Team Science and Translation:
The Manchester Cancer Research Centre Approach

Translation Manchester – Nov 16 2022

Professor Robert Bristow MD PhD FRCPC FMedSci

Director, Manchester Cancer Research Centre and CRUK Manchester Centre
Chief Academic Officer - The Christie Foundation NHS Trust
University of Manchester Cancer Studies

MANCHESTER CANCER RESEARCH CENTRE

Patients At The Heart of the A Comprehensive Cancer Research Centre

"Answering the Daily Questions from Patients and Researchers"

Is Cell Therapy or Immunotherapy right for me?

How are you continually tracking my success of treatment?

Can you cure me when there is spread of disease?

I am concerned about my own cancer risk - so what can I do and what trials are ongoing?

I have severe heart problems – will this make them worse?

Can I get protons instead of photons?

Should I stop Metformin/Statins or other non-cancer drugs?

Does my ancestry or bloodline matter for my cancer response and preventing cancer in loved ones ?

Innovation is "a new idea, creative thoughts, new imaginations in form of device or method".

- **Innovation** is often also viewed as the application of better solutions that meet new requirements, unarticulated needs, or existing market needs.

- **Innovation** is a prerequisite of commercialisation

- The MCRC is committed to creating “Synergies and Soil” for **innovation** through **team science**

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A Few Areas to Explore Together

- The concept of the MCRC and Team Science
- Team Science: Definitions and Exemplars
- Effective Building of New Teams and ROI
- New Environments and Impact on Team Science

I have no disclosures

A Few Areas to Explore Together

- **The concept of the MCRC and Team Science**
  - **Pulling it under one roof and driving big programmes**
- Team Science: Definitions and Exemplars
- Effective Building of New Teams and ROI
- New Environments and Impact on Team Science

I have no disclosures

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- **Team Science & Strong Investment:** CRUK, UoM, The Christie NHS Foundation Trust
- **Breaking down silos:** affiliations with MFT, SRFT, GMCP, MAHSC and HInM
- 1 of 5 **Research Beacons** at University of Manchester and part of **UMRI**
- Competitively designed as an NCI-Designated **Comprehensive Cancer Research Centre**
- Increasing focus on complex populations, data and models - **EDI and Multimorbidity**

A Nexus of Research Excellence

TRANSLATION MANCHESTER

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wellcome

Personalised Cancer Medicine in Manchester

NHS Long Term Plan 55,000 more survivors in 2028

Large patient population
Broad trial portfolio
Real World Outcome
iMATCH
DETERMINE, TARGET
NATIONAL

NHS The Christie NHS Foundation Trust
Experimental Cancer Medicine and CRF

Clinical and Experimental Pharmacology
Genomics and Bioinformatics
CRUK Centre, ACED, RadNet
Proton Beam Therapy
Circulating biomarkers

CANCER RESEARCH UK

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Sample collection
infrastructure and SOPs

MANCHESTER CANCER RESEARCH CENTRE
Biobank

MANCHESTER 1824
The University of Manchester
Division of Cancer Sciences

Principal Investigators
Recruitment
Teaching and training

University Hospitals NHS NHS Foundation Trust
Centre for Genomic Medicine

Clinical Pathology Accreditation
Wide expertise in genomic medicine
Genetic counselling

Greater Manchester Cancer

NHS in Greater Manchester

GMCA GREATER MANCHESTER COMBINED AUTHORITY

Manchester Academic Health Science Centre

MCRC Adding Value to Commercialisation

CANCER RESEARCH UK

MANCHESTER

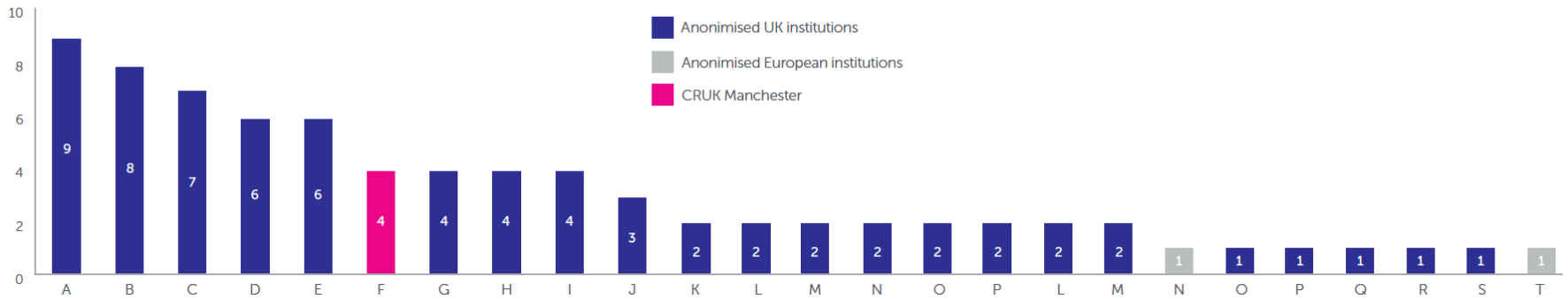
Commercial Partnerships Annual Review 2020/21

Together we will beat cancer

Next steps

- New Commercialisation post with Innovation Factory, CRUK, MCRC
- Focus on Digital assets and Advanced Materials

Number of Disclosures 20/21



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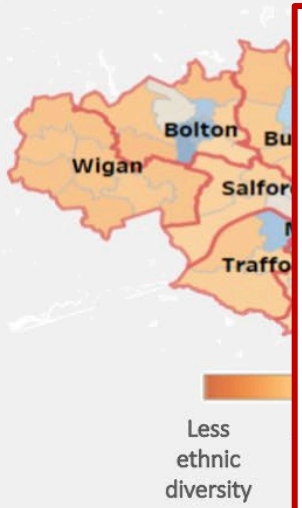
MANCHESTER 1824 The University of Manchester

The Manchester Challenge and Opportunity



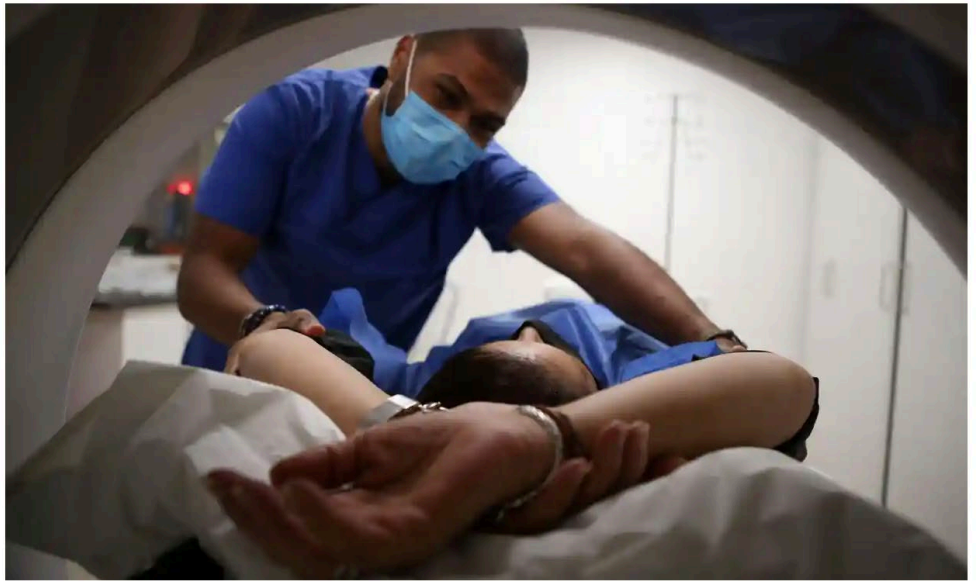
Cancer

Study reveals stark disparities in cancer rates between ethnic groups

Black people twice as likely to get prostate cancer while white people have double the chance of lung cancers

Andrew Gregory *Health editor*

Wed 2 Mar 2022 01.00 GMT



A radiographer gives a woman a lung scan. Photograph: Pascal Pochard-Casabianca/AFP/Getty Images

Stark disparities in cancer rates between different ethnic groups have been laid bare in new research showing black people are twice as likely to get prostate cancer while white people have double the chance of getting skin and lung cancers.

The analysis of NHS Digital cancer registration data by Cancer Research UK provides the most complete recording ever of cancer rates by ethnicity in

Greater Manchester Cancer

In som

each locality

and

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“Cancer Precision For All”

Harnessing inclusive translational science and driving clinical excellence to create a future free from the burden of cancer”

- Address the needs of medically and socially complex patients, many of whom are currently excluded from precision trials through an EDI lens
- Attention to patients’ underlying health that impact cancer behaviour, including comorbid metabolic or pathologic states (e.g., diabetes mellitus, atherosclerosis) and their attendant medications.
- Recognise that these factors and ethnic diversity leads to distinct tumour biologies including genetic instability levels, types of cancer drivers, differential toxicities and treatment outcomes.
- Ignoring patient and population complexity leads to imprecision in pre-clinical tumour biology with unrepresentative models and in clinical stratification and appropriate design of clinical trials.

The complexity and diversity of the Vision defined by the MCRC can only be addressed by team science

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The Digital Team and Digital Cancer Centre

Data Sciences in Everything We Do - Tackle Patient Complexity

A Rapid Learning Digital Cancer Centre System

E-linked Biobank & Models

Patient Data Promise

Capture
Real-World Data

(Real Time Christie, GP and other Trust data)

Analyze
Real-World Evidence

(AI-driven clinical decision support)

Implement
Practical Assessment
Improve Care

(Inclusion & Impact)

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Inclusive And Diverse Team Leads

Dirivng MCRC-designed interventions

Manchester-Barts Centres: EDI Series with foci on gender, ethnicity, social deprivation and LGBTQ+

GMCP-Health Inequalities Team

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Oyebanji Adewumi

Nalin Thakkar

EDI Directorate and Social Responsibility

Take the **trials and early detection** out to deprived communities

Increasing high school students and PhD offers to diverse trainees

#PrideIn Research

Precision in clinical trials using **orthogonal data from diverse populations** in Greater Manchester (GM)

NHS
The Christie
NHS Foundation Trust

Kelly Picard Smith

KUTRRH
Outcome Hub

George Njoroge

Diversity in **Genomics, Data and Models**

Comprehensive EDI training for all

Community Leads VOCAL-PPIE

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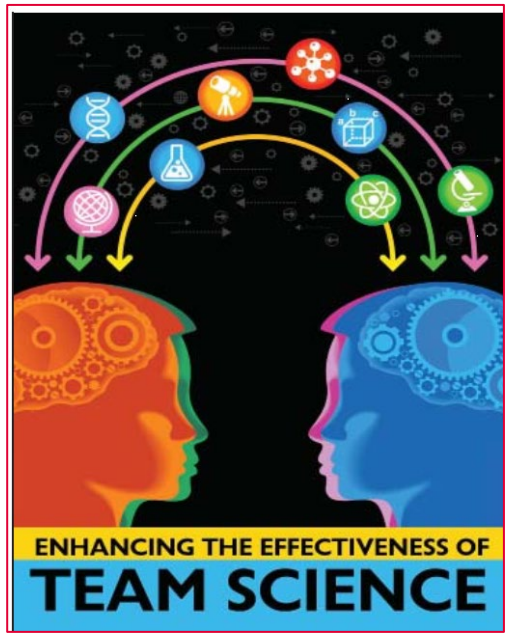
A Few Areas to Explore Together

- The concept of the MCRC and Team Science
- **Team Science: Definitions and Exemplars**
  - **Intramural and Extramural**
- **Effective Building of New Teams and ROI**
  - **Town Hall Concept**
- New Environments and Impact on Team Science

I have no disclosures

MCRC and Cancer Team Science

Creating "Synergies and Soil"



The nation turns to the National Academies—National Academy of Sciences, National Academy of Engineering,

MCRC Town Hall Concept:

- Build teams with complementary expertise and knowledge integration
- Patients, Scientists, Clinicians
- Collaborate to overcome the biggest cancer research challenges
- Goal Alignment across teams
- Break down research silos
- Forge long term multidisciplinary projects and collaborations
- Permeable and dynamic boundaries
- High diversity of membership

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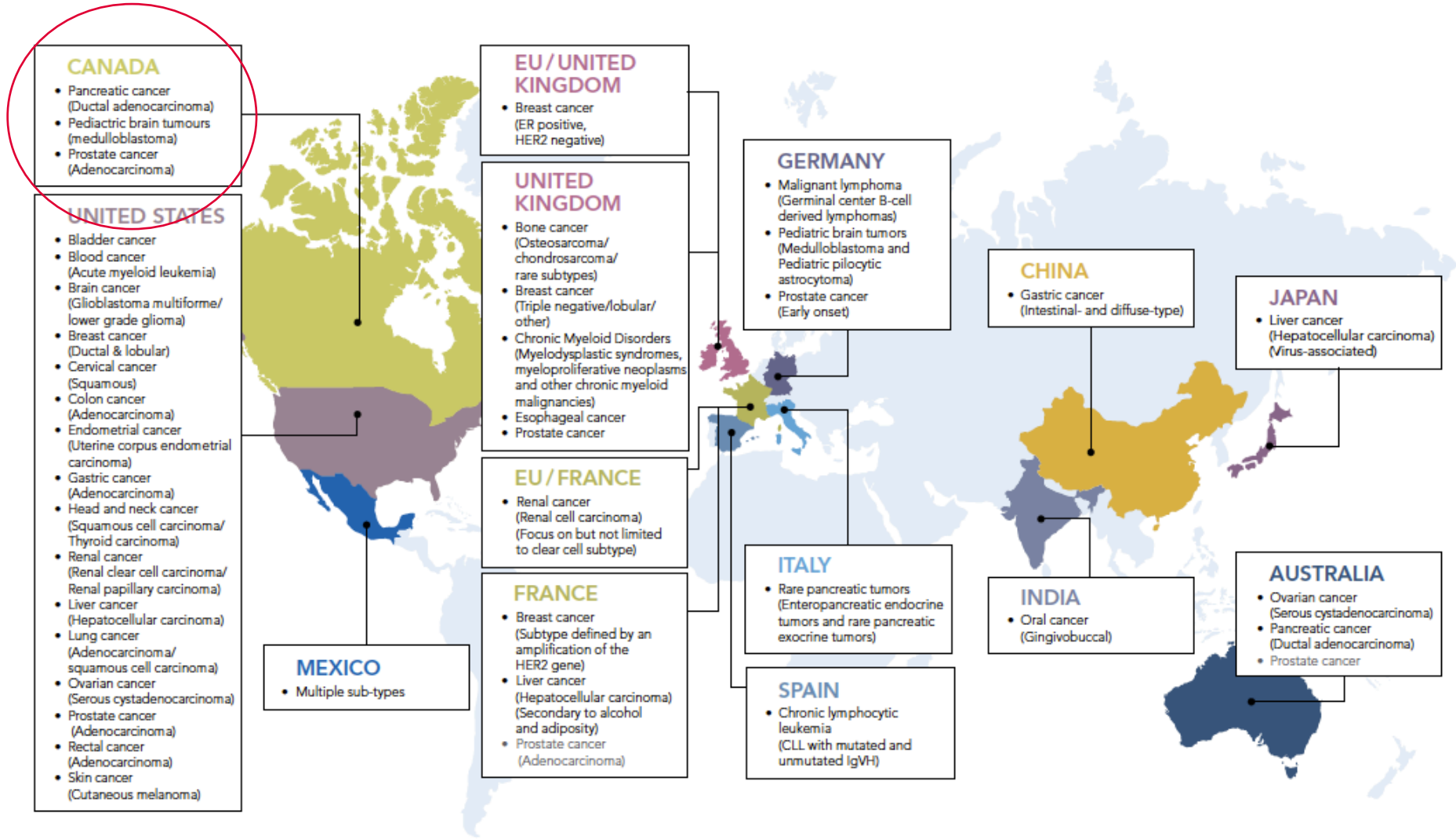
Academic Approaches: Team Science and Big Data



Canadian Prostate Cancer Project: $20 million to deliver 500 genomes

Side Projects became Careers for 4 new ECRs:
circular RNA, proteogenomics, enhancers and silencers, miRNA

Main Project = Metastatic Prostate Cancer Signature

Cell
Cancer Cell
Nature
Nature Medicine
Nature Comms
Nature Genetics
Lancet Oncology

2011
0 WHOLE GENOMES

Monthly Meetings-Strict Outputs
Change in lexicon amongst researchers
Troubleshooting shared across disciplines
SAB to keep to tight timelines
Shared first and senior authorships up front
Keep the politics within the seniors

2018
556 WHOLE GENOMES
PREFERRED COLLABORATOR

PAN PROSTATE CANCER GROUP

New Cancer Genomics – Spatial Multi'Omics Build & New Models

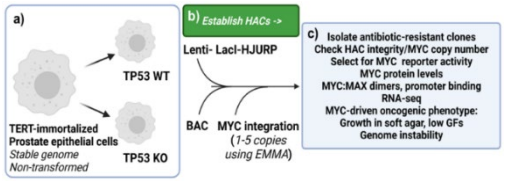
1. Clinical specimens and WGS of recurrent and metastatic prostate cancer

ManTRa Diagnostics

PAN PROSTATE CANCER GROUP

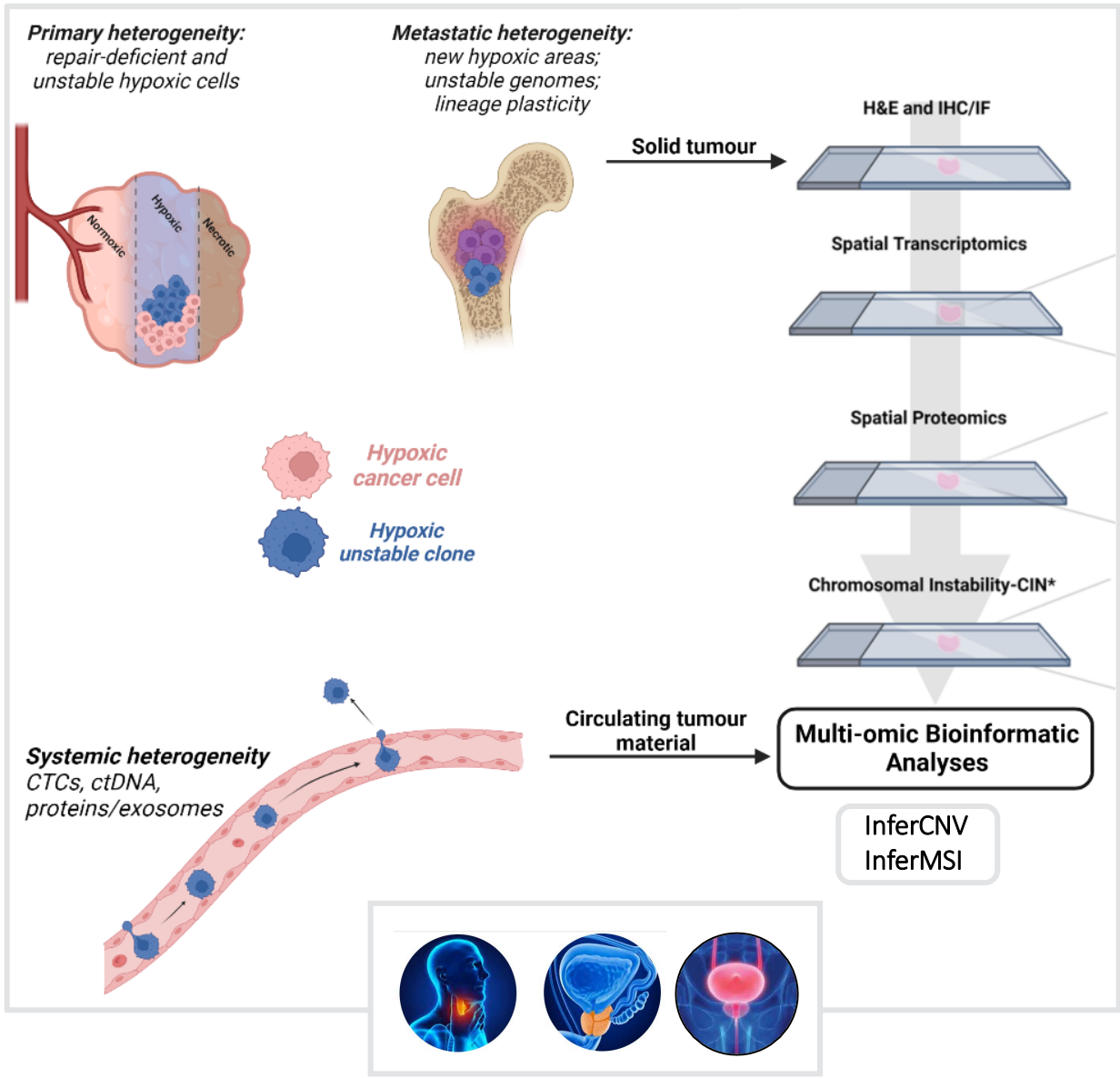
PROSTATE CANCER UK

2. Novel bioengineering of HACs containing chromosomal gains – exemplar Chr8 and MYC

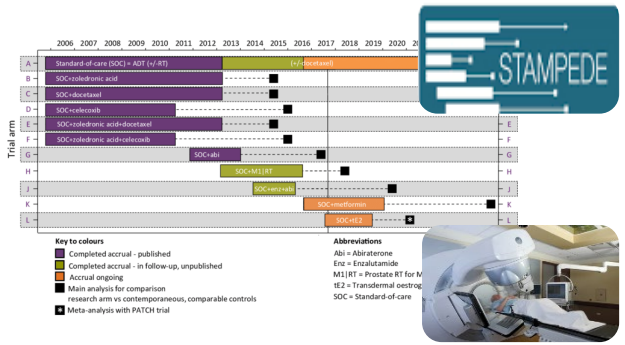


UKRI Biotechnology and Biological Sciences Research Council

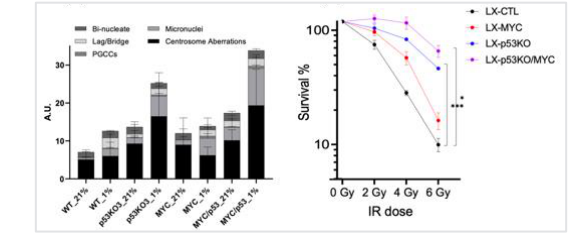
UKRI Engineering and Physical Sciences Research Council

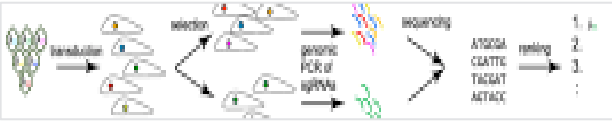


3. Germline determinants of prognosis in combined modality RT trials with RAPPER specimens

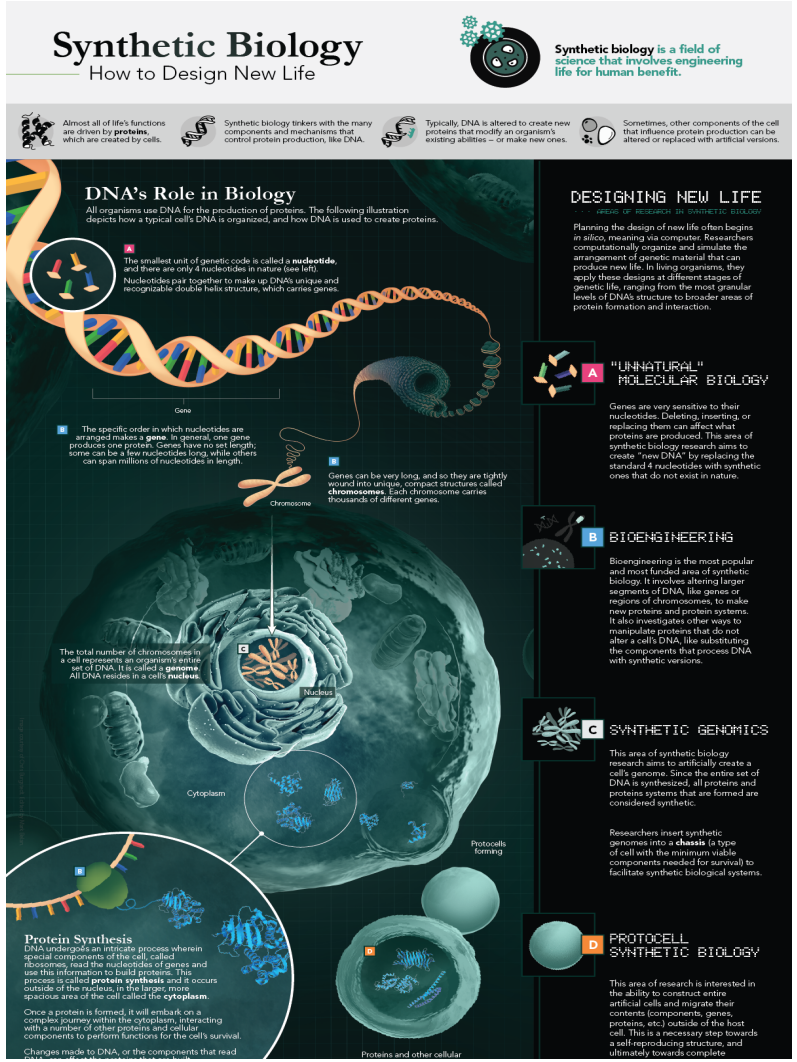


4. CRISPR screens for radioresistance genes in isogenic cells with AZ

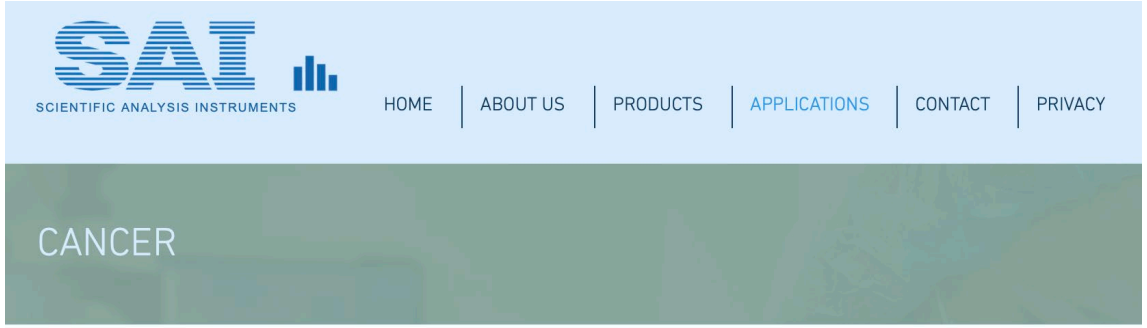




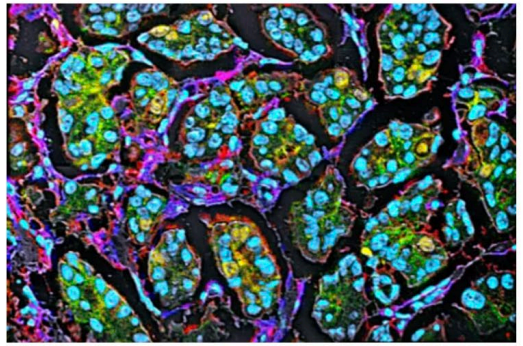
New Transdisciplinary Cancer Science: UKRPIF and Grants



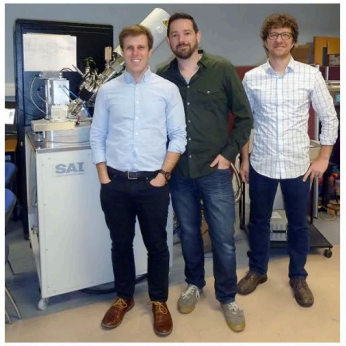
Manchester Institute of Biotechnology-BBSRC
BioEngineers – Cancer Models for Chromosomal Gains



SAI MidiSIMS ToF HR for MIBI
(Multiplexed Ion Beam Imaging)



The location and abundance of six proteins—e-cadherin (green), vimentin (blue), actin (red), estrogen receptor, progesterone receptor, and Ki67—found in breast cancer cells are seen in this multiplexed ion beam image. Cells positive for estrogen receptor a, progesterone receptor, and Ki-67 appear yellow; cells expressing estrogen receptor a and the progesterone receptor appear aqua. (Image courtesy Robert Michael Angelo See full article here.)



Leading cancer researchers from Stanford University, California putting the SAI ToF SIMS through its paces in Manchester UK for their MIBI application.
Left: Harris Fienberg, CEO, Ionpath Inc
Middle: Prof Sean Bendall
Right: Dr Robert Michael Angelo

Biologists, Engineers, Chemists -EPSRC
MIBI-TOF- Subcellular Imaging and Proteomics

Building Teams: The MCRC Town Hall Concept

- Open invitation to all, widely disseminated
  - Representation from wide range of professions
  - Junior up to extremely senior
  - Patients/representatives

- 2 hour town hall meeting:
  - Highly interactive
  - Chaired by MCRC Director
  - NOT a board meeting
  - NOT an exec/strategy meeting
  - NOT with a preset agenda, no decisions made in advance

MANCUNIAN SPEED DATE 2h
SESSION = "The New Idea"

Real Time Outcome
Genomics
Biobanking
Cancer Economics
Trainees

Problems/challenges of this approach…

- **Resistance** from Principal Investigators and Senior Leadership – why are we doing this? Why are we involving so many people rather than celebrating the individual ?

- **Involve and Align more** than just one (Christie NHS Foundation) Trust

- Securing involvement of **patient advocates** – having patients in the room changes the dialogue, and holds us to account on what we are really trying to do!

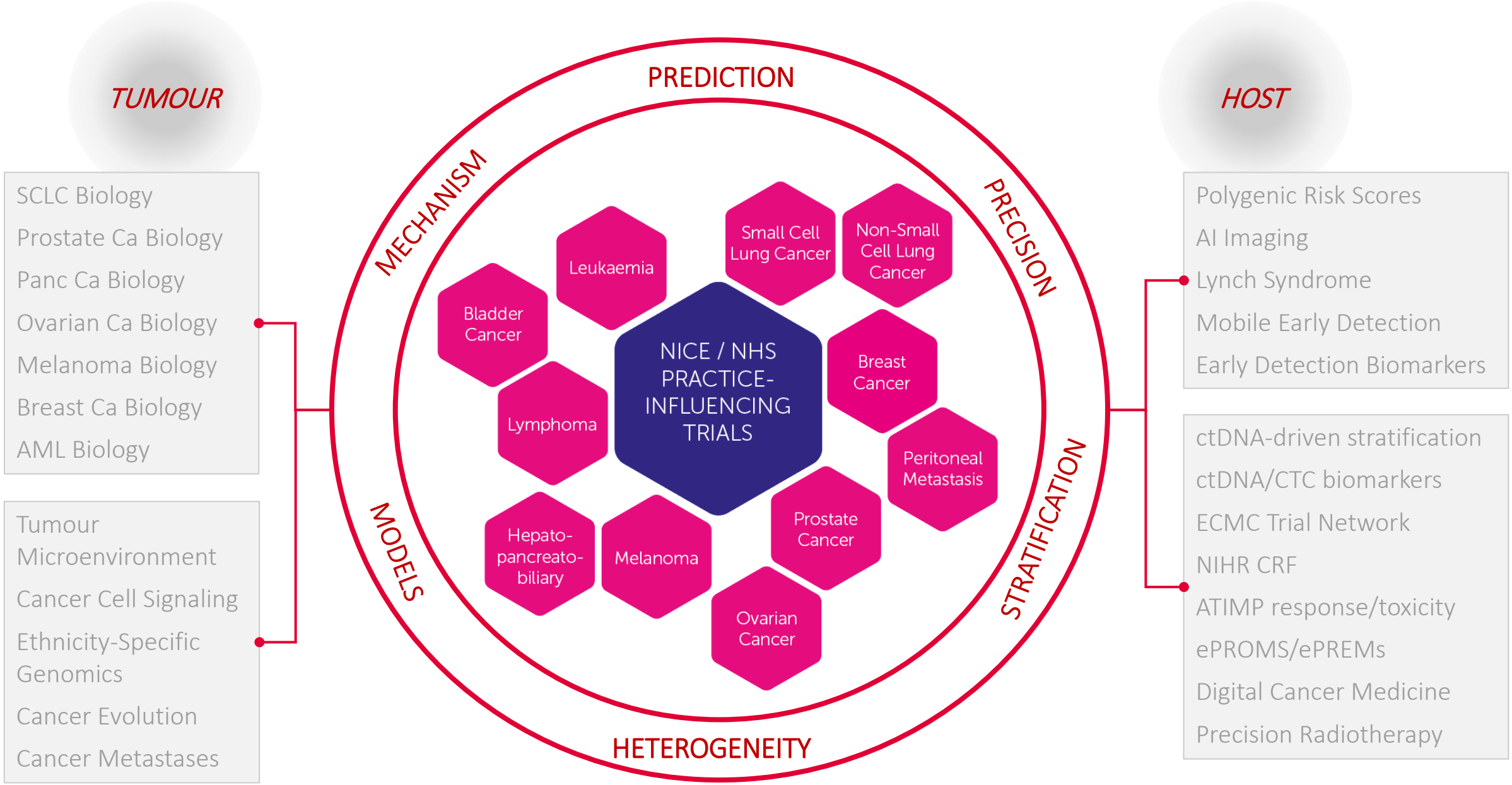
- **Projects that don't fit the remit…**
  - must be new teams, not existing teams
  - achievable within 3 years
  - progress towards a real change in clinical care
  - uplift junior faculty and staff
  - high-risk, high impact ideas only
  - unique to Manchester – cannot be done anywhere else

Team Science Projects Developed

Disease Group	Project title	Lay Headline
Breast	Breast cancer risk assessment pre-screening age	*'Young Women and Breast Cancer- Reaching the unreached"*
Melanoma	Towards melanoma and other skin cancer prevention in UK: the case for banning sunbeds	*'Manchester bans sunbeds'*
HaemOnc	Combining mass spectrometry platforms to deliver precision medicine for haematopoietic stem cell transplantation and graft versus host disease	*'Silent killer of bone marrow transplants stopped in tracks'*
Lung	Whether Manchester NSCLC patients have different molecular biology and genetics relative to other jurisdictions	*'Manchester lung cancer patients different to others in the UK'*
Hepato-pancreato-biliary (HPB)	MFT and Christie-hepatobiliary	*'Manchester improves survival in most difficult cancers by attacking cancer "scars"*

Prostate, ovarian, peritoneal, CNS, HEENT sites developed through grants and other meetings/approaches

ROI reported to Christie and University: ACED, new ECR (MRC Clinician Scientist), new Social Policy, Trust alignment



Across Trusts: Pairing Pre-Clinical Scientists with Clinical Acceptors

Benefits of the approach to translational teams…

- New collaborations and narratives and grant opportunities- builds beyond the silos of traditionally funded research
  - *"Chance only favours the prepared mind"*

- Pump priming funds and leveraged support from MCRC: including biobanking and samples, access to data, genomics, operational support

- Varired return on investment (ROI) based on teams formed – ROI can vary amongst funders and stakeholders

- **New strategic priorities** – MCRC will promote this research and support it moving forward at an accelerated pace = **RESEARCH BRANDs**

- Further opportunity for funding through links to University philanthropy teams, and our network of other funders across multiple disciplines

- Chance for ECRs to "shine"

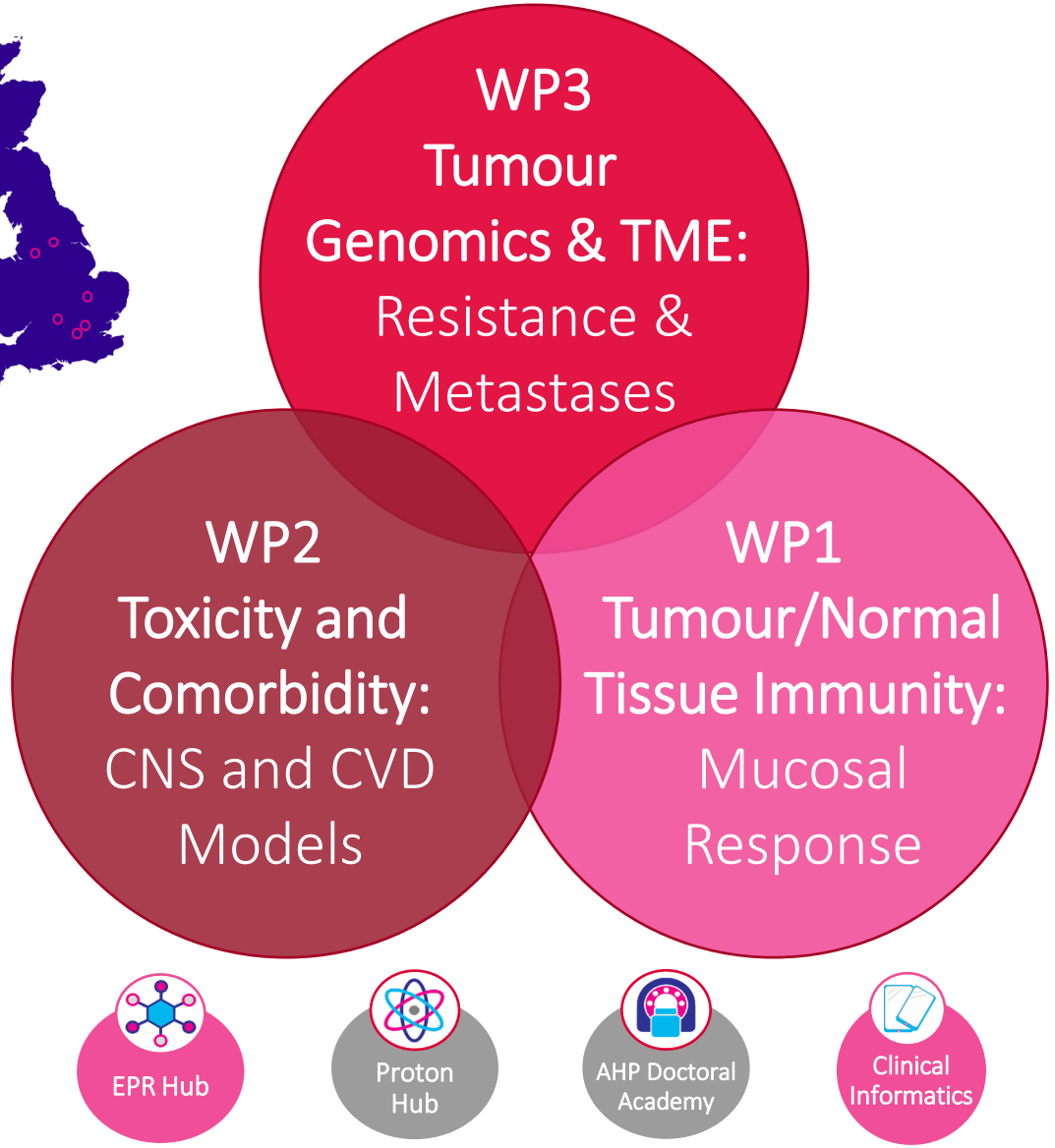
ROI: Alliance for Cancer Early Detection (ACED)

- **11** ACED PhD students
- To date, Manchester ACED has been awarded in excess of **£4.5M** in research and infrastructure funding:
  - £3.2M MERCADO original Award
  - **£2.3M* in subsequent ACED funding**
  - **£5M in Big Idea Grant in immune**
- Hosted ACED Summer School 2021
- Foci in biomarkers, big data, hereditary cancers, bioreactor models, PRS, genomics

CANCER RESEARCH UK · CANARY CENTER AT STANFORD · UNIVERSITY OF CAMBRIDGE · OHSU KNIGHT CANCER Institute · UCL · MANCHESTER 1824 The University of Manchester

ROI: CRUK RadNet as Intramural & National Team Science (£18M)

VISION: Understand the mechanistic interactions between the immune response, comorbidity/toxicity and genomics, for personalised RT



IMPACT

Insight from real-time outcome data

Address the challenges of diverse patient characteristics

Individualise physical and biological targeting

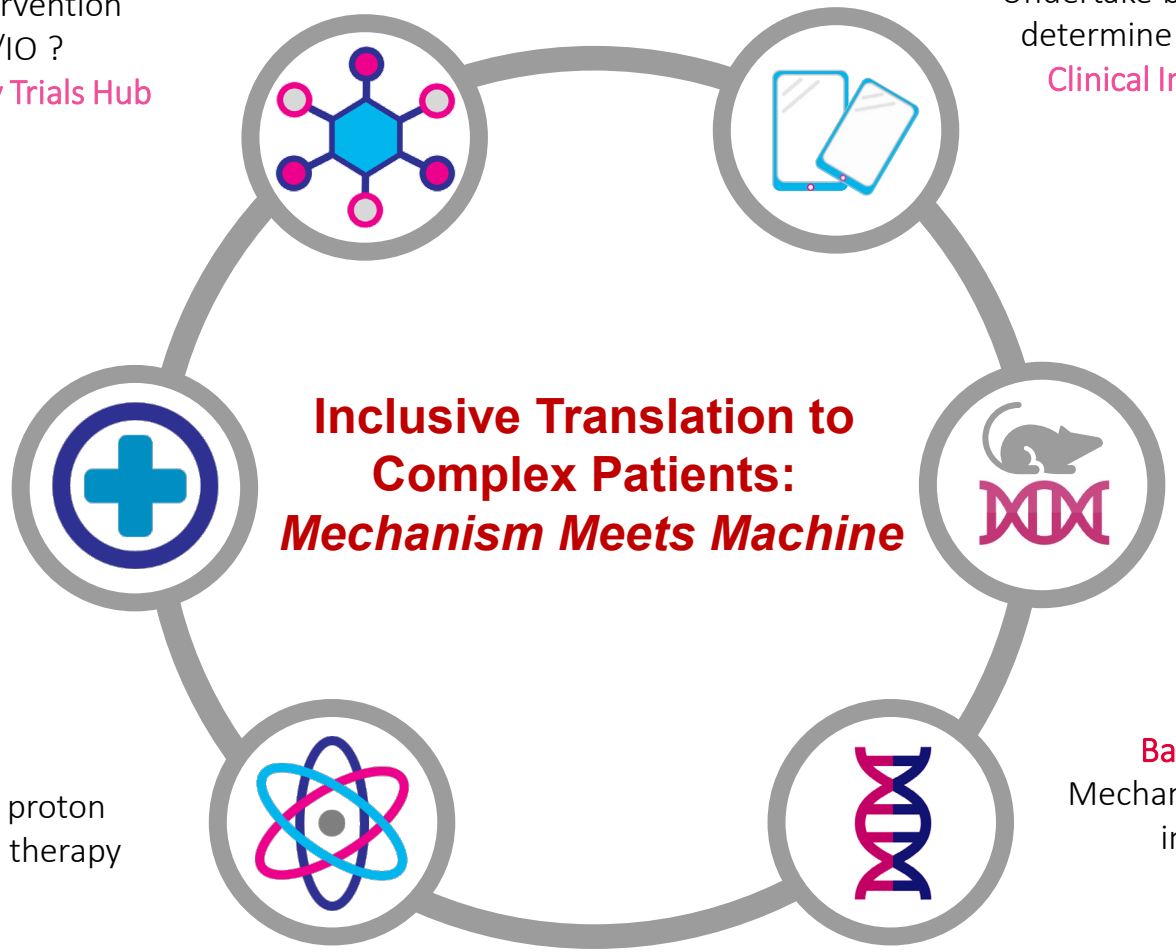
Additional role of systemic therapies

Levered 22M in grants and 19 PhD students

CANCER RESEARCH UK | RADNET MANCHESTER

Clinical Translation & Validation
Implementation & intervention
Protons ? RT-Drug/IO ?
Early Phase Radiotherapy Trials Hub

Big Data Analysis
Undertake big data analysis & determine causal structure
Clinical Informatics Hub



Nano-omics Biomarker Discovery
Radiation-induced molecular pathways & plasma proteomics
WP2

New Hypotheses and Novel Model Development
Modelling complex co-morbidities
WP1; WP2, WP3

Proton Research
Exploring in vitro and in vivo proton versus photon effects of each therapy
Proton Biology Hub

Back Translation
Mechanistic insight; novel interventions
WP1; WP2

Biomarkers

NEW SCIENCE

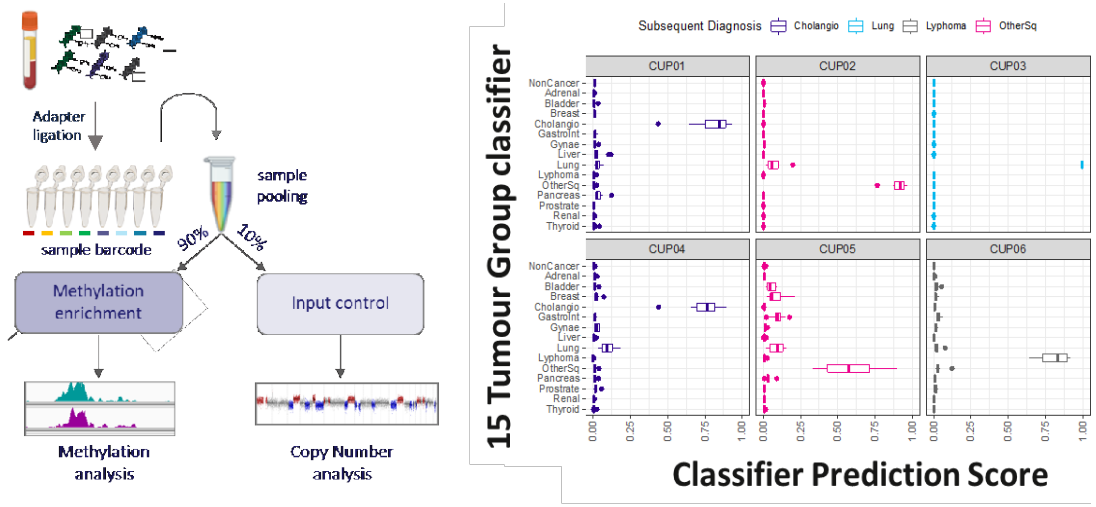
- **New ctDNA methylation utilities for unmet needs** (detection of 2nd cancers, tissue of origin in CUP)
- **New liquid biopsies** for paediatric cancers, brain cancer, leptomeningeal disease (blood, tears, CSF)
- **CTCs and ctDNA** and **early immune landscape** for early detection
- **New targets** in small cell lung cancer with **molecular subtyping** for personalised medicine

VFM

- **National Biomarker Centre and Experimental Cancer Medicines Centre collaborations**
- **Critical mass of specialist biomarker leads/ analysts/ technologists enhancing all themes**

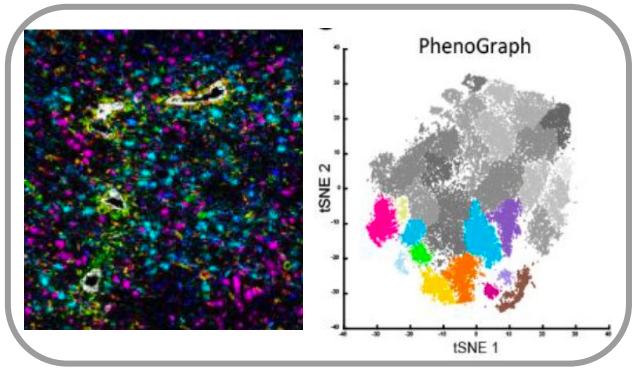
Taking the 'U' Out of CUP !

Tissue of origin reported in methylated ctDNA to support treatment decision-making - 5th leading cause of death in UK



- **International excellence** and best practice in biomarker science
- **Supports Primary Endpoint** liquid biopsies and clinical unmet needs to direct therapy

Integrative Pathology



NEW SCIENCE

- **"Architecture in Evolution":** rapid tissue procurements for resistance and recurrence
- **Patient-derived models** with full molecular pathological evaluation and outcome data
- **Multi-omic discoveries to inform biomarker development**

VFM

- **E-linked biobank for local and national researchers to test hypotheses and technology build with researchers and academic pathologists**

Radiotherapy BioAdaption

NEW SCIENCE

- **Dynamic 4D changes in TME** during radiotherapy using **fMRI & OE-MRI**
- **Aligned serial ctDNA to develop biomarkers of resistance and normal tissue toxicity**

VFM

- **Cross-training in medical physics, machine learning and biology at the intersection of radiomics and genomics – feedback into RadNet network**

Team BRAINatomy

- Paediatric radiation dosimetry and outcomes research
- Annotated clinical trial cohorts SJMB96 & SJMB03
- COG and PBTC biostatistical core

- **Largest childhood radiotherapy centre in N America**

St Jude

- Normal tissue effects of radiation
- Validated animal model
- Research particle irradiation facility
- Small animal imaging
- Sequencing facility

- **Only Netherlands paediatric proton centre**

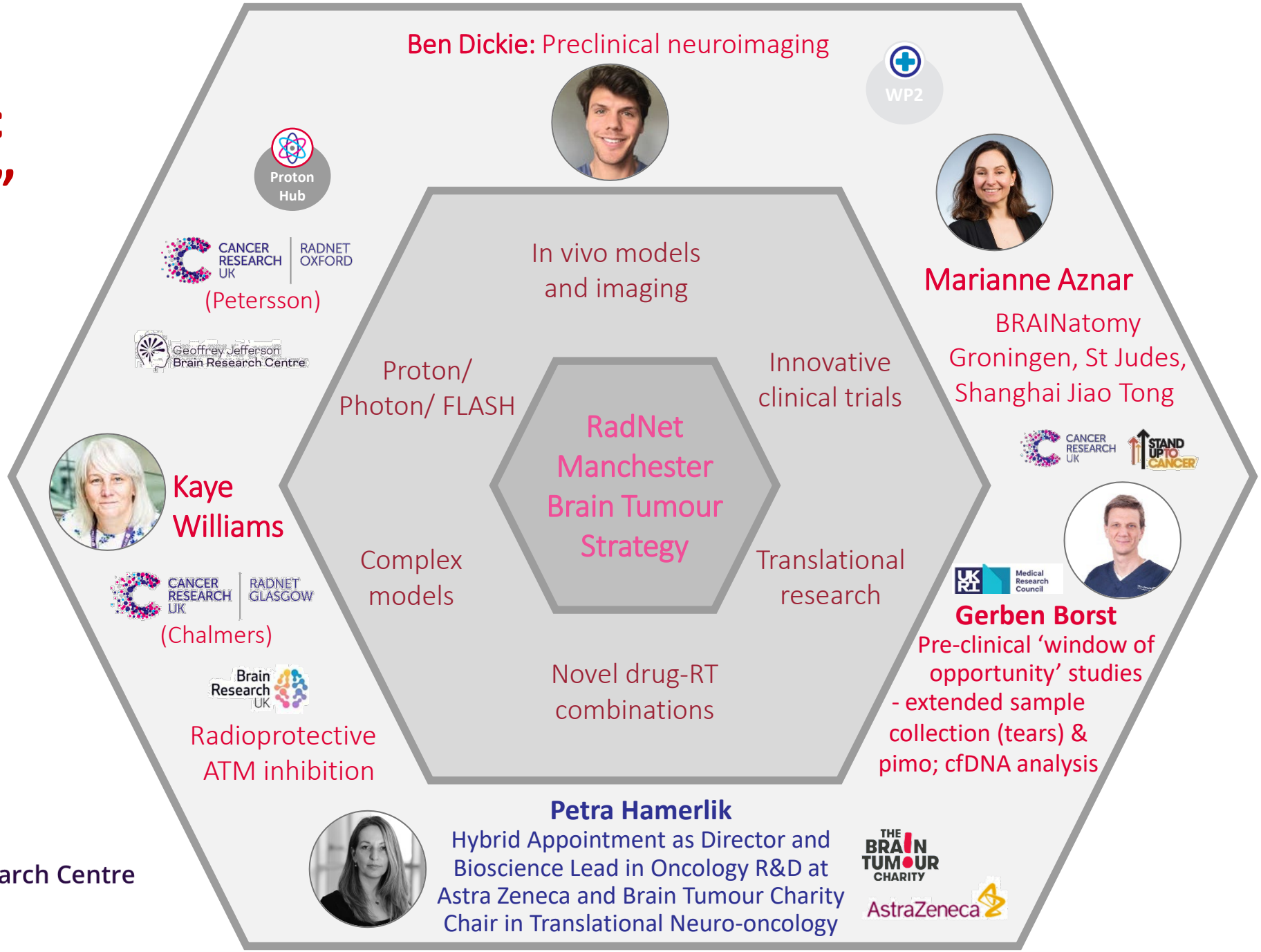
Groningen

- Real world clinical cohort
- Radiation physics and modelling
- AI / machine learning
- Single cell sequencing
- Research infrastructure: RADNET, ARTNET, Bioproton, INSPIRE

- **Only UK paediatric proton centre**

Manchester

Exemplar of Creating Scientific "Synergy and Soil"



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Geoffrey Jefferson Brain Research Centre

Team Science Informed The MCRC's USPs and Over-Arching Strategic Areas

Presented to the IAB-MCRC Nov 2022

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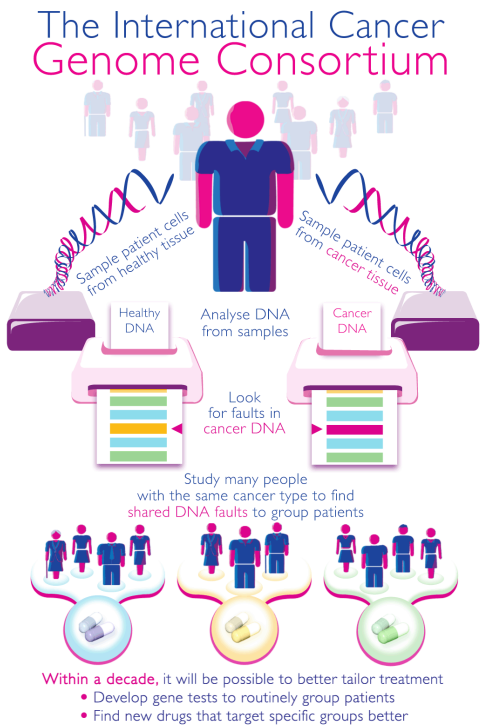
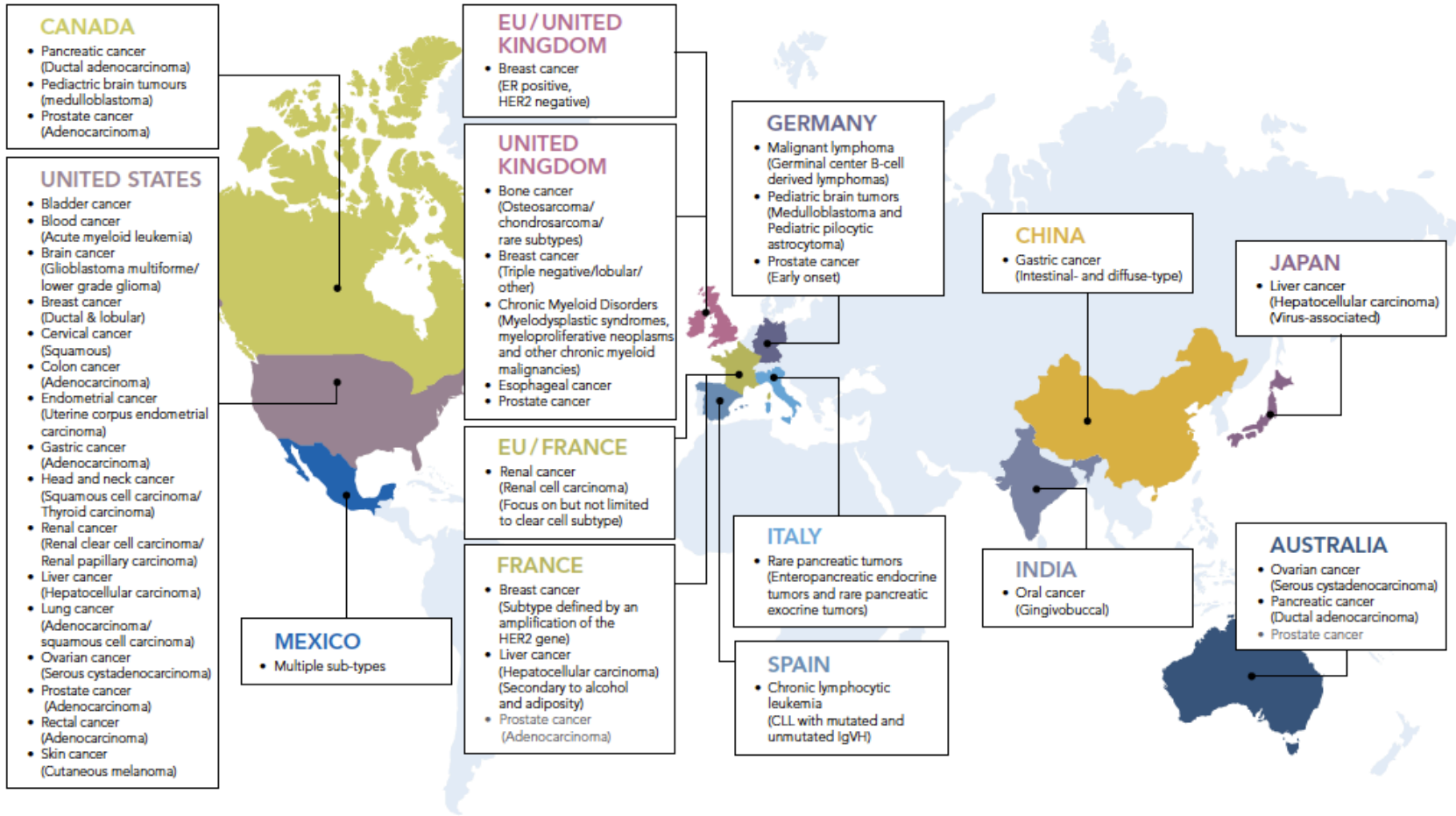
CANADA
Toronto - Princess Margaret
STARS21
EDx: Advanced Materials
EUROPE
FLASH consortia
OncoRay Dresden
ASIA
Shanghai-France partnership
Singapore - A*Star
USTRALIA
bourne - Peter Callum Cancer Centre
USA
ACED partnership:
OHSU & University of Stanford
MD Anderson
Baylor
KENYA
Oesophageal and breast cancer
Fellows training
INDIA
PDRAs-Tata Consulting Service
Genomics and AI Teams
International Team Science
Peer review and iterative critical appraisal for best research practice and models
Health care systems' research
Scientific innovation and co-creation
Intersections within national patient diaspora
Different skillsets and scientific interpretations
Granting opportunities
Altruism & Humanity
Frankly, it's the future for impactful work

ICGC: Where's Africa In This International Genomics Ambition?





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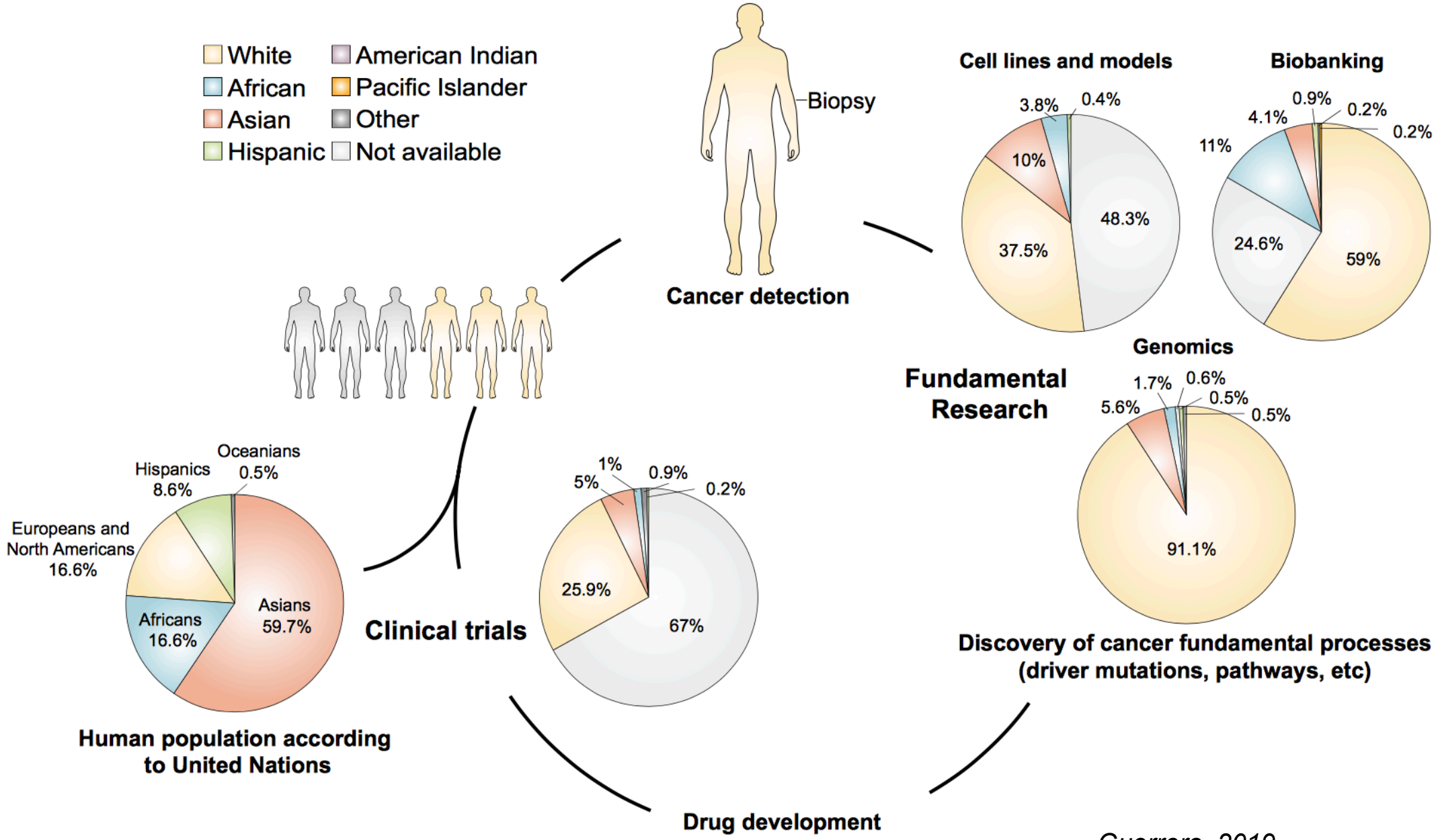


Guerrero, 2019

Strong ongoing partnership

Three Applied Health Research Aims

AIM 1	AIM 2	AIM 3

Reduce burden of disease

Cost efficiency

Multiple uses

Outputs -Initial and Sustained

MANCHESTER

A sustainable and growing
ivering on
better

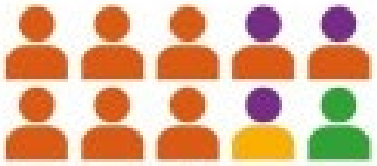
Best urban and rural engagement – KUTRRH and communities

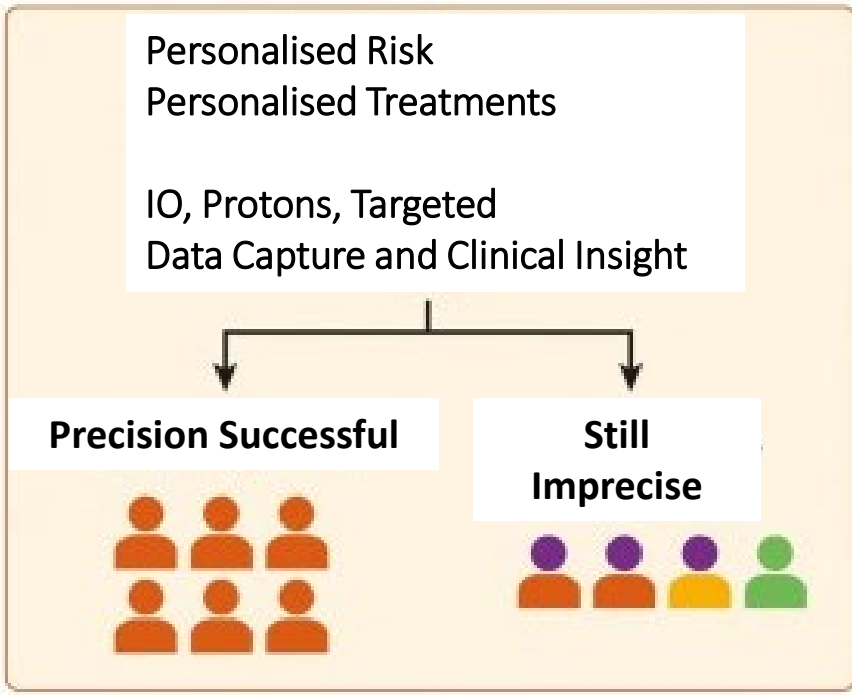
Internationalisation as a Road to Inclusive Team Science

- Co-creation of the early detection work between Manchester-Christie NHS Trust and Kenyatta University Teaching, Referral and Research Hospital in Nairobi
- Exemplar of active listening to our scientific partners and in this case co-creating and designing a cancer research and healthcare strategy using team science
- East African and Sub-Saharan Biology, Genetics, Enagagement
- £2.8M from NIHR

'By Kenya and for Kenya'

Profiled cancer
Patient cohort





Cancer Intelligence

- Social Deprivation
- Ethnicity
- Comorbidity & Mental Heath
- Geography
- Incidence
- Mortality
- Engagement
- Priorities
- Cancer Models

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A Few Areas to Explore Together

- The concept of the MCRC and Team Science
- Team Science: Definitions and Exemplars
- Effective Building of New Teams and ROI
- **New Environments and Impact on Team Science**

I have no disclosures

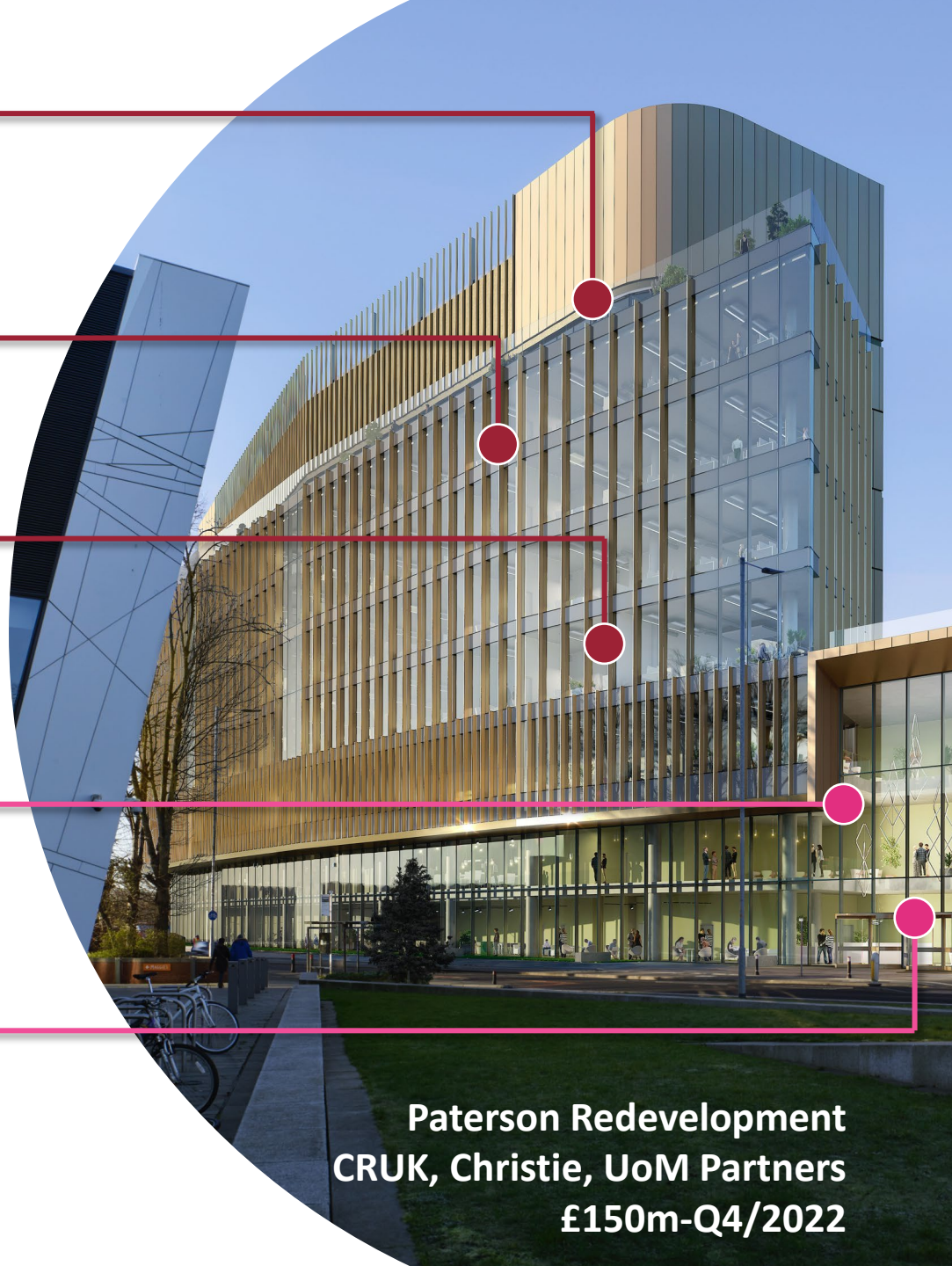
Proposed cancer education hub for CRUK trainees to collaborate

State-of-the-art UoM and CRUK laboratories with collaboration zones

Biomarker Centre and Integrative Pathology co-location

Connecting a CRUK Institute and Centre with the largest single site cancer centre in Europe

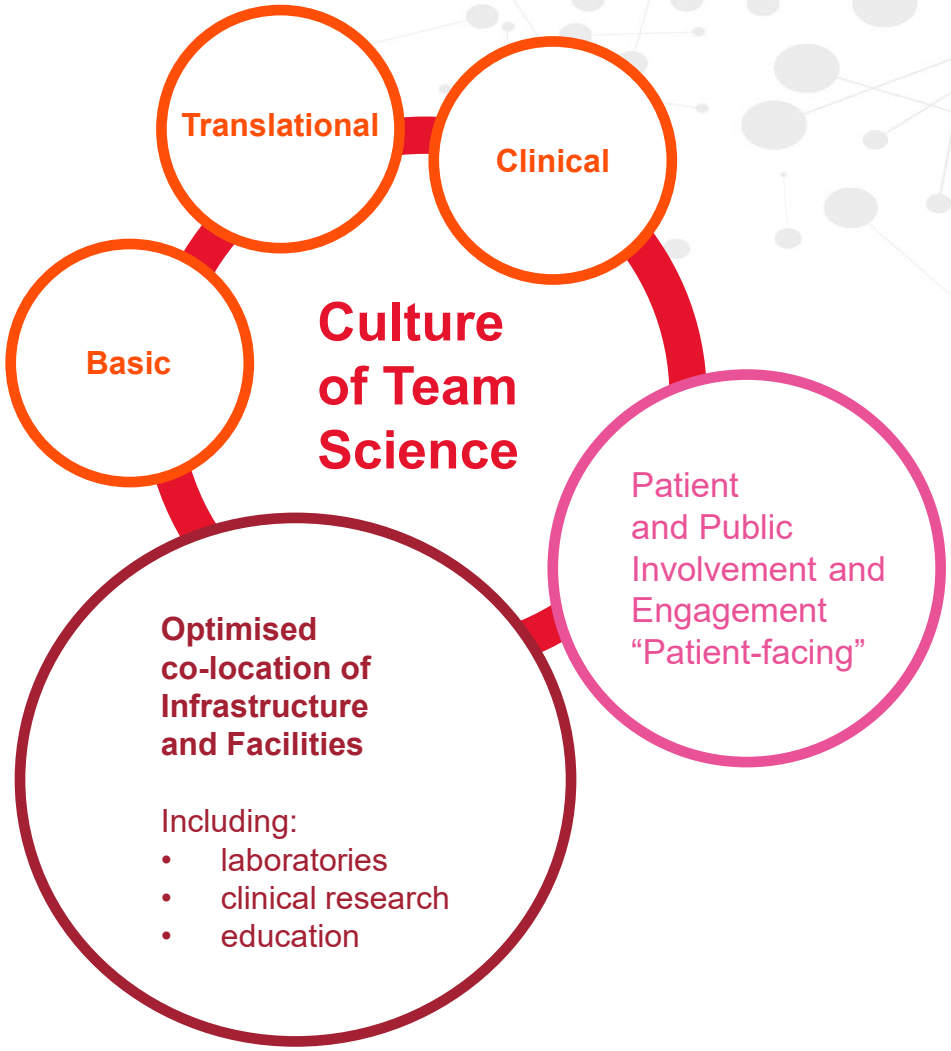
Interactive touch screen technology outreach to describe our research to both public and patients



Paterson Redevelopment
CRUK, Christie, UoM Partners
£150m-Q4/2022

Guiding Principles

A research-centric building to facilitate the partners' ambition to be one of the world's premier comprehensive cancer centres



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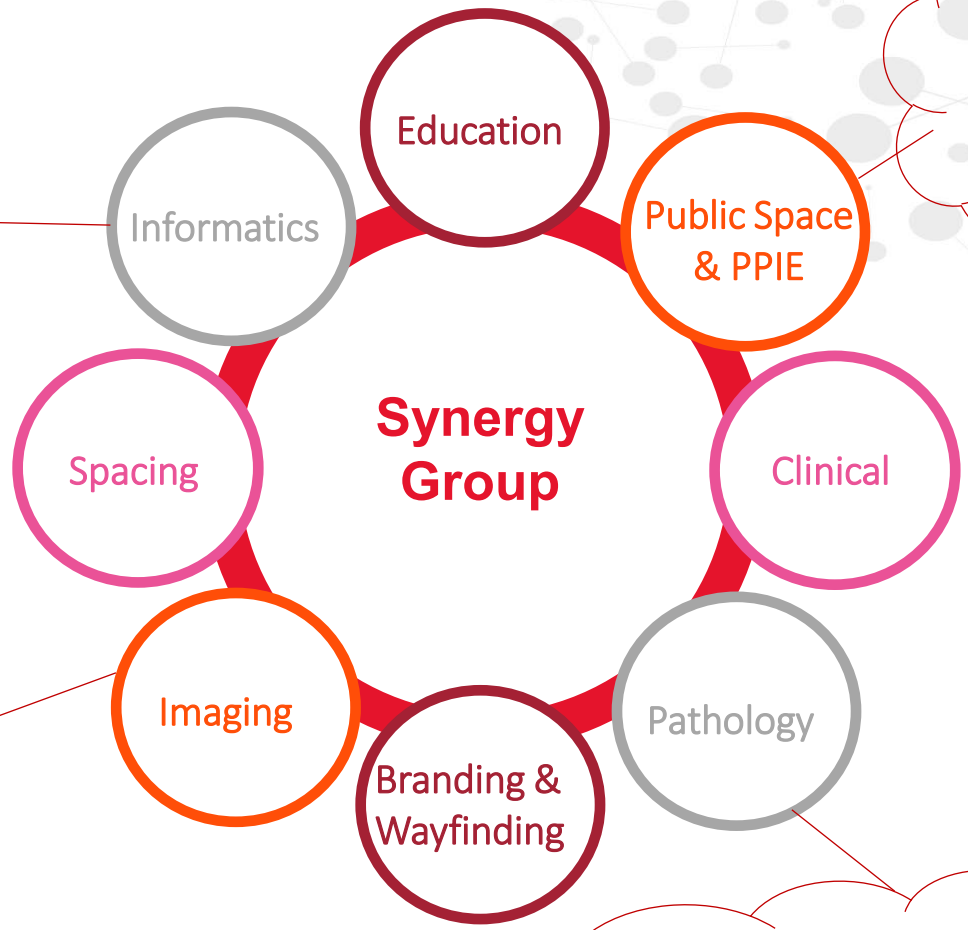
CANCER RESEARCH UK

NHS The Christie NHS Foundation Trust

Synergy Group-2023 onwards

MI/MCRC bioinformatics
TCS partnership
Clinical informatics
Pankhurst/CRUK/DCC

PPIE Public Meeting Space
Scientific Pop-Ups
(Trainees, Cancer Revolution)
Should it be a destination ?
Information KIOSKs
Mirror within OCRB



In Situ Scientific imaging Consultation
Adjoined Med Phys and Imaging
Fellows spacing

Scientific Pathology Consultation
Academic Integrative Pathology
CRTFs in Pathology
Novel technologies
Global Genomics

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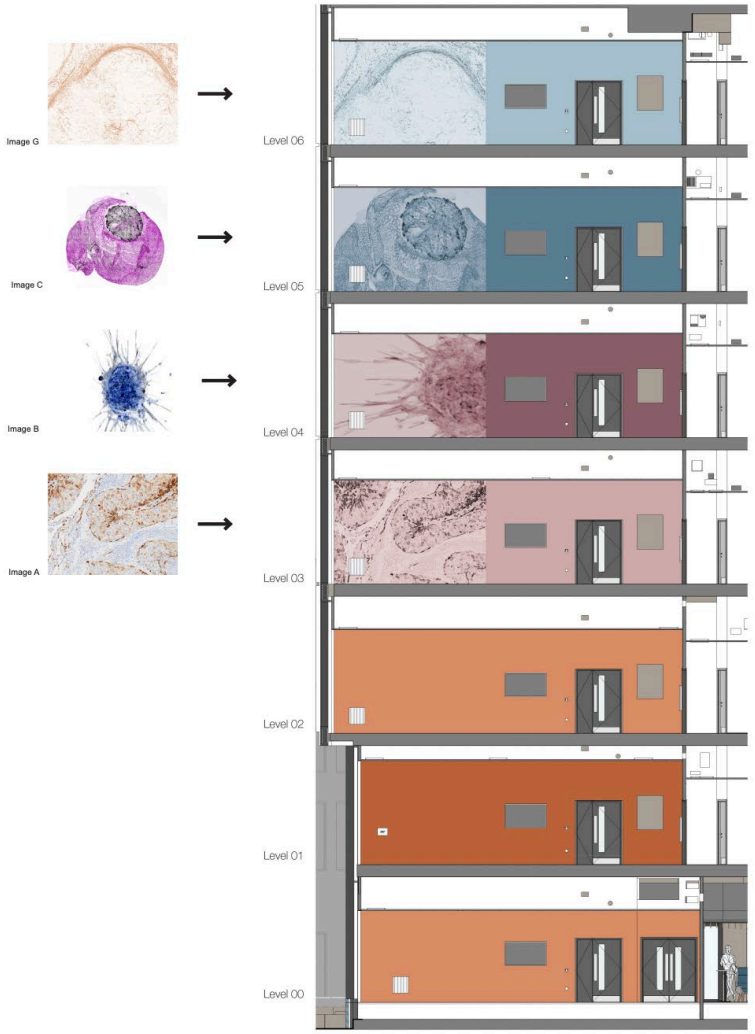
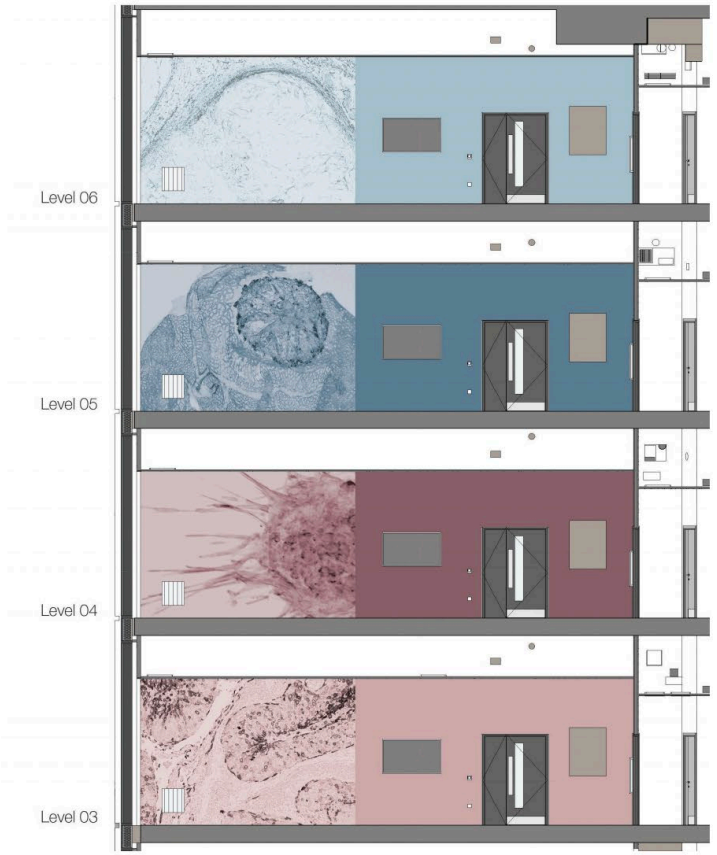
- Short explanation of what the image is capturing.
- QR code linking to a patient story relating to the work being done on the floor.
- Opportunity for clinical trials and genomics imagery on floors 1 and 2





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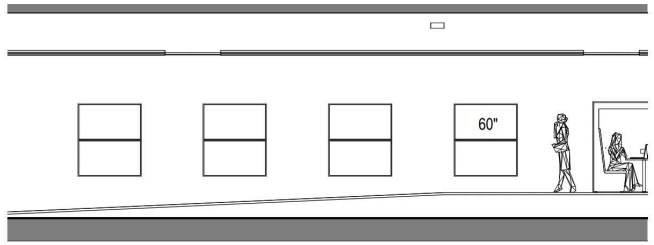
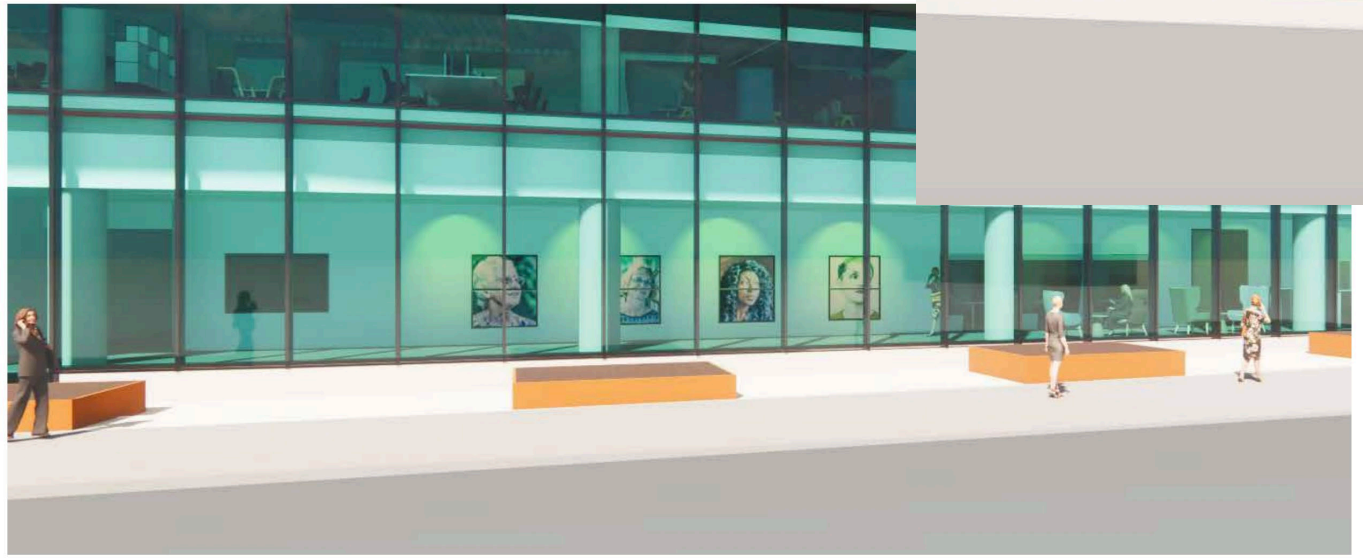


Corridor wall
Agreed screen configuration
8 no. 60" screens



View towards main entrance

The Next Era for Team Science and an Inclusive MCRC

Continue to build our strong translational team science conduit

- Drive basic & discovery science into novel trials; planned reverse-translation

Holistic approach to the "host" as well as the tumour

- The study of, and with, complex patients will lead to novel mechanistic insights to decrease their morbidity and mortality from cancer

Inclusive approaches in all our research programming

- To place scientific relevancy to the forefront and new science cascade into diverse models, trainees, leaders and clinical trials

National/International training lead in complex cancer data

- Collaborator of choice within the CRUK network for integrated data studies

TranslationManchester
Research Network

Download the booklet
https://bit.ly/3dEBTEs
Available in the useful links box

> 70 partners

- Research and Technology Transfer Support
- Industry
- Research Facilities
- Networks
- Biobanks
- Clinical Trials Support
- NHS

Supporting Translational Research

D1 D2 D3 D4 T1 T2 T3 T4

wellcome

Thank you

Manchester,
Top 3/13th Best Cities in World
(Time Out 2021/2022)