NIHR | Leeds Biomedical Research Centre

UNIVERSITY of York

UNIVERSITY OF LEEDS

NHS The Leeds Teaching Hospitals NHS Trust

NIHR Leeds Biomedical Research Centre Histopathology theme

Professor Philip Quirke

Theme lead, NIHR Leeds BRC

Pathology at Leeds

Previous high impact research

Improving surgery:

- Anterior resection
- Abdominoperineal resections
- Colonic Cancer

Safety trials with surgery:

- MRC Classic – keyhole surgery
- EME Rolarr – Robotic surgery

Treatment trials

- Foxtrot and Piccolo with oncology
- MRC CR07 with radiotherapy

Single cell genotyping

Pathology at Leeds

- University of Leeds
  - Largest academic pathology department in UK
  - Current major research programmes
    - Microbiome
    - Artificial intelligence and digital pathology
    - Clinical trials
    - Bowel cancer improvement programme
    - Super resolution microscopy
- NHS
- Supraregional/Regional service
- Leader in digital pathology
- Site specialised consultants
- Major training centre

The BRC histopathology theme team

Lead Theme Phil Quirke
Lead work package 1 as above
Deputy Dr Caroline Young recently appointed consultant pathologist
Dr Henry Wood
Mr Bottomley

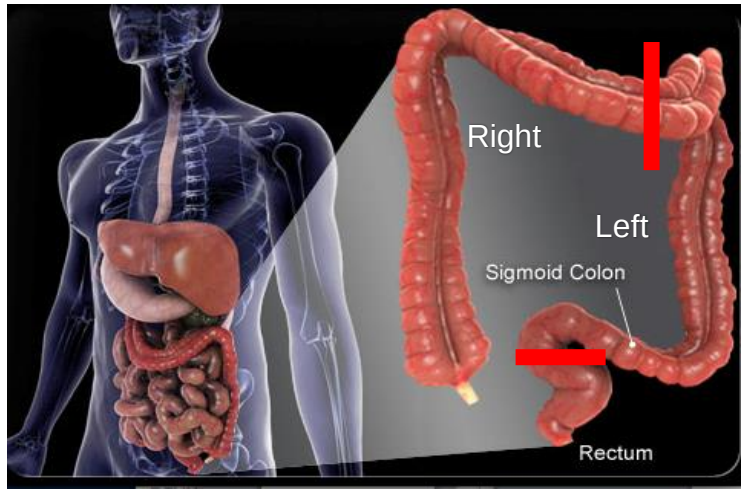
Lead work package 2 Professor Heike Grabsch
Deputy Dr Nick West
Professor Kather
Dr Derek Magee (Heterogenius)
Dr Susan Richmond
Dr Hannah Muti
Dr Jon Laye

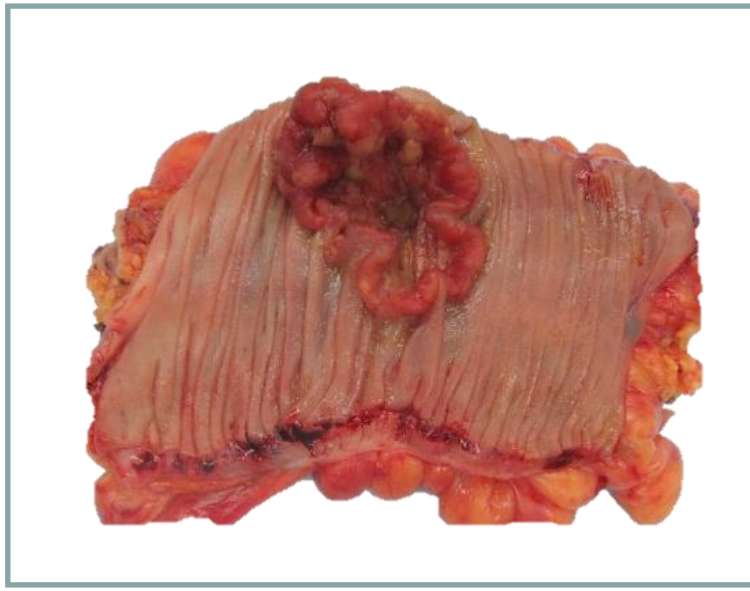
Improved screening bowel cancer

Improved GI cancer diagnostics and outcomes

Large bowel cancer

Global incidence 1.9M 2020
Global deaths 935,173 2020
5 year UK survival 60%



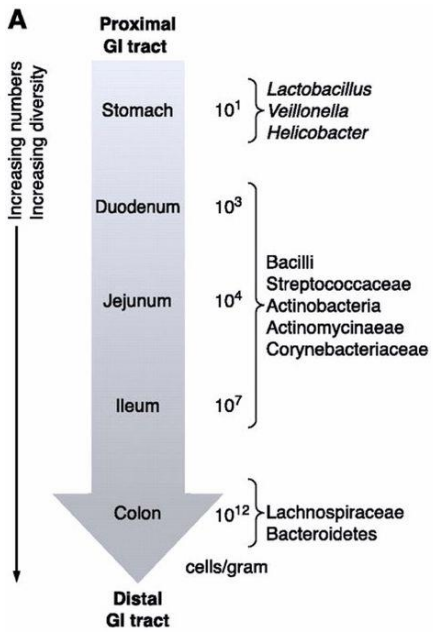


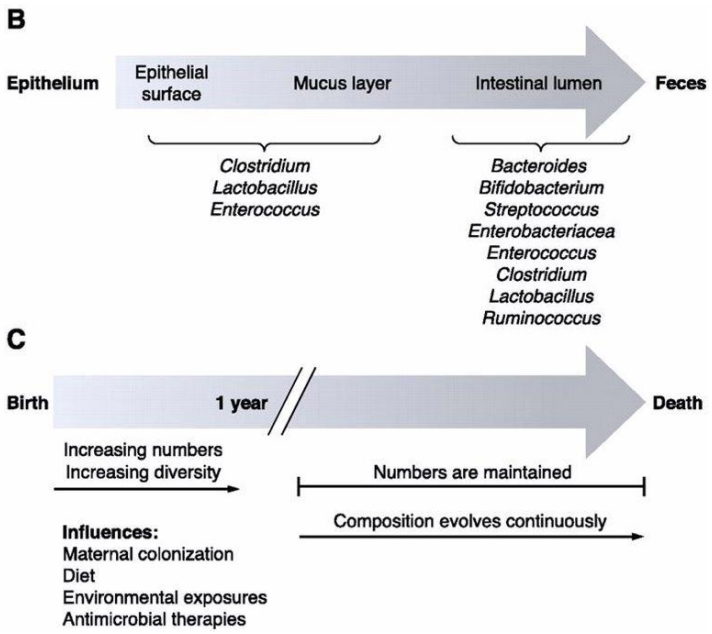
Disease of elderly average age 72
Now increasing in younger age groups <50

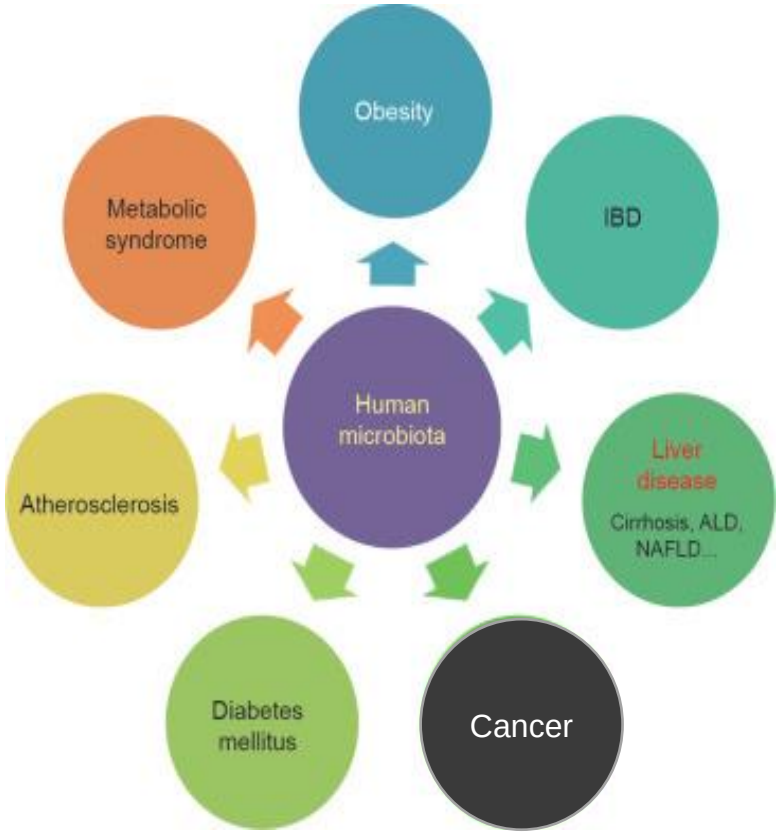
Screening available
Surgery main form of treatment
Additional radio/chemo/immunotherapy

Microbiome may have a role in:
Causation
Prevention
Screening
Treatment

Microbiome

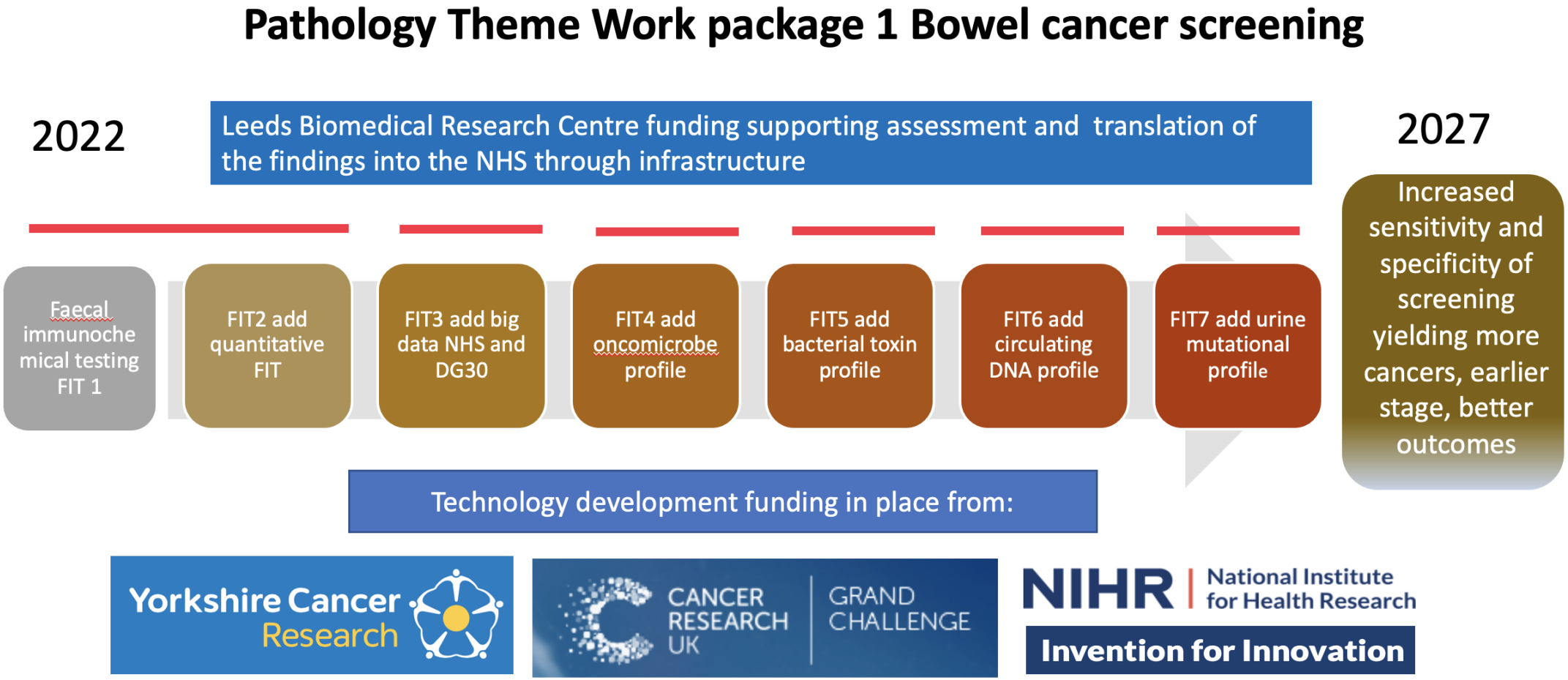

A
Proximal GI tract
Increasing numbers
Increasing diversity
Stomach
Duodenum
Jejunum
Ileum
Colon
10^1
10^3
10^4
10^7
10^{12}
Lactobacillus
Veillonella
Helicobacter
Bacilli
Streptococcaceae
Actinobacteria
Actinomycinaeae
Corynebacteriaceae
Lachnospiraceae
Bacteroidetes
cells/gram
Distal GI tract


B
Epithelium
Epithelial surface
Mucus layer
Intestinal lumen
Feces
Clostridium
Lactobacillus
Enterococcus
Bacteroides
Bifidobacterium
Streptococcus
Enterobacteriacea
Enterococcus
Clostridium
Lactobacillus
Ruminococcus
C
Birth
1 year
Death
Increasing numbers
Increasing diversity
Numbers are maintained
Composition evolves continuously
Influences:
Maternal colonization
Diet
Environmental exposures
Antimicrobial therapies


Obesity
Metabolic syndrome
IBD
Human microbiota
Atherosclerosis
Liver disease
Cirrhosis, ALD, NAFLD...
Diabetes mellitus
Cancer

Work package 1

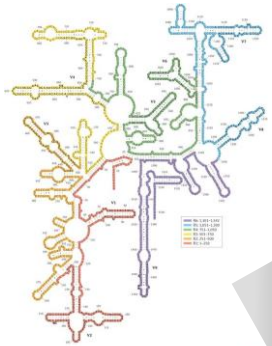
Screening available but limited effect can we improve it?



NHS
Bowel Cancer
Screening Programme

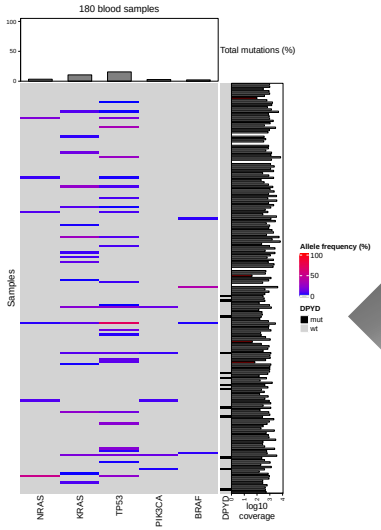
15,000

2000



16s rRNA

CT DNA



Bacterial toxins

Pks
ETBF
FadA

Issues

Access to NHS data still very difficult

Early tumours limited DNA release

Colonoscopy data on low blood negative samples

Cancer vs 'not'

Fusobacterium
Peptostreptococcus
Parvimonas
Porphyromonas
Gemella
Odoribacter
Faecalibacterium

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Work package 1

Applications in screening programme

- Identifying high risk individuals below the 120ug/g current positive threshold
- Identifying people above 120ug/g who are low risk and can avoid colonoscopy

New applications

- Can a microbiome test help identify cancer carriers in straight to FIT
- Discussions with Nottingham to examine this question

Does a microbiome test help identify ethnic minority/younger patients

Table 1: Median age (interquartile range shown in brackets (IQR)) of individuals diagnosed with colorectal cancer, by ethnic group

	YCRBCIP region	England
White	72 (65-80)	73 (64-81)
Asian	63 (51-75)	64 (55-75)
Black	61 (52-81)	66 (55-78)
Other, mixed and multiple	63 (50-74)	63.5 (52-76)
Unknown	72 (63-81)	71 (62-81)

The BRC histopathology theme team

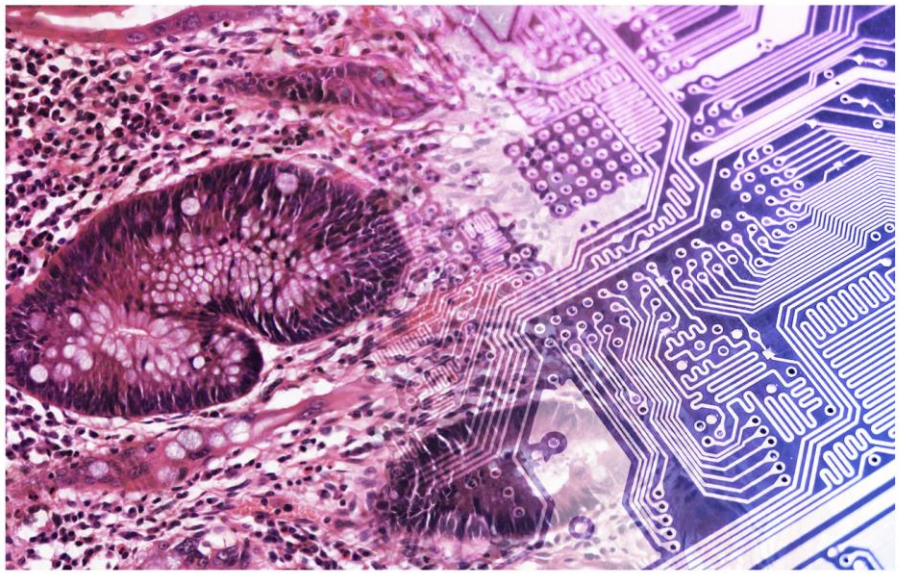
Improved GI cancer diagnostics and outcomes

2022 **Pathology Theme Work package 2 GI cancer artificial intelligence** 2027

Only 3 confirmed tests to predict response to GI cancer treatment available e.g.dMMR, Ras mutation and Her2
None to common chemotherapies e.g Fluoropyrimidines, platinum agents, Irinotecan

No prediction of response to radiotherapy possible

No AI tests
In routine use
In bowel cancer



Contributions to funding in place from:

Yorkshire Cancer Research

CANCER RESEARCH UK

NIHR | National Institute for Health Research
Invention for Innovation

Using current and new DP clinical trials archive developed predictive markers

AI algorithms that predict response to chemotherapy in bowel cancers

AI algorithms that predict response to radiotherapy in rectal cancers

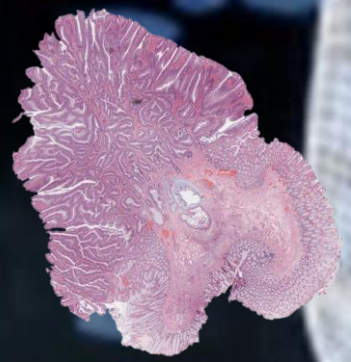
Introduction into NHS practice

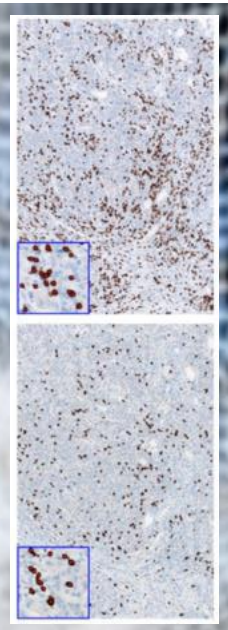
Lead work package 2
Professor Heike Grabsch
Deputy Dr Nick West

Professor Kather Dresden
Leading expert AI group

Dr Derek Magee
AI expert and Heterogenius

Pathology AI



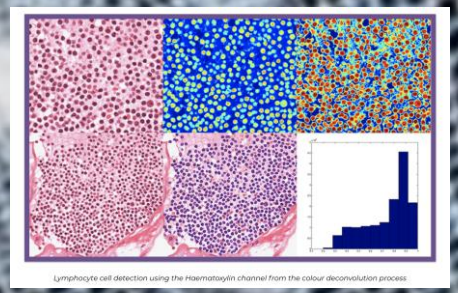


Predictions

New biology

Weakly supervised

Supervised



Validation

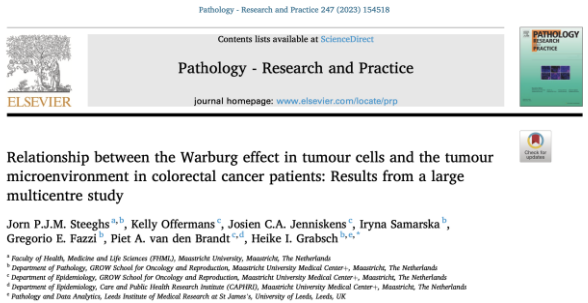
Validation

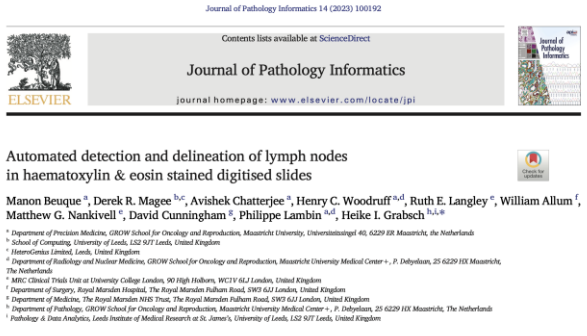
Validation

In clinical populations around the world

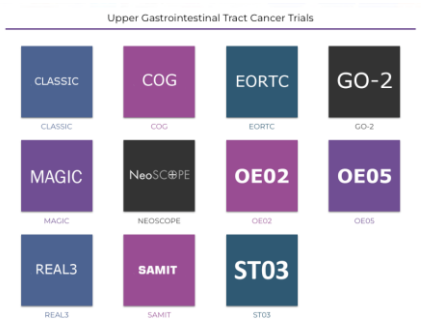
Translation into NHS

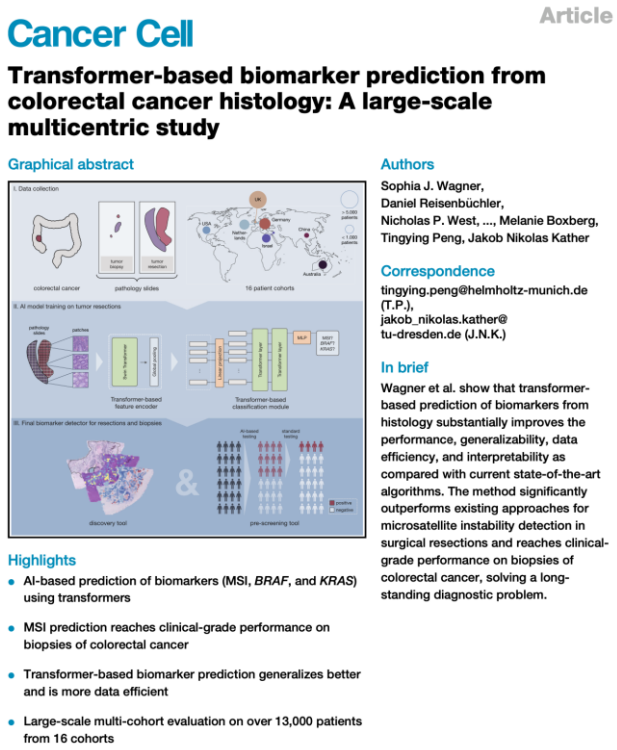
Lower GI trials





Upper GI trials





AI identification of dMMR and mutations

dMMR – high risk of Lynch syndrome
resistant to chemotherapy
sensitive to immunotherapy

Issues are introduction to practice
Cost of exploitation
Public software
NHS????
Partner with companies?

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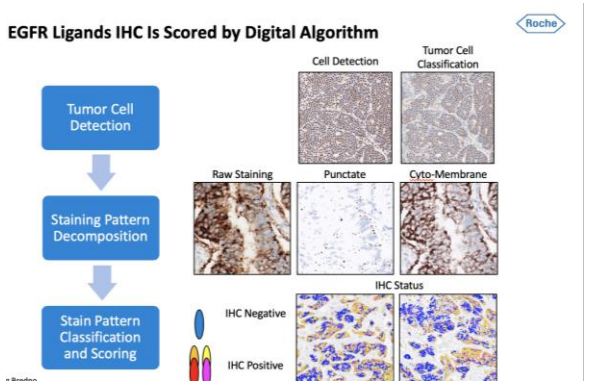
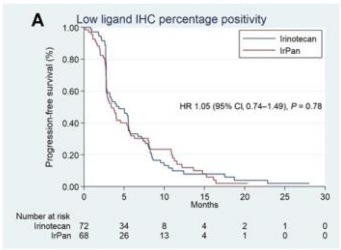
New funding

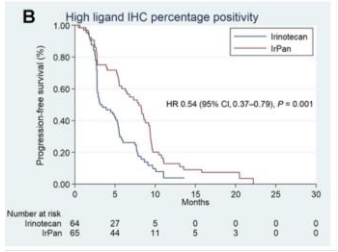
2 new projects for AI - 280K
Roche – extension of patent Application
Supervised AI – markers of response
Further project under discussion



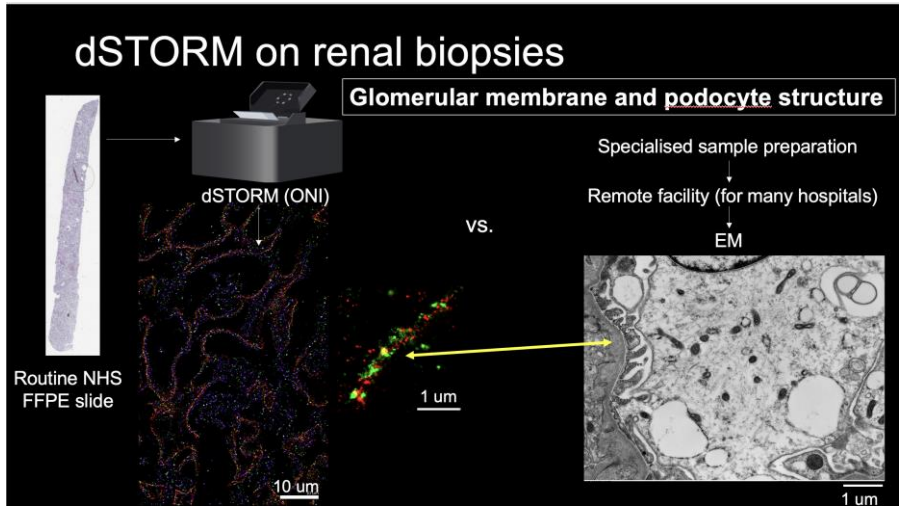
Low Areg/Ereg IHC

High Areg/Ereg IHC





Extension of AI to NIHR ONI project on super resolution microscopy yielding proof of principle of application to renal Biopsies and cancer. 200K new AI spend



Education

3 AI Phd students
3 Clinical Research Fellows
New NIHR CTRF
Joint Surgery/pathology/microbiology

Young CL Oakley lecturer/medal

Roche Sponsored Academic pathology network

30K

WT N4 PhD's
Manchester-Leeds CRUK PhDs

Research culture

Creating the next generation

Largest pathology clinical academic training programme in UK
CTRF/Post doc fellowships – WT, MRC, CRUK, Innovate UK
Inspire, Research Masters, Academic foundation, IAT

Training for academic and service success

Academic skills – grants, management, leadership, mentorship, sponsorship
Service skills – FRCPath, management, translation, liaison

EDI
State school visits, pathology female predominant programme, IAT programme representative of local population
https://eprints.whiterose.ac.uk/169926/

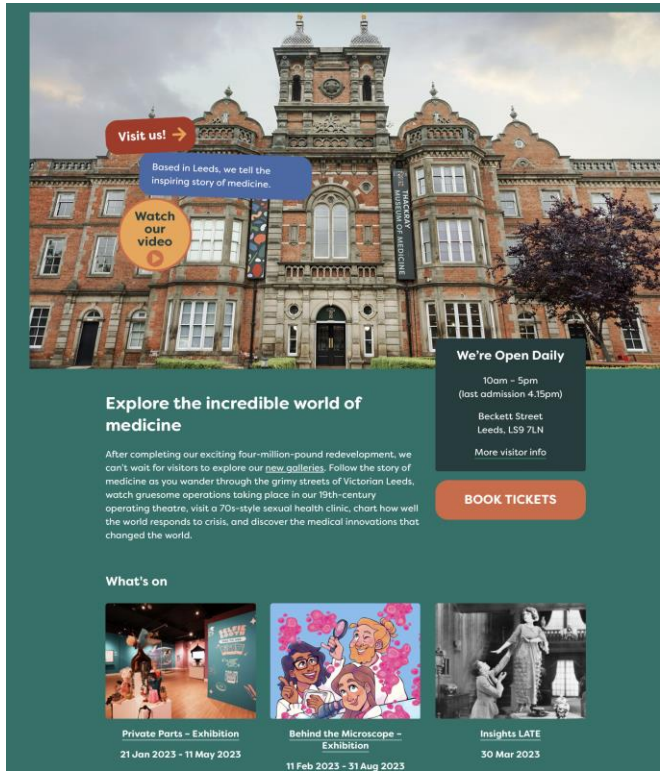
Recent promotions Pathology BRC
Caroline Young to LTHT Consultant*
Kate Marks NIHR UoL CL
Henry Wood UoL Lecturer
Susan Richman UoL Lecturer

PPIE Pathology Theme

Know Your St: Inside Our Guts**

Episode 2

University of Leeds professor Phil Quirke discussed 'warrior poos' and analysed a cancerous bowel during his feature on the show. Photo: Channel 4



Horrible Histologies
Public Exhibition

Pathology PPIE groups
YCR BCIP
NIHR i4i – ONI, GeneFirst
OPTIMISTICC CRUK

Thackray Medical Museum eye dissections

Leeds University Be Curious

Global Colon Cancer Concern webinar

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Good progress
Looking forward to the future work
Thank you for listening