

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



NHS Pathology

University Pathology

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

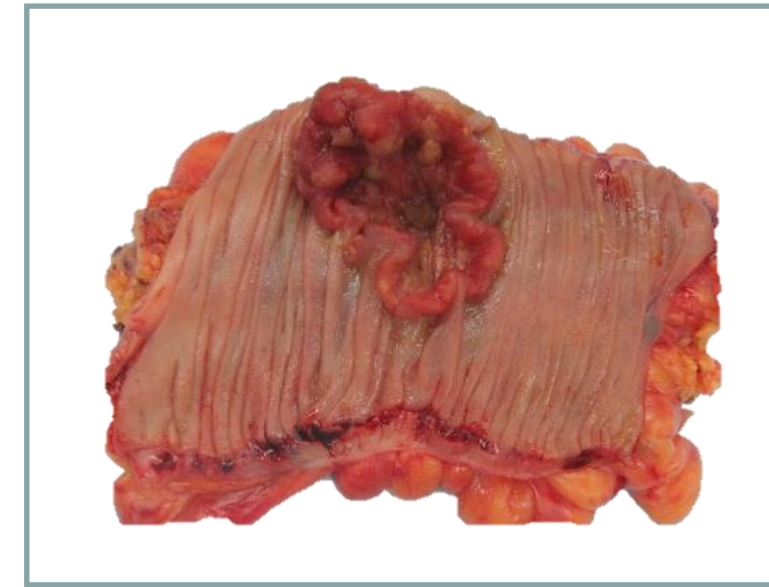
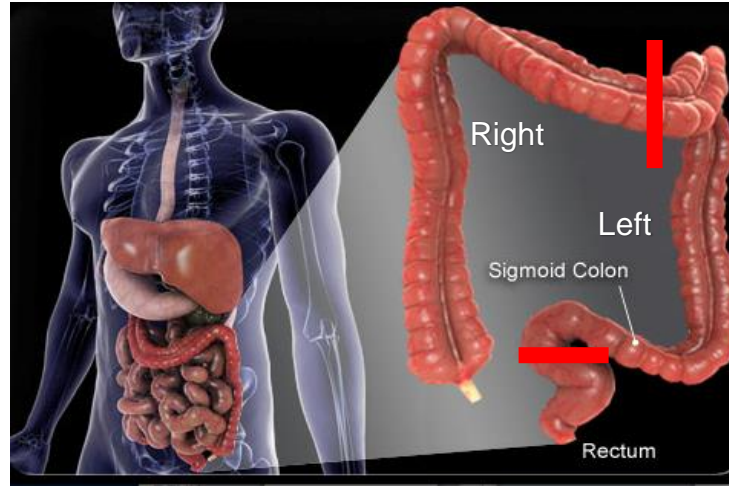
Lead work package 2 Professor Heike Grabsch
Deputy Dr Nick West
Professor Kather
Dr Derek Magee (Heterogenius)
Dr Susan Richmond
Dr Hannah Muti
Dr Jon Laye

**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%

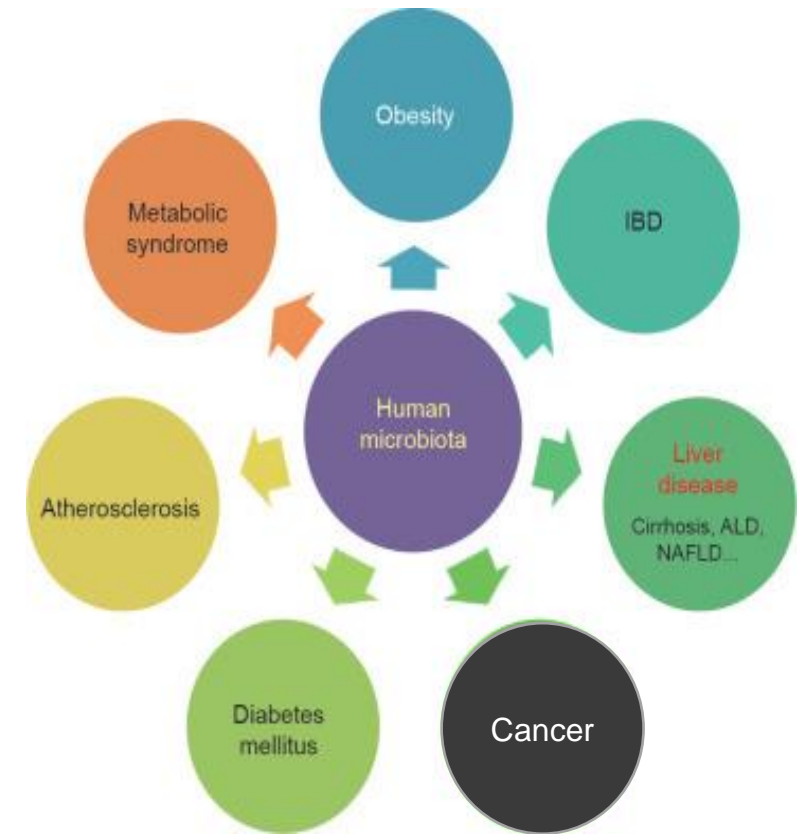
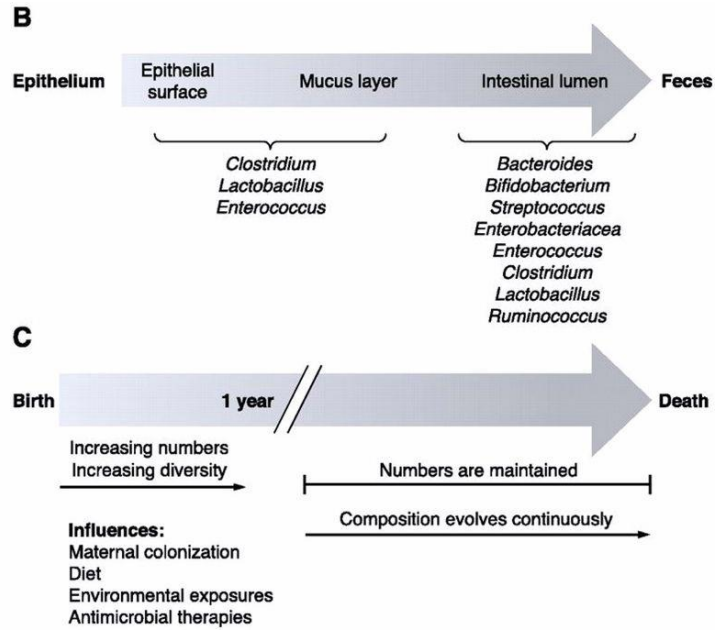
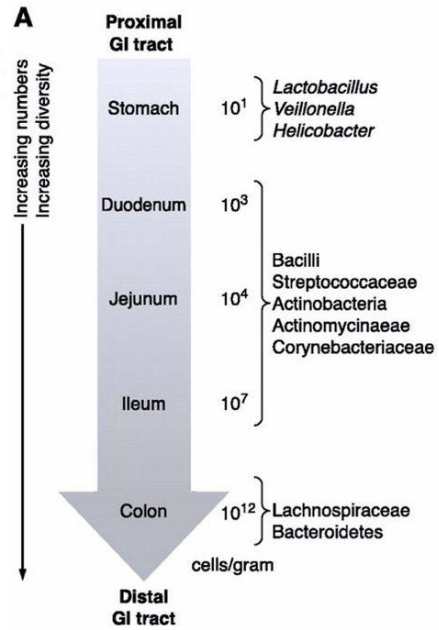


Disease of elderly average age 72
Now increasing in younger age groups <50

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

Microbiome may have a role in:
Causation
Prevention
Screening
Treatment

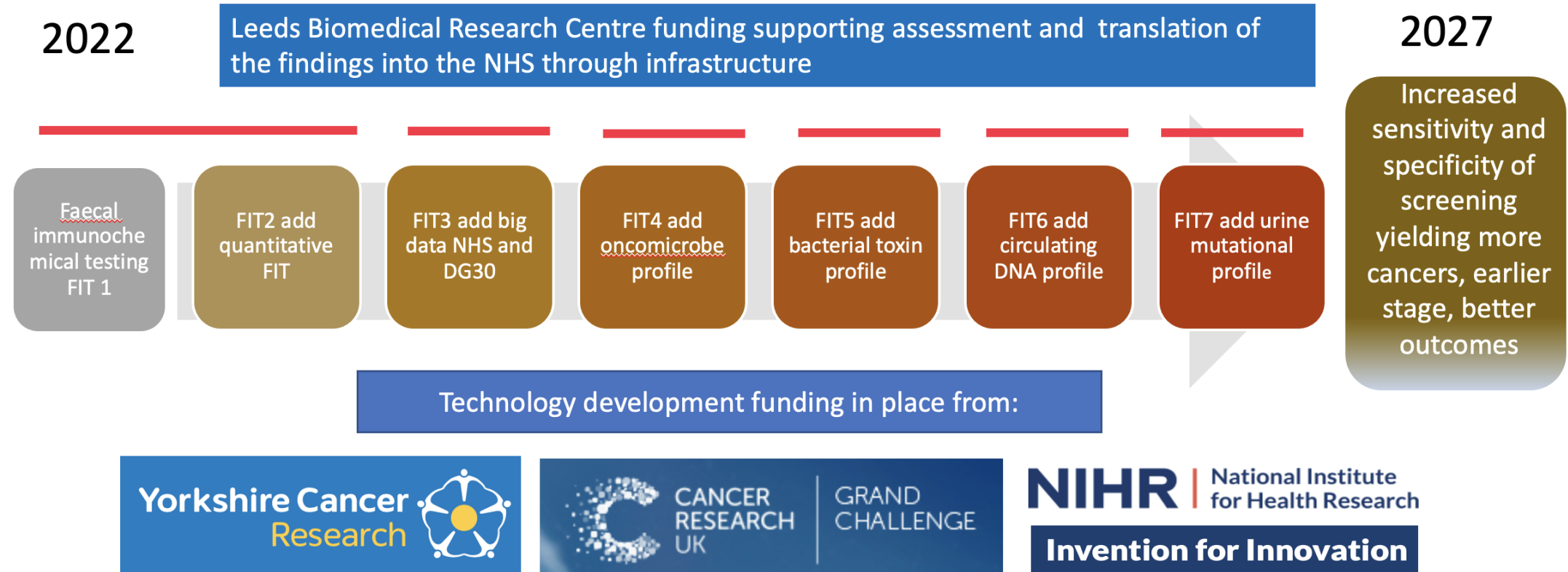
Microbiome



Work package 1

Screening available but limited effect can we improve it?

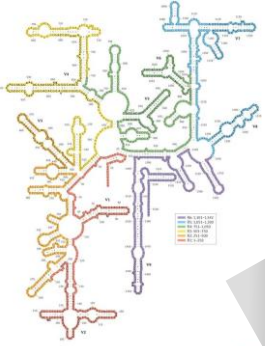
Pathology Theme Work package 1 Bowel cancer screening





15,000

2000

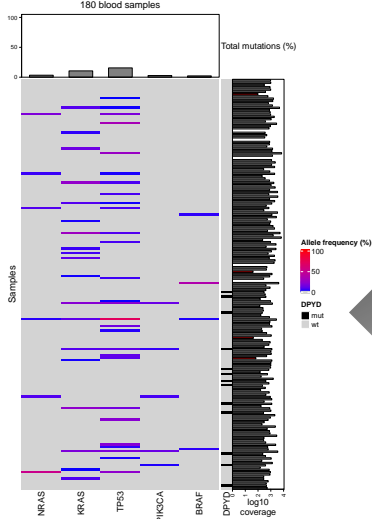


16s rRNA

Issues

- Access to NHS data still very difficult
- Early tumours limited DNA release
- Colonoscopy data on low blood negative samples

CT DNA



Bacterial toxins

Pks
ETBF
FadA

- Cancer vs 'not'
- Fusobacterium*
 - Peptostreptococcus*
 - Parvimonas*
 - Porphyromonas*
 - Gemella*
 - Odoribacter*
 - Faecalibacterium*

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

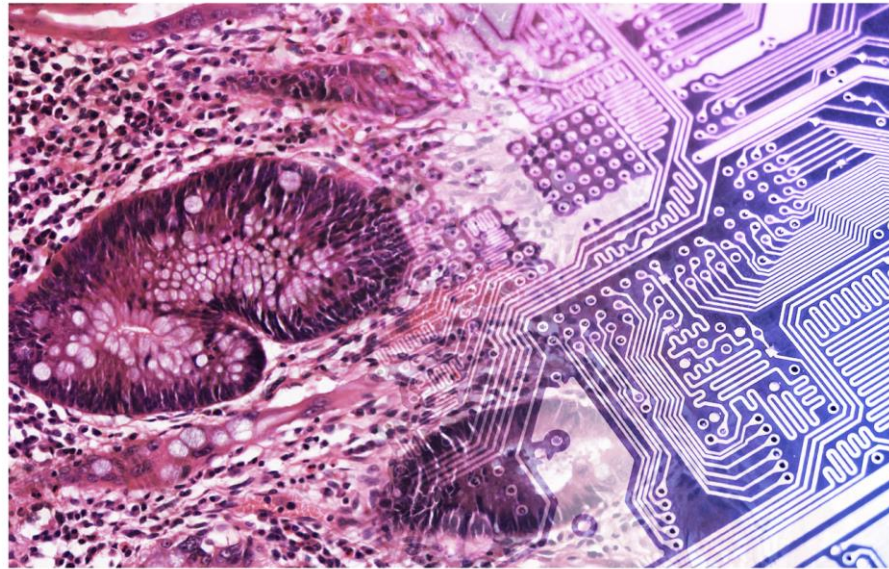
Improved GI cancer diagnostics and outcomes

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.



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.

Contributions to funding in place from:



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

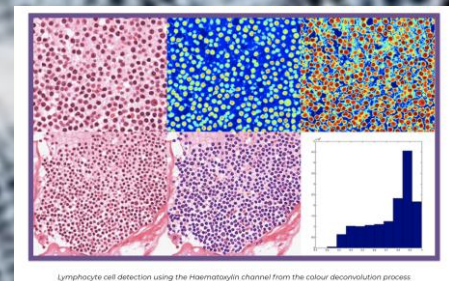
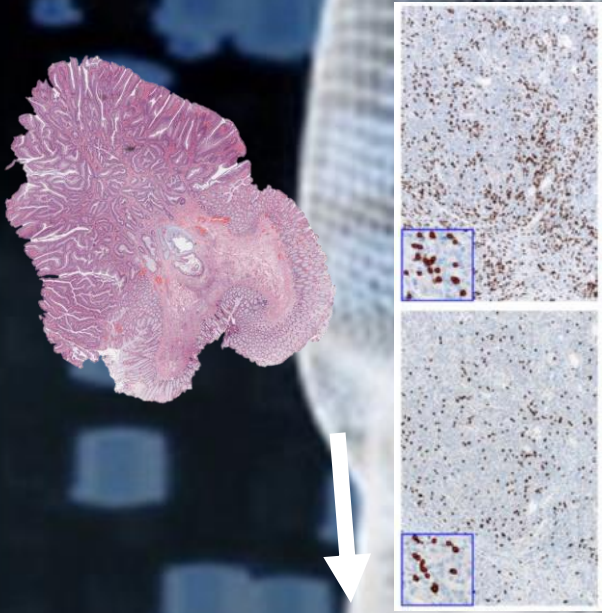
Validation

Validation

Validation

Predictions

New biology



Weakly supervised

Supervised

In clinical populations
around the world

Translation into NHS

Lower GI trials

Upper GI trials

Virtual Pathology at the University of Leeds

Home Public Slides EQA Teaching Research **Clinical Trials** NDIR

Colorectal Small Bowel Upper GI Anal Microbiome

Colorectal Clinical Trials

APHRODITE	ARIEL	ARISTOTLE	AURORA
BACCHUS	CLASICC	COPERNICUS	CORE
CR07	EnROL	EXCITE	FI Study
FOCUS	FOCUS2	FOCUS3	FOCUS4
FOXROT	FOXROT 2	FOXROT 3	GLiSten
InstAct	Mercury	Mercury2	Piccolo
QUASAR	RICE	RMHvs12	ROLARR
SCORT	octo	STAR-TREC Phase 2	STAR-TREC Phase 3
STARRCAT	Stockholm III	T-REX	TREC
TRIGGER			

Pathology - Research and Practice 247 (2023) 154518

Contents lists available at ScienceDirect

Pathology - Research and Practice

journal homepage: www.elsevier.com/locate/prp

Relationship between the Warburg effect in tumour cells and the tumour microenvironment in colorectal cancer patients: Results from a large multicentre study

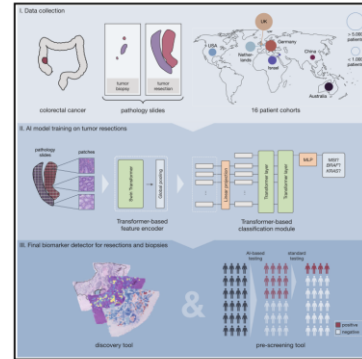
Jorn P.J.M. Steeghs^{a,b}, Kelly Offermans^c, Josien C.A. Jenniskens^c, Iryna Samarska^b, Gregorio E. Fazzi^d, Piet A. van den Brandt^{e,f}, Heike I. Grabsch^{g,h,i}

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^b Department of Pathology, GROW School for Oncology and Reproduction, Maastricht University Medical Center+, Maastricht, The Netherlands
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^d Department of Epidemiology, Care and Public Health Research Institute (CAPIRI), Maastricht University Medical Center+, Maastricht, The Netherlands
^e Pathology and Data Analytics, Leeds Institute of Medical Research at St James's, University of Leeds, Leeds, UK

Cancer Cell

Transformer-based biomarker prediction from colorectal cancer histology: A large-scale multicentric study

Graphical abstract



Highlights

- AI-based prediction of biomarkers (MSI, BRAF, and KRAS) using transformers
- MSI prediction reaches clinical-grade performance on biopsies of colorectal cancer
- Transformer-based biomarker prediction generalizes better and is more data efficient
- Large-scale multi-cohort evaluation on over 13,000 patients from 16 cohorts

Article

Authors

Sophia J. Wagner, Daniel Reisenbüchler, Nicholas P. West, ..., Melanie Boxberg, Tingying Peng, Jakob Nikolas Kather

Correspondence

tingying.peng@helmholtz-munich.de (T.P.), jakob_nikolas.kather@tu-dresden.de (J.N.K.)

In brief

Wagner et al. show that transformer-based prediction of biomarkers from histology substantially improves the performance, generalizability, data efficiency, and interpretability as compared with current state-of-the-art algorithms. The method significantly outperforms existing approaches for microsatellite instability detection in surgical resections and reaches clinical-grade performance on biopsies of colorectal cancer, solving a long-standing diagnostic problem.

Journal of Pathology Informatics 14 (2023) 100192

Contents lists available at ScienceDirect

Journal of Pathology Informatics

journal homepage: www.elsevier.com/locate/jpi

Automated detection and delineation of lymph nodes in haematoxylin and eosin stained digitised slides

Manon Beuque^a, Derek R. Magee^{b,c}, Avishek Chatterjee^a, Henry C. Woodruff^{d,e}, Ruth E. Langley^a, William Allum^f, Matthew G. Nankivell^g, David Cunningham^h, Philippe Lambin^{h,i}, Heike I. Grabsch^{j,k,l}

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^h Department of Pathology, GROW School for Oncology and Reproduction, Maastricht University Medical Center+, P. Debylaan, 25 6229 EX Maastricht, The Netherlands
ⁱ Pathology & Data Analytics, Leeds Institute of Medical Research at St James's, University of Leeds, LS2 9JT Leeds, United Kingdom

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?

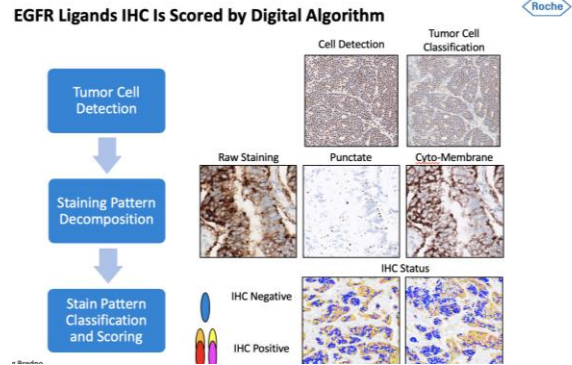
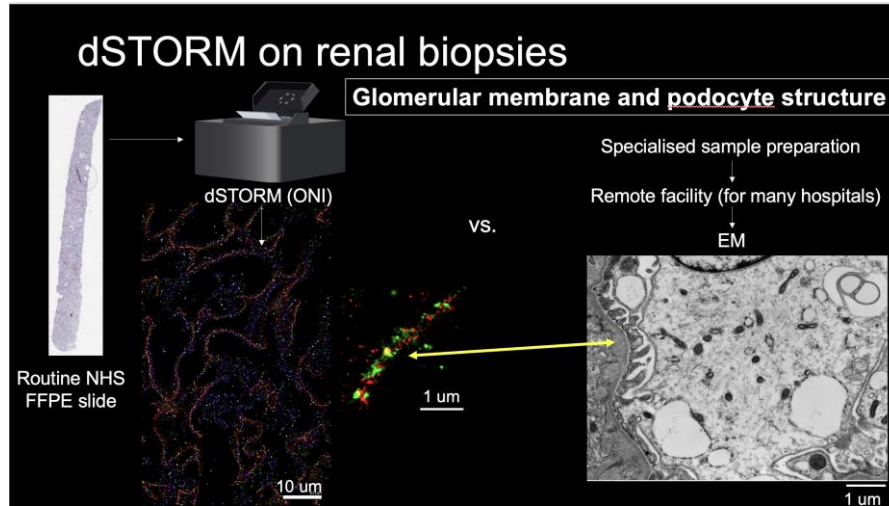
Upper Gastrointestinal Tract Cancer Trials

CLASSIC	COG	EORTC	GO-2
MAGIC	NeoSCoPE	OE02	OE05
REAL3	SAMIT	ST03	

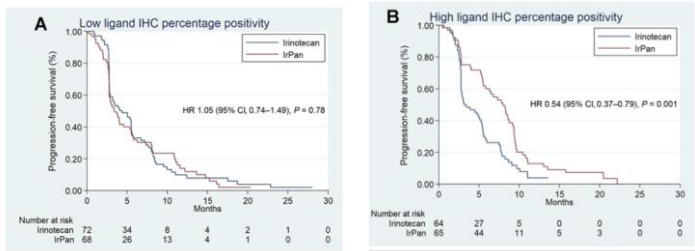
New funding

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

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



Low Areg/Ereg IHC High Areg/Ereg IHC

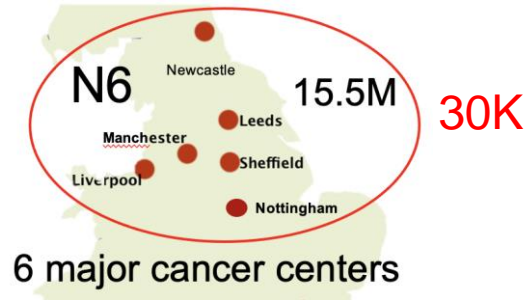


Education

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



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

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

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/>

PPIE Pathology Theme

Know Your S**t: 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

A promotional graphic for the Thackray Medical Museum. The top half features a photograph of the museum's grand, red-brick building. Overlaid on the photo are several call-to-action buttons: 'Visit us!' with a right-pointing arrow, 'Watch our video' with a play icon, and 'We're Open Daily' with a clock icon. Below the photo, there is a section titled 'Explore the incredible world of medicine' with a paragraph of text. At the bottom, there is a 'What's on' section with three small images and their respective dates: 'Private Parts - Exhibition' (21 Jan 2023 - 11 May 2023), 'Behind the Microscope - Exhibition' (11 Feb 2023 - 31 Aug 2023), and 'Insights LATE' (30 Mar 2023). A 'BOOK TICKETS' button is also present.



Horrible Histories
Public Exhibition

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

Thackray Medical Museum eye dissections

Leeds University Be Curious

Global Colon Cancer Concern webinar



Good progress

Looking forward to the future work

Thank you for listening