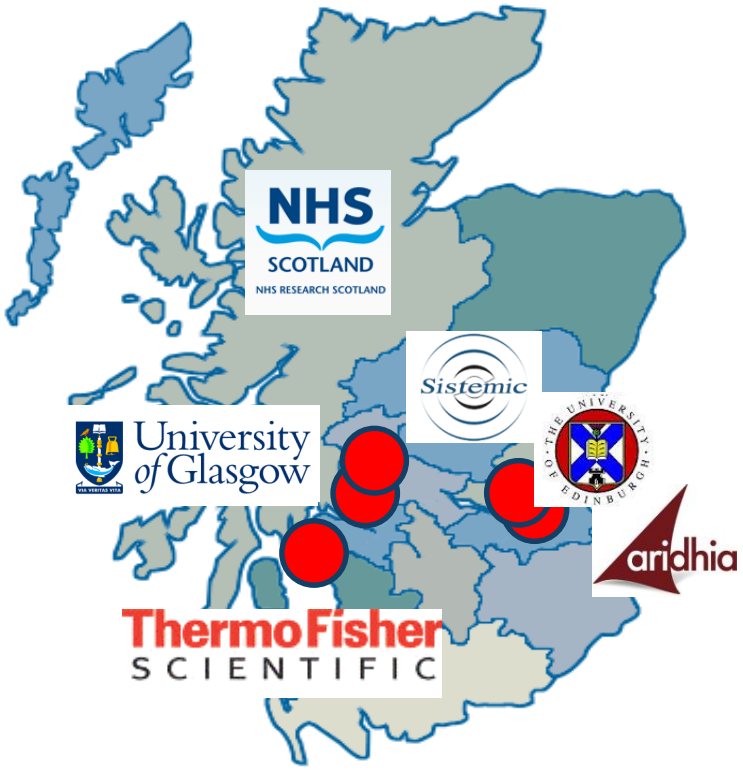
International Cancer Genome Consortium

CHIEF SCIENTIST OFFICE

PANCREATIC CANCER ACTION NETWORK

APGI

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

University of Glasgow

Glasgow – Swedish GWAS of HTN

OPEN ACCESS Freely available online

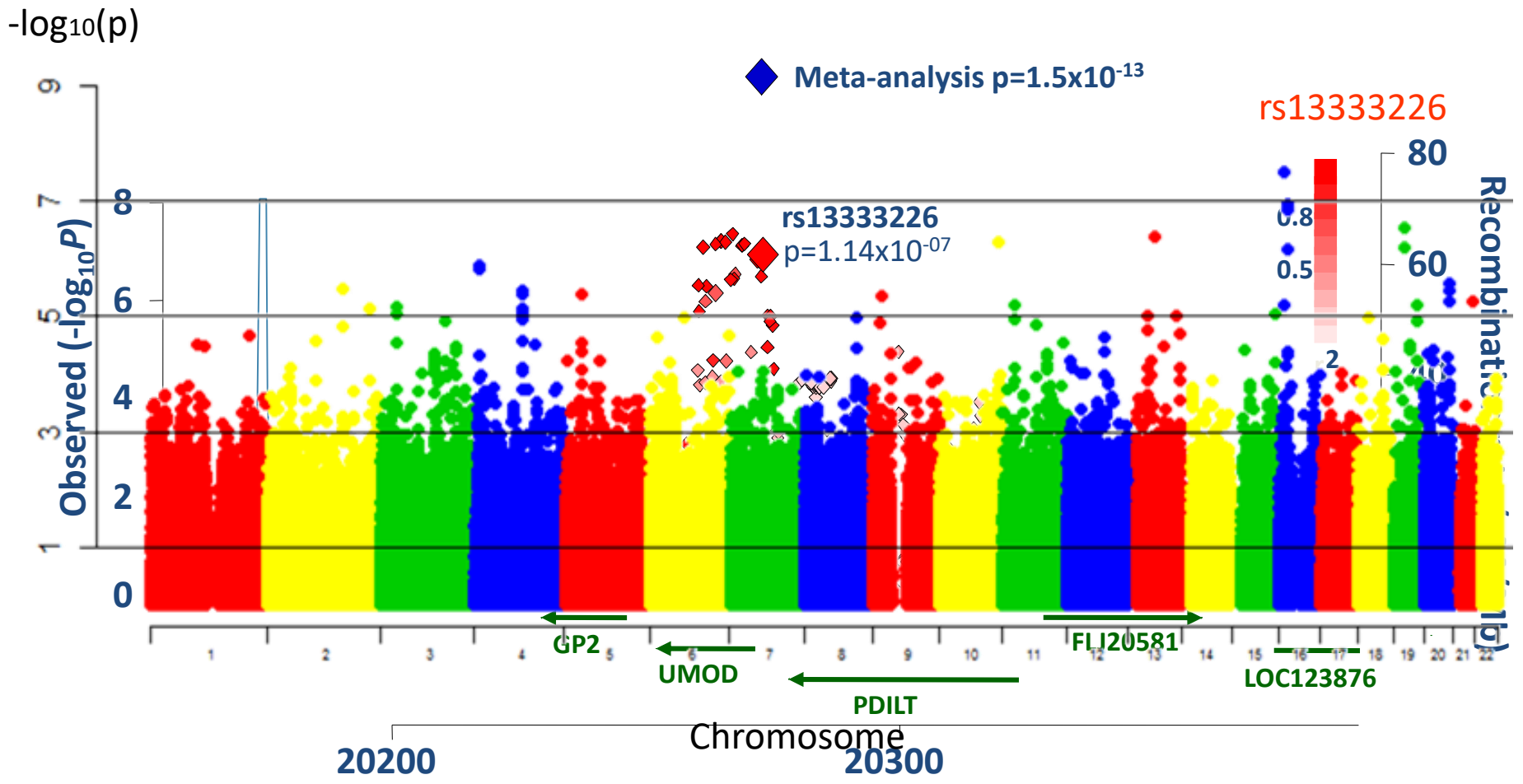
PLoS GENETICS

Genome-Wide Association Study of Blood Pressure Extremes Identifies Variant near *UMOD* Associated with Hypertension

Sandosh Padmanabhan[1], Olle Melander[2], Toby Johnson[3], Anna Maria Di Blasio[4], Wai K. Lee[1], Davide Gentilini[4], Claire E. Hastie[1], Cristina Menni[1,5], Maria Cristina Monti[4,6], Christian Delles[1], Stewart Laing[1], Barbara Corso[4,6], Gerjan Navis[7], Arjan J. Kwakernaak[7], Pim van der Harst[8], Murielle Bochud[9], Marc Maillard[10], Michel Burnier[10], Thomas Hedner[11], Sverre Kjeldsen[12], Björn Wahlstrand[11], Marketa Sjögren[2], Cristiano Fava[2,13], Martina Montagnana[2,14], Elisa Danese[2,14], Ole Torffvit[15], Bo Hedblad[2], Harold Snieder[16], John M. C. Connell[17], Morris Brown[18], Nilesh J. Samani[19], Martin Farrall[20], Giancarlo Cesana[5], Giuseppe Mancia[5], Stefano Signorini[21], Guido Grassi[5], Susana Eyheramendy[22], H. Erich Wichmann[23,24], Maris Laan[25], David P. Strachan[26], Peter Sever[27], Denis Colm Shields[28], Alice Stanton[29], Peter Vollenweider[30], Alexander Teumer[31], Henry Völzke[32], Rainer Rettig[33], Christopher Newton-Cheh[34,35], Pankaj Arora[34,35], Feng Zhang[36], Nicole Soranzo[36,37], Timothy D. Spector[36], Gavin Lucas[38], Sekar Kathiresan[34,35], David S. Siscovick[39], Jian'an Luan[40], Ruth J. F. Loos[40], Nicholas J. Wareham[40], Brenda W. Penninx[41,42,43], Ilja M. Nolte[16], Martin McBride[1], William H. Miller[1], Stuart A. Nicklin[1], Andrew H. Baker[1], Delyth Graham[1], Robert A. McDonald[1], Jill P. Pell[44], Naveed Sattar[1], Paul Welsh[1], Global BPgen Consortium[¶], Patricia Munroe[3], Mark J. Caulfield[3], Alberto Zanchetti[4,45], Anna F. Dominiczak[1*]

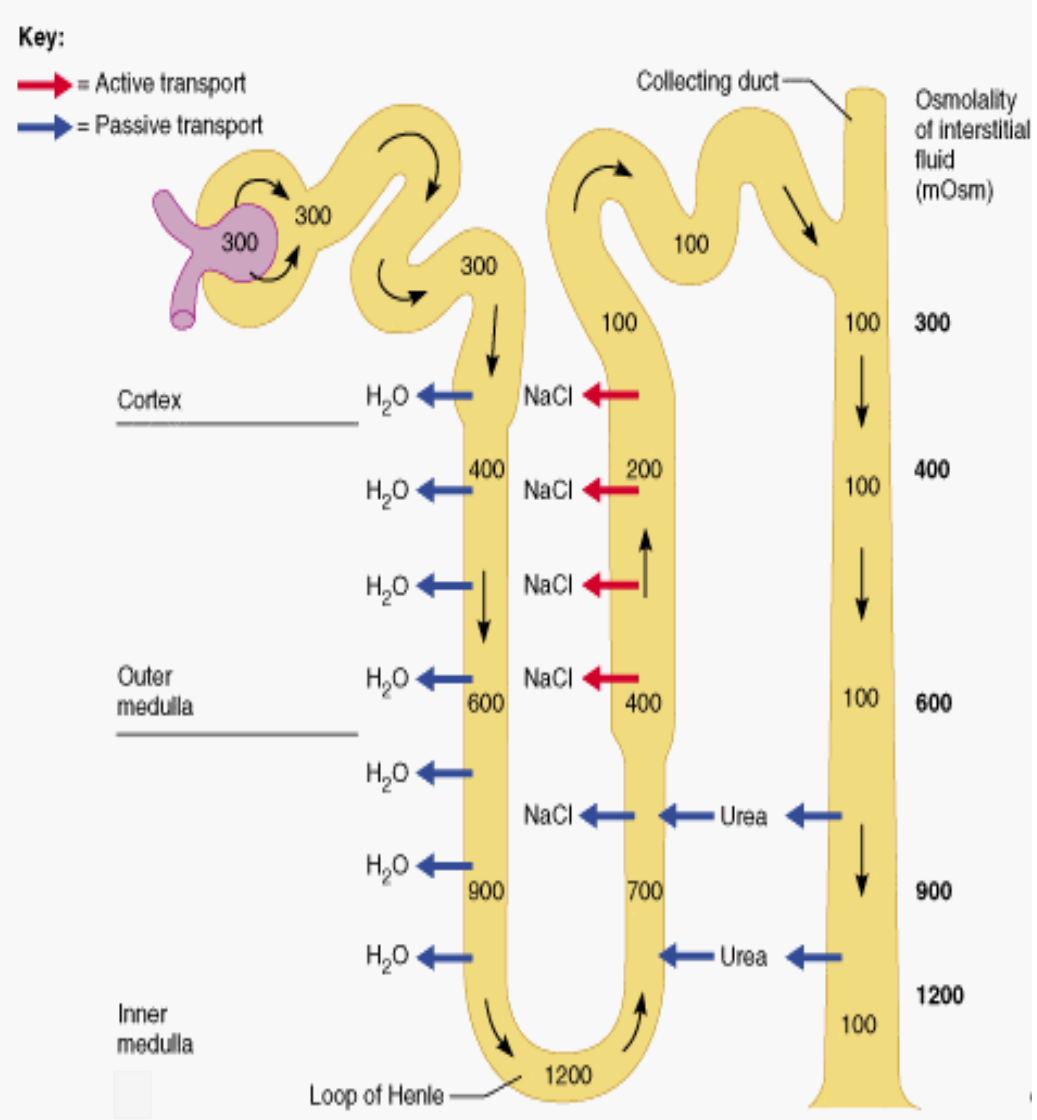
Padmanabhan S et al. PLoS Genetics 2010;6:e1001177

Uromodulin regulates sodium homeostasis in the kidney



Padmanabhan S et al. PLoS Genetics 2010;6:e1001177

Uromodulin



Previously called Tamm– Horsfall protein

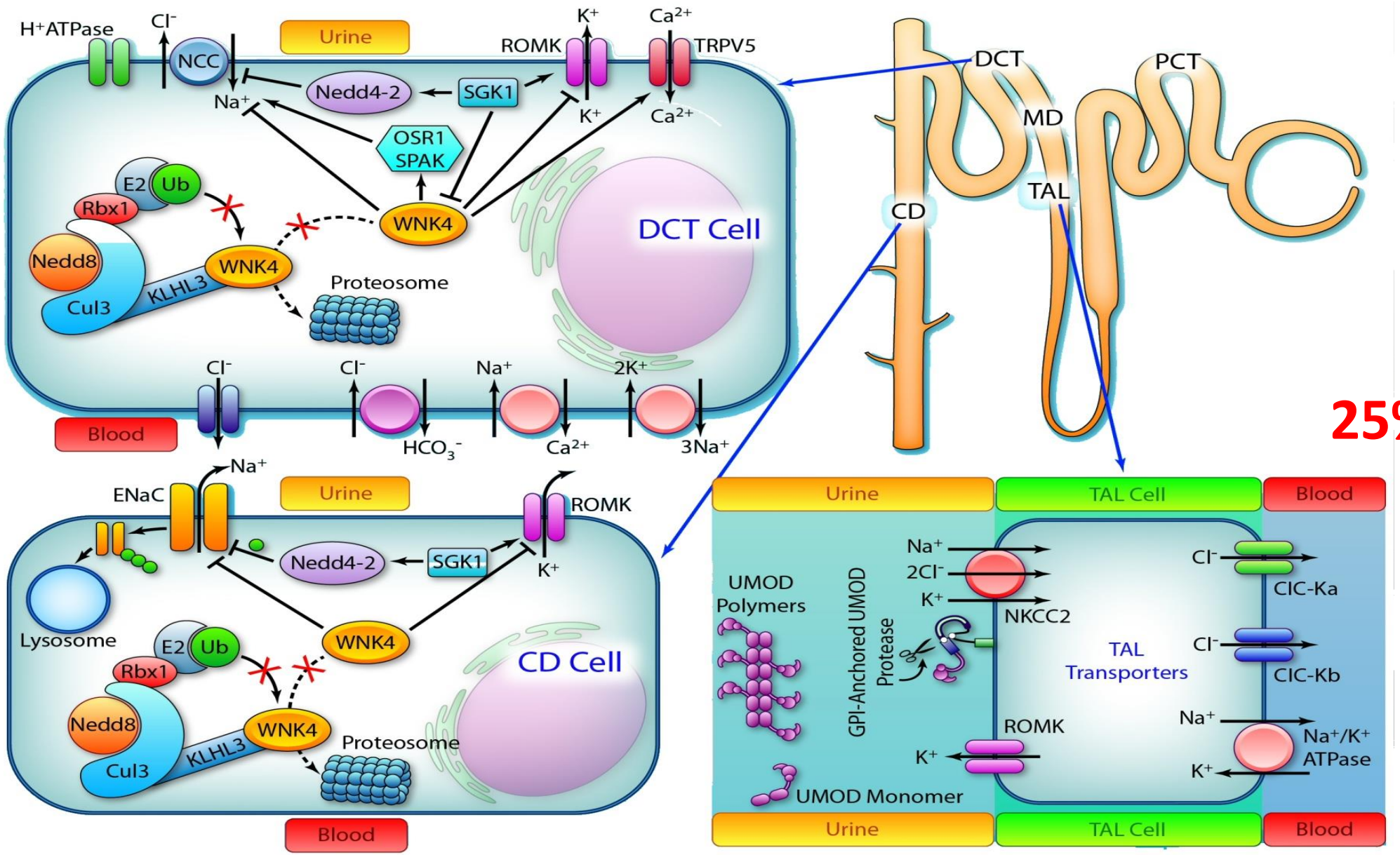
Expressed exclusively by the **thick ascending limb of the loop of Henle** and released into urine from the apical cell membrane.

The thick ascending limb of Henle is impermeable to water and is the site where 25% of filtered Na^+ is reabsorbed.

In physiological range it is the most abundant urinary protein.

It is a protective factor for UTI and renal stones.

Molecular pathways affecting sodium transport

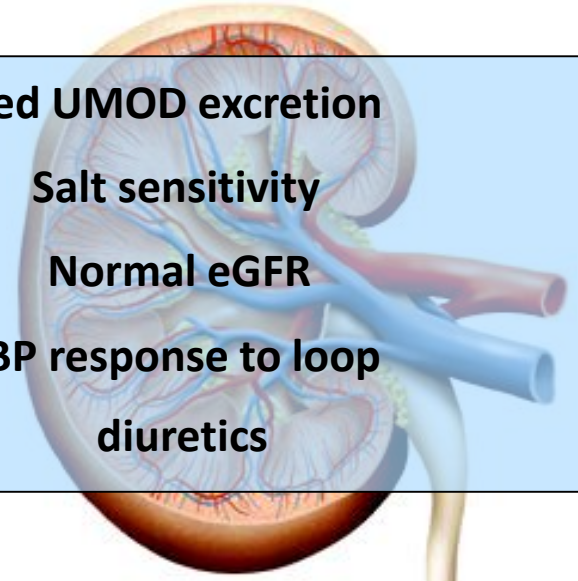


Padmanabhan et al, Circ Res 2015;116:937

UMOD & Precision Medicine

Hypertension Strata by *UMOD* rs13333226

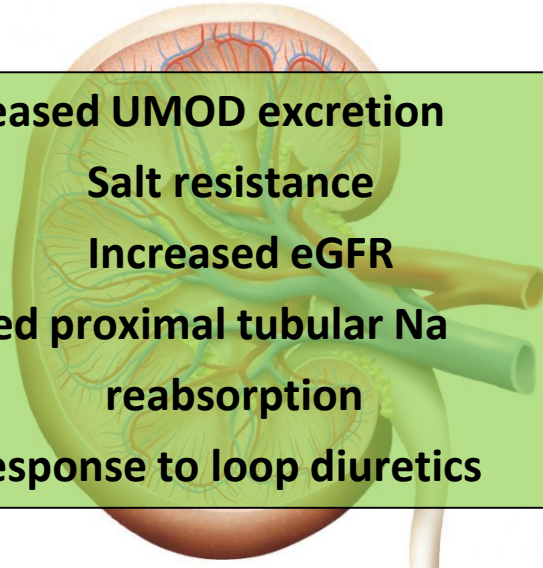
High-UMOD Hypertension



- Increased UMOD excretion
- Salt sensitivity
- Normal eGFR
- Greater BP response to loop diuretics

AA genotype – 67%

Low-UMOD Hypertension



- Decreased UMOD excretion
- Salt resistance
- Increased eGFR
- Increased proximal tubular Na reabsorption
- Poor BP response to loop diuretics

AG/GG genotype – 33%

Uncontrolled Hypertension → genotype guided algorithm to determine use of loop diuretic → early add-on loop diuretics in those with AA genotype

Precision Medicine Clinical Trial

Dundee

Clinical Research Centre
Health Informatics Centre&Memo
CRUK laboratories

Glasgow
Integrated CRF

Queen Elizabeth University Hospital
Royal Infirmary
Beatson Oncology Centre

Repurposing of Torasemide based on genetic make up

Screening
Uncontrolled Hypertension
BP>140/90

2 week run in
Discontinue diuretics if prescribed

Bloods
Ambulatory Blood
Pressure Monitoring

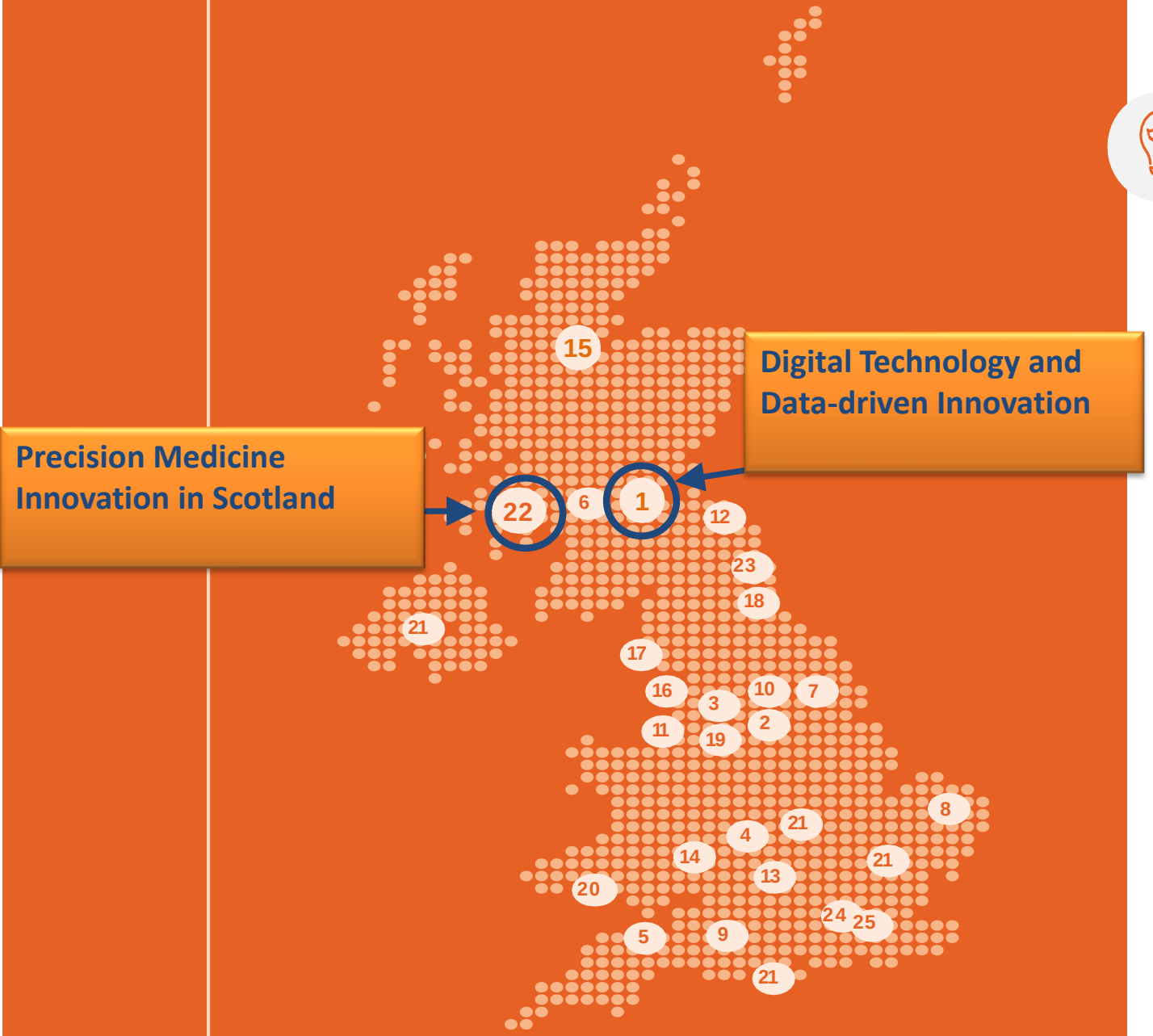
28days | 56days | 84days | 112days

Torasemide 5mg OD

Wellcome CRF
Institute Med Cell Biol

Commenced May 2017

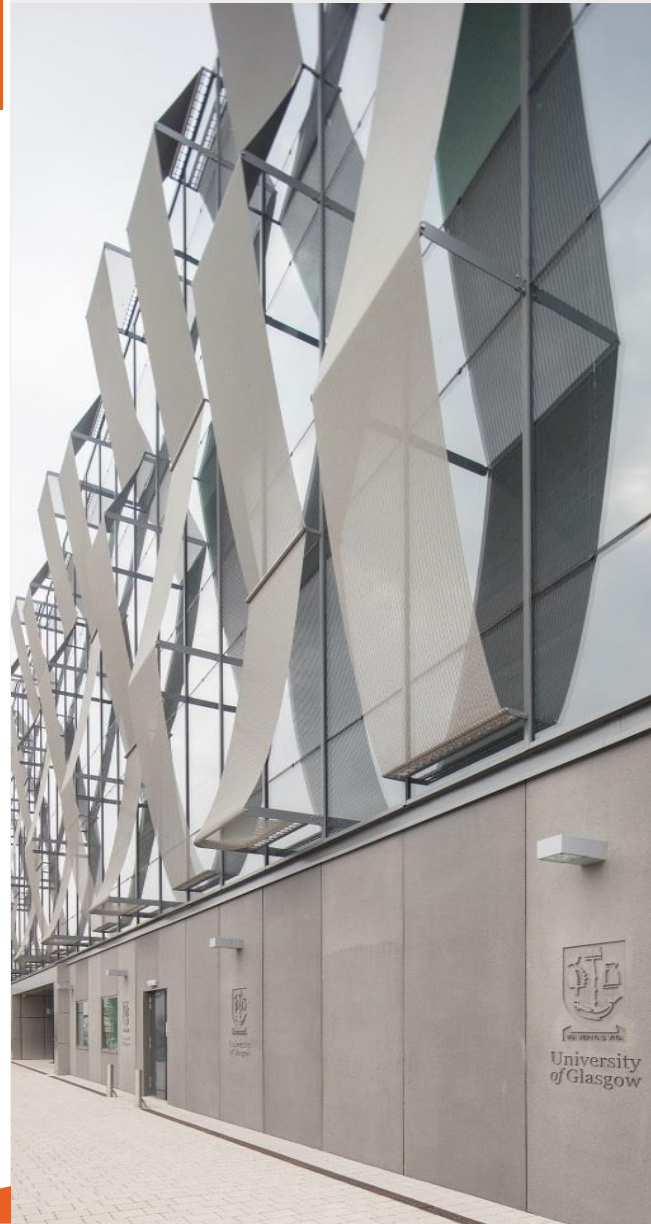
Recruitment End Nov 2019



INDUSTRIAL STRATEGY

University of Glasgow

'Science and Innovation Audits help local organisations map their research and innovation strengths, and identify areas of potential global competitive advantage.'



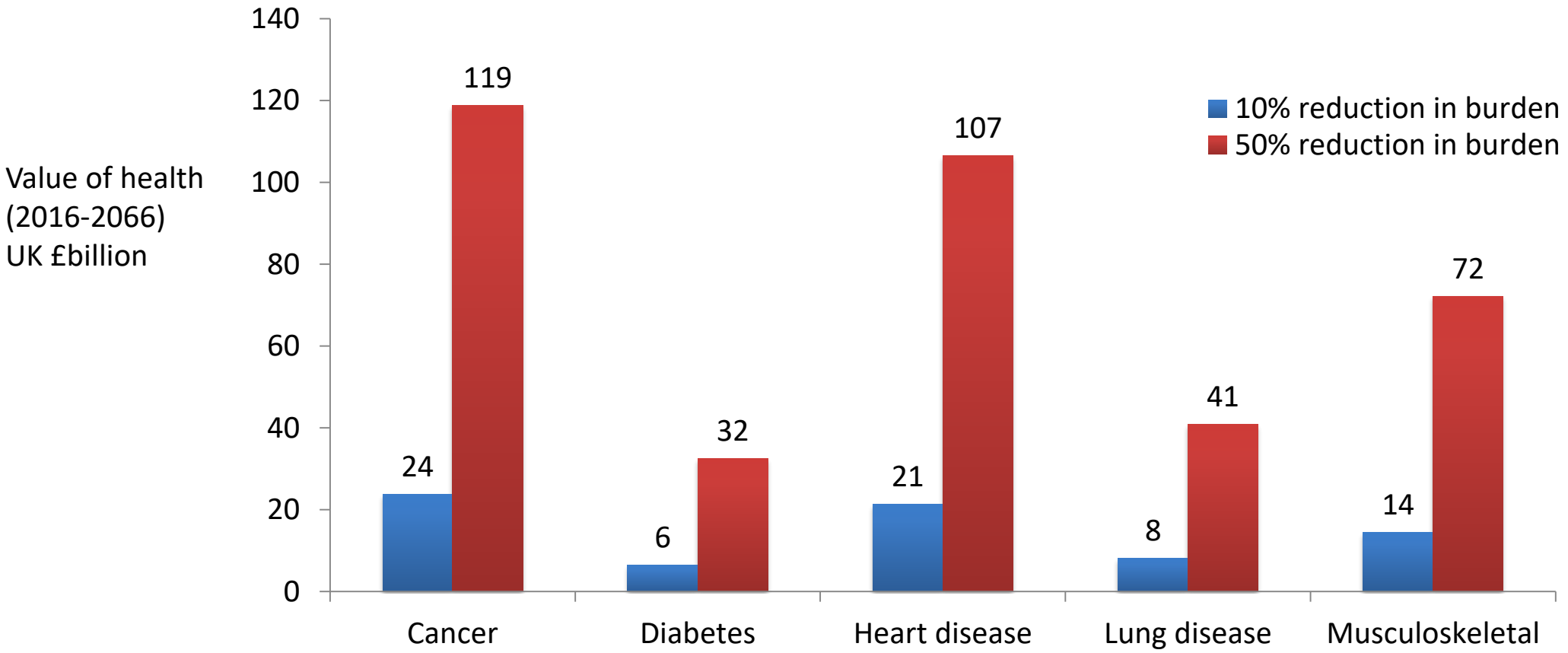
Precision Medicine: the economic opportunity

www.gla.ac.uk/precisionmedicine/SIA

"The global market value:
2016 - $43bn
2025 - $134bn "

In Scotland PM could save the NHS - £1.5bn over 5 years

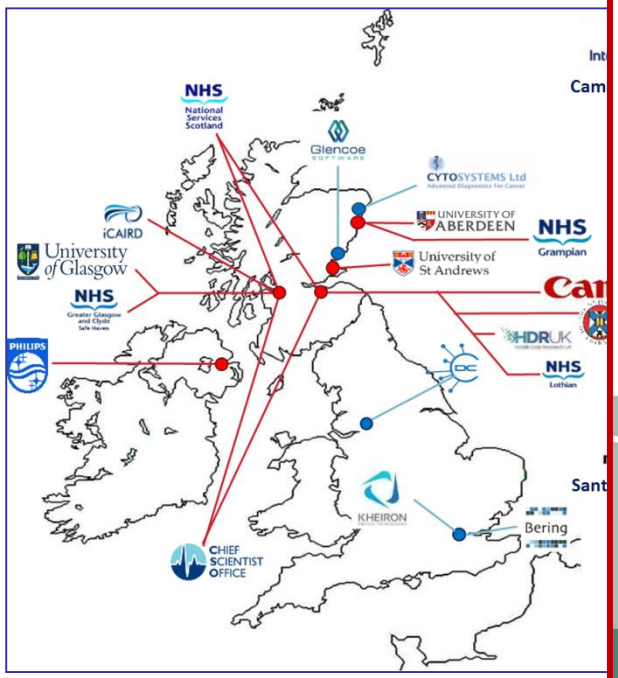
Potential value of Precision Medicine in Scotland



- Uses methodology adapted from Dzau et al, The Lancet (2015)
- Annual Burden of Disease from The Scottish Burden of Disease Study, 2015 available from http://www.scotpho.org.uk/media/1474/sbod2015-overview-report-july17.pdf
- Assumes 10% and 50% reduction in burden from hypothetical precision medicine innovations in five major disease groups
- Additional QALYs valued at £20,000 in line with lower accepted UK threshold

‘Game-changing’ Opportunities for Scotland

1. Next generation clinical dec
support tools



Department for Business, Energy & Industrial Strategy

Precision Medicine Innovation in Scotland:
Accelerating Productivity Growth for Scotland and the UK

INDUSTRIAL STRATEGY | UK Research and Innovation

. QEUH as a ‘living laboratory’ to
ealise the potential of PM and drive
conomic growth

ThermoFisher SCIENTIFIC
Stratified Medicine Scotland
Bio Clavis
NHS Greater Glasgow and Clyde
aridhia
Spiritus
SIEMENS Healthcare
MR CoilTech

PF full proposal in progress……

Safe Haven AI Platform at ICE - SHAIP

Clinical Cockpit

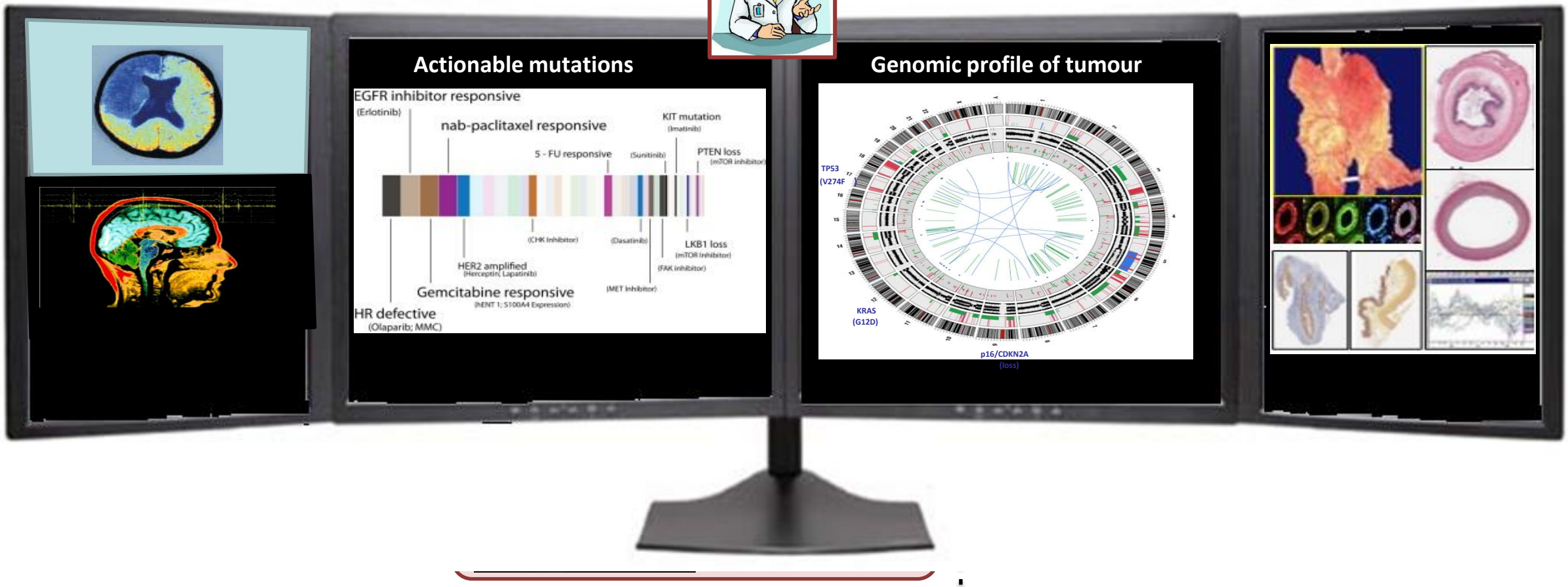
Healthcare Enterprise | Technology Company

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

Clinician

Data Controller

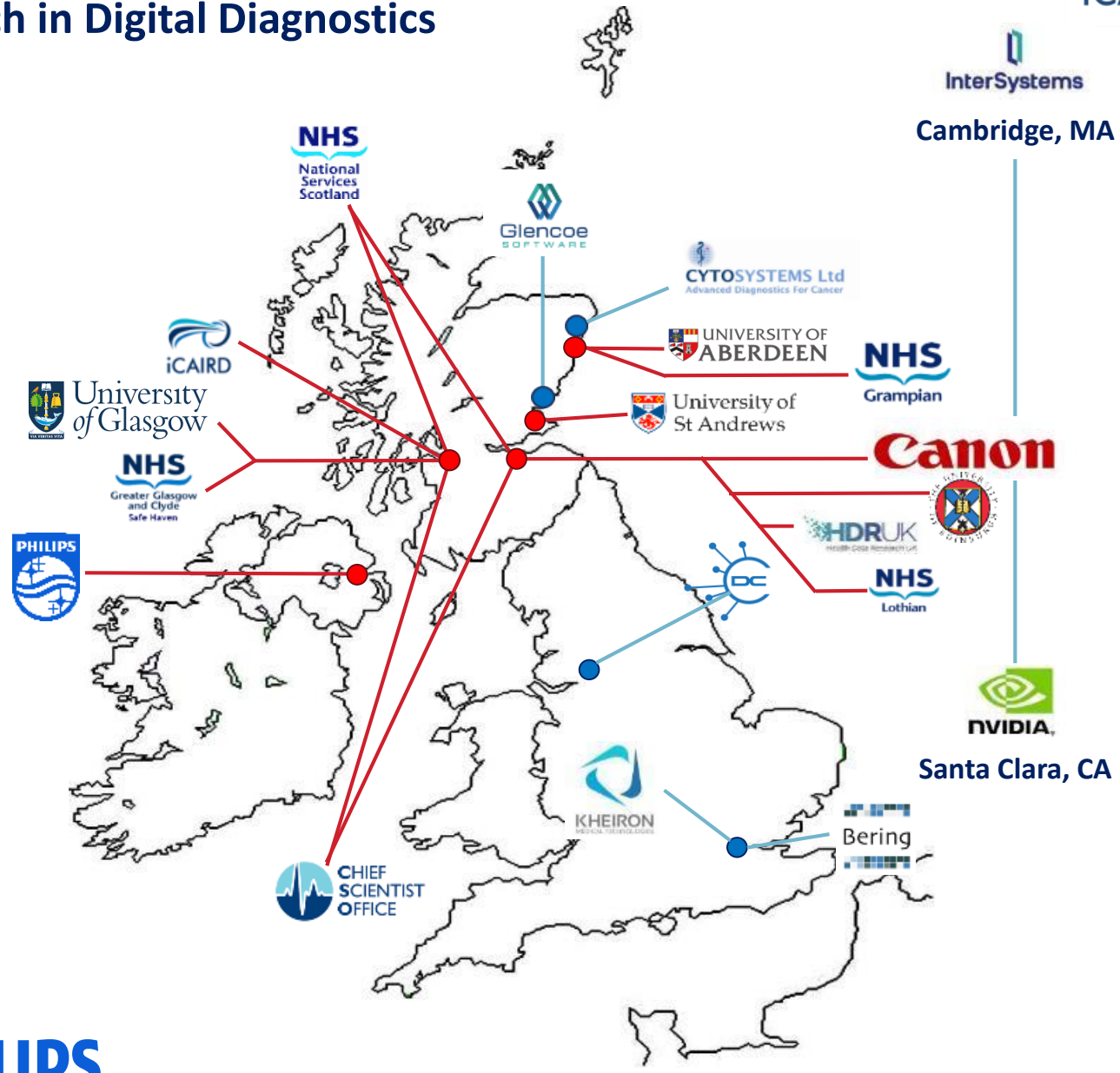
Researcher



Dr Ken Sutherland

iCAIRD

Industrial Centre for Artificial Intelligence Research in Digital Diagnostics



Key features

- University of Glasgow led
- Pan-Scotland initiative
- £10M from Innovate UK
- £6M from industry partners
- 6 SME partners involved in exemplars
- Brings Philips and SMEs to Clinical Innovation Zone

‘The Living Laboratory’ Proposal

University of Glasgow

NHS Greater Glasgow and Clyde

- Environment and ecosystem for Business Growth
- Proximity to world-class academic/ clinical/ industry expertise
- Health Innovation Hub with enabling infrastructure for innovation and clinical adoption

Real World Implementation of PM

Industry Use Cases

Accelerating Commercial Innovation

- Accelerating productivity growth for Scotland
- Healthcare cost avoidance
- Improving patient outcomes

ThermoFisher SCIENTIFIC

Bio:Clavis

Stratified Medicine Scotland

SIEMENS Healthcare

MR CoilTech

aridhia

Canon

Living Laboratory: Use Case

Analysis of Initial Glasgow Cohort

ThermoFisher: diversification in Scotland; Coriell: new to Scotland

Initial Cohort Analyzed: Aged 65+ on multiple medications

Data de-identified, economic analysis conducted upfront

- Average number of medications per member: 8
- Most prevalent condition: High blood pressure
- Most costly condition: Diabetes

Nearly 22% of this cohort (36,000 people) at risk of medication failure or significant adverse reaction from at least 1 medication prescribed

71% taking at least one drug with known genetic implications

Predicted cost savings of >£85M over three years upon implementation

165k 65+ year old Poly-pharmic Individuals

>£450M Annual pharmaceutical spend

£2.7B Annual health care spend

~£85M Potential Savings in 3 years

ThermoFisher SCIENTIFIC

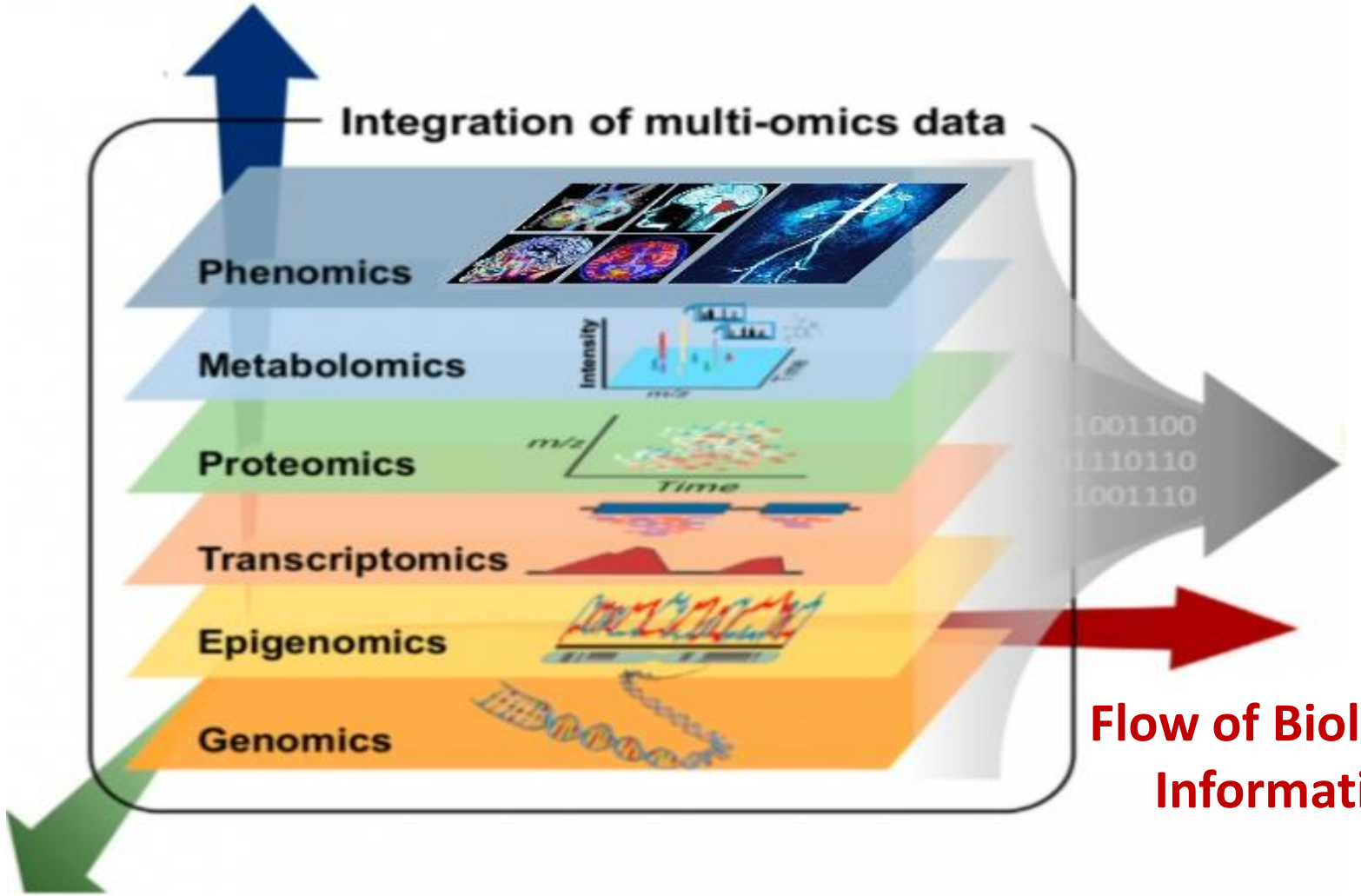
Precision Medicine: Report by the World Innovation Summit for Health (WISH)

Case study 8: Scotland Precision Medicine Ecosystem

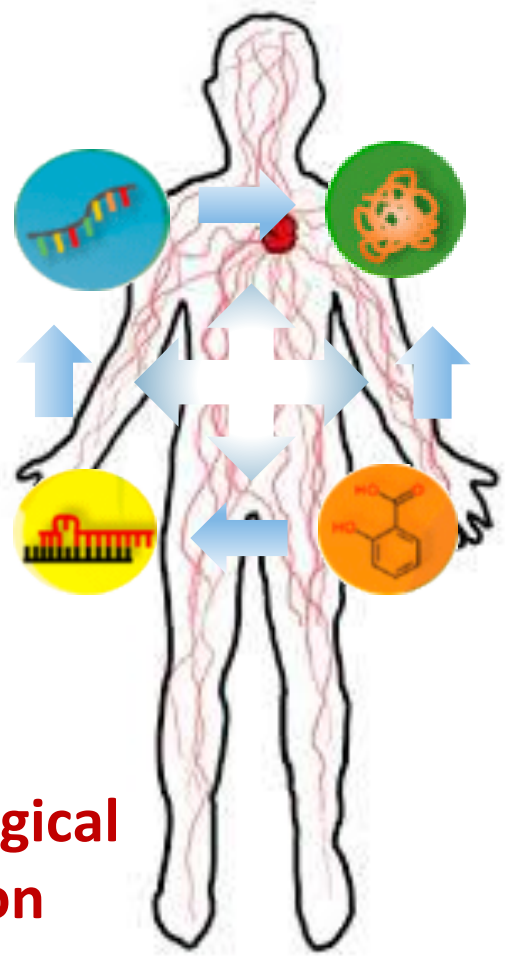
The SMS-IC will help organizations develop capabilities and assets to create PM solutions that attract commercial investment and have the potential to generate revenue for Scottish partners. This model is intended to accelerate the adoption of genomic services and enable broader academic, industrial and NHS participation across Scotland.

Precision Medicine is ready for clinical use

Analysis



Flow of Biological Information



Clinical utility

Network Modelling
Functional annotation

\+ digital radiology & digital pathology


University of Glasgow
VIA VERITAS VITA
Thank You
SUPPORT
INSPIRING
PEOPLE

University of Glasgow

Scotland's Ecosystem for Precision Medicine

- Connected Ecosystem
- Broad Industry Base
- Advanced Exemplars
- Academic Leadership
- Forward-thinking NHS
- Electronic Health Records
- Chronic Disease, Patient Trust
- Data Integration and Analysis
- Rapid NHS Adoption
- Diagnostics
- Clinical Trials
- Commercial Products
- Fast Regulatory Approval

NHS SCOTLAND

SHARE

Scottish Enterprise

HDRUK Health Data Research UK

Innovate UK

Scottish Funding Council
Promoting further and higher education

Queen Elizabeth University Hospital (QEUH)

UNIVERSITY OF ABERDEEN

University of Dundee

THE UNIVERSITY of EDINBURGH

University of Glasgow

HERIOT WATT UNIVERSITY

University of St Andrews

University of Strathclyde Glasgow

SCOTTISH DEVELOPMENT INTERNATIONAL

#SCOTLANDISNOW

ESH European Society of Hypertension

International Society of Hypertension

BIHS British and Irish Hypertension Society
Committed to preventing cardiovascular disease

Clinical Innovation Zone (CIZ) for Precision Medicine

CLINICAL INNOVATION ZONE

- Total of 22,000 sq ft
- Purpose-built industry space
- Located within QEUH
- Facilitated access to clinicians
- Flexible space – wet lab, dry lab, office space
- Hot-desk facilities for industry
- UK Science Parks Association (UKSPA)

Stratified Medicine Scotland

SIEMENS Healthcare

SIEMENS Healthineers

Canon

Spiritus

Bio:Clavis

aridhia

University of Glasgow

NHS Greater Glasgow and Clyde

MR CoilTech

CAUSEWAY THERAPEUTICS

LUCID

Thank you for attending the LUCID Conference