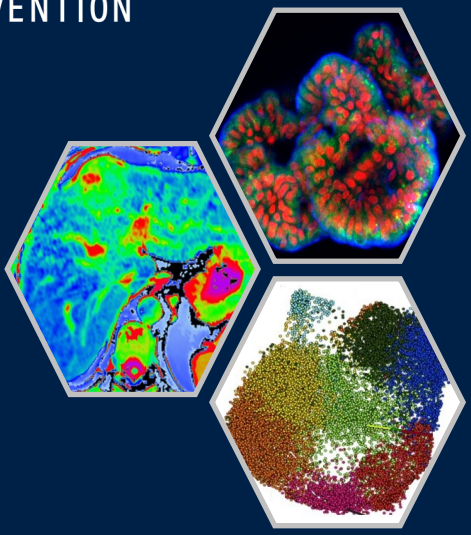
OXFORD CENTRE FOR CANCER EARLY DETECTION AND PREVENTION

UNIVERSITY OF OXFORD



Oxford Centre for Cancer Early Detection and Prevention 5-Year Symposium

10-11th December 2024

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Welcome

I am delighted to welcome you to this Symposium in celebration of five years since we launched the Oxford Centre for Cancer Early Detection and Prevention (OxCODE). Since 2019, OxCODE has grown from 40 PIs to over 375 members, who have received >£75m in external grants and industry funding, of which OxCODE grant-writing support contributed to >£38m. We've now funded 14 OxCODE pump-prime awards, generating >£8.5m leveraged research funding, and 12 OxCODE travel awards to allow early career researchers to present their cancer early detection and prevention research at key international conferences.

This event is a celebration of the breadth of our research in cancer early detection and prevention. We have four excellent keynote speakers: Victor Velculescu, Dame Molly Stevens, Sam Janes and Georgia Black. We are also grateful to our patient and public representatives, who will share their insights into how to make sure your research will benefit patients and how to increase your chances of funding success.

For the first time, we welcome audience members external to Oxford and are excited about the new opportunities for collaborations that this provides. We have included ample networking breaks, so please take the time to talk to someone new and learn about an area of research that is different from yours. You never know where these chance conversations may lead!

Finally, I would like to thank all the speakers, poster presenters and chairs at today's event, our event sponsors Moderna and Veritie Diagnostics, and Cancer Researh UK, the Medical Sciences Division John Fell Fund, the CRUK Oxford Centre and the NIHR Oxford BRC for their support of OxCODE and this event.

Xin Lu

OxCODE Director

Schedule - day 1

09.30-09.40 Welcome

Xin Lu, OxCODE Director

09.40-11.00 Session 1: Technology for early detection and prevention

Chair: Chunxiao Song

09.40 **Keynote talk: Victor Velculescu** - Early detection of cancer using cell-free DNA fragmentomes

10.20 **James McCullagh** – Metabolomics as a tool for early cancer detection

10.40 **Sarah Blagden & Eleni Adamopoulou** – BRCA-Vax: Mapping the antigenic landscape to discover targets for a preventive vaccine

11.00 *Coffee*

11.30-12.30 Session 2: Translating research for patient benefit & lightning talks

Chair: Ellie Barnes

11.30 **Panel Discussion: How do you translate your cancer early detection and prevention research for patient benefit?**

- **Hazel Beaver**, Patient and Public representative
- **Claire Brown**, Partner, Life Sciences, Oxford Science Enterprises
- **Anna Dowrick**, Senior Researcher in Healthcare Implementation, University of Oxford
- **Victor Velculescu**, Professor of Oncology, Pathology, Medicine, and Genetic Medicine, Johns Hopkins University School of Medicine

12.10 **Lucy Denly** – Whole-genome urinary DNA methylation for earlier detection of bladder cancer recurrence

Cont.

Schedule - day 1

12.15 **Dimitris Vavoulis** – Nanopore whole genome sequencing of liquid biopsies for cancer detection

12.20 **Yi-Jhih Huang** – Targeting c-MET for endoscopic detection of dysplastic lesions within Barrett's Esophagus using EMI-137 fluorescence imaging

12.25 **Lucy Goudswaard** – Using Mendelian randomization to identify circulating proteins involved in multiple myeloma risk

12.30 *Lunch & posters (13.00-14.00)*

14.00-15.00 Session 3: Preventive cancer vaccines

Chair: Karin Hellner

14.00 **Catriona Gilmour Hamilton & Anna Fry** – PPI and cancer vaccination: lessons learned so far

14.20 **Nancy Zaarour** – Harnessing the power of tissue resident memory T cells (TRMs) to prevent ovarian cancer

14.40 **David Church** – LynchVax – a precision prevention vaccine for Lynch Syndrome

15.00 *Coffee*

15.30-16.50 Session 4: Early detection technologies

Chair: Jens Rittscher

15.30 **Fergus Gleeson** – Lung cancer screening big data collection in the NHS

15.50 **Michael Pavlides** – Abbreviated Magnetic Resonance Imaging vs ultrasound surveillance for liver cancer detection - AMULET

16.10 **Keynote talk: Dame Molly Stevens** – New bio-engineering approaches to treat and detect cancer

16.50-17.00 Closing remarks

Sarah Blagden, OxCODE Associate Director

17.00 *Drinks reception and canapés*

18.30 *VIP dinner, St Anne's College (invited guests only)*

Schedule - day 2

09.30-09.40 Welcome

David Church, OxCODE Operational Group Member

09.40-11.00 Session 5: Early cancer biology

Chair: David Church

09.40 **Asger Jacobsen** - Understanding the mechanisms of pre-leukaemic clonal selection

10.00 **Simon Leedham** – Using spatial biology to quantitively map and understand cell interactions in colorectal adenoma-carcinoma progression

10.20 **Keynote talk: Sam Janes** – Pre-invasive lung cancer progression

11.00 *Coffee*

11.30-12.25 Session 6: Risk identification and stratification & lightning talks

Chair: Ruth Travis

11.30 **Ling Yang – Chronic pathogen infections and risk of cancers**

11.50 **Pradeep Virdee** – Blood test trends for cancer detection in patients presenting with unexpected weight loss in primary care: a diagnostic accuracy, longitudinal cohort study

12.10 **James Yarmolinsky** – Proteogenomic and observational evidence implicate ANGPTL4 as a therapeutic target for colorectal cancer prevention

12.15 **James Chettle** – The RNA binding protein LARP1 drives tumorigenesis by promoting metabolic plasticity and resistance to oxidative stress

12.20 **Natalie Jooss** – Excess galectin-1 in myeloproliferative neoplasms induces platelet activation and pro-fibrotic megakaryocytes

12.25 *Lunch*

Schedule - day 2

13.20-14.00 Session 7: Getting your research funded

Chair: Sarah Blagden

13.20 **Panel Discussion: Getting grant funding for your cancer early detection/prevention research**

- **Françoise Howe**, OxCODE Scientific Coordinator
- **Talisia Quallo**, Research Programme Manager, Cancer Research UK
- **Janette Rawlinson**, Patient and Public representative
- **Florence Theberge**, MRC Programme Manager, Translation (Vaccines, Antibodies, Protein & Peptide Therapeutics)

14.00-15.20 Session 8: Diagnosing cancers with non-specific symptoms

Chair: Brian Nicholson

14.00 **Fergus Gleeson & Claire Friedemann Smith** – Cancer, serious disease diagnoses, and clinically significant incidental findings in the first six years of the Oxford Suspected CANcer (SCAN) pathway

14.20 **Julie-Ann Moreland & Aduke Onafowokan** – Understanding barriers to research participation alongside the SCAN Pathway

14.40 **Keynote talk: Georgia Black** – Doing "detective work": how are non-specific symptom pathways for cancer investigation organised, and what are the implications for safety and quality of care?

15.20-15.30 Closing remarks

Simon Leedham, OxCODE Associate Director

About OxCODE

The Oxford Centre for Early Cancer Detection launched under the leadership of Professor Xin Lu in June 2019 to build on the existing momentum and galvanise early cancer detection research in Oxford. We have recently expanded OxCODE's remit to also include biologically informed cancer prevention research, changing the name to the Oxford Centre for Cancer Early Detection and Prevention (OxCODE).

The formation of OxCODE consolidated our significant expertise to realise the full potential of cross-disciplinary discourse and collaboration for advancing early cancer research for patient benefit. The Centre comprises >350 members from >20 Departments, Units and Institutes from the University of Oxford and the Oxford University Hospitals NHS Foundation Trust (OUHFT). OxCODE aims to stimulate more cancer prevention and early detection activity in Oxford. We are expanding our multidisciplinary research community by hosting a series of events and increasing the scale and scope of this research at Oxford by providing infrastructure funding for new projects, grant writing support and travel awards.

All University of Oxford or OUHFT researchers with an interest in cancer prevention and early detection are welcome to join. If you wish to be added to the mailing list to hear about future events and funding opportunities, or have an idea for a new research project, please email the OxCODE Scientific Coordinator (francoise.howe@ludwig.ox.ac.uk).

OxCODE is supported by:

UNIVERSITY OF OXFORD

John Fell Fund

NIHR | Oxford Biomedical Research Centre

CANCER RESEARCH UK | OXFORD CENTRE

OxCODE Committees

OxCODE Management Committee

The OxCODE Management Committee determines the overarching vision and strategy for OxCODE.

Xin Lu - Director

Ellie Barnes

Sarah Blagden

David Hunter

Simon Leedham

Paresh Vyas

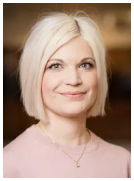
OxCODE Operational Group

The OxCODE Operational Group reviews, supports and guides the activities of OxCODE, within the overarching strategy set by the OxCODE Management Committee.

Simon Leedham

Sarah Blagden

David Church



Karin Hellner

James McCullagh

Brian Nicholson

Beth Psaila

Jens Rittscher

Chunxiao Song

Ruth Travis

OxCODE Funding Scheme

The OxCODE Funding Scheme aims to advance innovative Oxford-based research that can be applied to cancer early detection and/or prevention. OxCODE aims to pump-prime this research by providing short-term awards that will enable the development of projects to a stage at which more long-term external funding can be sought.

Since 2021, funds have been awarded to:

- **Sarah Blagden** "Defining the immunopeptidomic landscape of ovarian cancer"
- **Alistair Easton** "Multiplex immunofluorescence: Developing a pipeline for early cancer phenotyping, diagnosis and research".
- **Skirmantas Kriaucionis** "A pilot study to investigate biomarkers predicting recurrence in patients with non-muscle invasive bladder cancer treated with intravesical BCG therapy"
- **I-Jun Lau** "Understanding the mechanisms of cancer evolution to Multiple Myeloma in patients with Monoclonal Gammopathy of Undetermined Significance"
- **James McCullagh** "Towards early detection of altered cancer metabolism"
- **Siim Pauklin** "Early detection of pancreatic cancer by identifying exosome marker signatures in blood"
- **Bethan Psaila** "Basophils and mast cells as non-canonical drivers of inflammation and cancer progression in patients with myeloproliferative neoplasms''
- **Monica Olcina** "Developing probes for ovarian cancer early detection"
- **Susie Shapiro** "Unprovoked venous thromboembolism and early detection of increased blood cancer risk"
- **Dimitris Vavoulis** "Precise and affordable cancer detection for resource-restricted healthcare systems through shallow long-read whole-genome sequencing of liquid biopsies"

The 2025 competition is open now: www.oxcode.ox.ac.uk

OxCODE Travel Award

The mission of the OxCODE Travel Award is to raise the profile of Oxford's cancer early detection and prevention research by competitively funding the attendance of early career researchers (students and post-doctoral researchers) at the Early Detection of Cancer and Cancer Prevention Research conferences. Applications from researchers working on fundamental scientific and/or clinical early detection and/or prevention research are welcome. Priority is given to applications with an abstract of high scientific quality with a clearly articulated relevance to the early detection and/or prevention of cancer, and applications with a strong justification for how the applicant will benefit by attending this conference.

This year's OxCODE Travel Award recipients were:

- **Jingfei Cheng** (Song group, Ludwig Institute for Cancer Research) "A human tissue atlas of DNA methylation and hydroxymethylation"
- **Holly Eggington** (Leedham group, Centre for Human Genetics) "BMP modulation suppresses the stem cell niche to prevent disease onset in a model of hereditary colorectal cancer"
- **Yi-Jhih Huang** (Vallis group, Department of Oncology) "Molecular imaging for the detection of Barrett's Esophagus, esophageal dysplasia and adenocarcinoma using a c-Met specific peptide"
- **Zhe Huang** (Travis group, Oxford Population Health) "Proteomic risk factors for prostate cancer: a case-cohort study in EPIC"
- **Joshua Moore** (Byrne group, Mathematical Institute) "Towards spatial hallmarks of cancer detection and treatment"

Look out for announcements via the OxCODE mailing list about future opportunities.

Sponsor - Moderna

At Moderna, our mission is to deliver the greatest possible impact to people through mRNA medicines. Since 2010 we have been pioneering the potential of mRNA to develop therapeutics and vaccines for infectious disease, immuno-oncology, rare diseases, cardiovascular disease and autoimmune diseases.

Most notably, these capabilities have come together to allow the authorised use of vaccines against the COVID-19 pandemic. We are relentlessly working to deliver on the promise of mRNA science to create a new generation of transformative medicines for patients.

Moderna has made a significant commitment to the UK over ten years as part of our strategic partnership with the UK government. Our new site on the Harwell Campus in Oxfordshire – the Moderna Innovation and Technology Centre – will enhance pandemic preparedness and provide the UK public with access to innovative mRNA vaccines for COVID-19 and potentially a range of other infectious diseases.

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Sponsor - Veritie Diagnostics

Veritie is developing a new-to-market first-in-kind In Vitro Diagnostic ('IVD') for cancers that examines the 'biochemical fingerprint' produced by biomarkers released into urine as opposed to quantifying a single biomarker.

Veritie are tackling difficult and novel challenges including the use of Machine Learning to identify signals in a highly complex matrix (urine) to achieve the sensitivity and specificity required by clinical users in order to achieve an IVD that is:

Faster: The aim is to deliver point-of-care testing in sub 3 minutes to reduce the number of clinical interactions (equating to cost/clinician workload) and compresses diagnostic workflow, resulting in faster time-to-therapy and reduced patient anxiety while waiting for test results.

Better: Using Surface Enhanced Raman Spectroscopy classification models with very high (90-10%) sensitivity, specificity, and overall diagnostic accuracy have been shown in academic literature.

Cheaper: A low-cost cartridge-based approach with limited consumables using a low-cost analysis system, together offering a cost-per-test below £10.

For instance, in prostate cancer, we target a sensitivity of 80-90%, versus that of PSA of 20-30%. This would transform the PPV and reduce unnecessary escalation to biopsy/MRI and free up resources for disease-positive patients as well as reducing clinical workload.

Session 1 Keynote

Early detection of cancer using cell-free DNA fragmentomes

Victor Velculescu

Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine

Dr Velculescu led the first genome-wide sequence analysis in human cancers, identifying key genes and pathways in tumorigenesis. He developed methods for global gene expression analyses and coined the word “transcriptome" to describe the patterns that could now obtained in cancer and other cells. This research has revealed the genomic landscape of several human cancers. These analyses identified a variety of genes not previously known to be involved in neoplasia, including *PIK3CA* as one of the most highly mutated genes in human cancer. His group’s discoveries have led to new FDA-approved therapies against PI3K and IDH1, and FDA-approved diagnostic tests for comprehensive tumor profiling. More recently, his group has created AI liquid biopsy approaches for early detection and monitoring of cancer patients. His work has provided new paradigms for understanding human cancer that have paved the way for precision medicine and benefited patients worldwide.

Dr Velculescu is a Professor of Oncology, Pathology, and Medicine, and Genetic Medicine and Co-Director of Cancer Genetics and Epigenetics at the Sidney Kimmel Comprehensive Cancer Center. Dr Velculescu attended Stanford University, where he graduated with Honors and Distinction in Biological Sciences. He obtained his MD and PhD in Human Genetics and Molecular Biology at the Johns Hopkins University School of Medicine.

Dr Velculescu has served as a member of the Board of Directors of AACR, as a Co-Leader of the SU2C Early Detection of Colorectal Cancer Dream Team, and as a member of several scientific advisory boards. He has been a Founder and Co-CEO of Personal Genome Diagnostics and a Founder and CEO of DELFI Diagnostics. His work has been recognized by a variety of national and international awards and honors, including for his entrepreneurial activities.

Session 1 Abstracts

Metabolomics as a tool for early cancer detection

James McCullagh

Department of Chemistry, University of Oxford

James McCullagh is Professor of Biological Chemistry at the University of Oxford and Director of the Mass Spectrometry Research Facility, in the Department of Chemistry. He runs a state-of-the-art mass spectrometry research facility supporting a broad range of mass spectrometry applications, services and collaborative projects. His research group is highly collaborative and develops novel bioanalytical techniques (with a particular focus on metabolomics and multiomics) and investigates fundamental biological and disease-related processes. His research involves biomarker discovery and identifying new targets in complex biochemical systems.

Growing evidence shows altered metabolism plays an important role in early tumorigenesis. IDH mutations probably precede tumour development in multiple cancers, elevating 2-hydroxyglutarate, and early liver cancers are characterised by aberrant metabolic processes. Mounting evidence suggests metabolic changes in early tumour biology have potential for early cancer detection. Metabolomics, sensitive technologies for measuring metabolic profiles in cells, tissues and biofluids, is an emerging technology for early cancer detection. I will discuss how we are using metabolomics for biomarker discovery with IDH mutations and early detection of hepatocellular cancer as examples.

Session 1 Abstracts


BRCA-Vax: Mapping the antigenic landscape to discover targets for a preventive vaccine

Sarah Blagden & Eleni Adamopoulou

Oncology Clinical Trials Office & Centre for Immuno-oncology, University of Oxford

Sarah Blagden, a medical oncologist, conducted her specialty training at the Royal Marsden Hospitals/Institute of Cancer Research and the University of Cambridge where she undertook a CRUK Clinician Scientist PhD Fellowship in fruit fly genetics. She led early phase trials at Imperial College (2006-2015) and was Director of Oxford's Early Phase Clinical Trials Unit (2017-2021) before directing the Oncology Clinical Trials Office specialising in Precision-Prevention and Early Detection studies. She is a strong advocate of patient and public involvement in clinical trial design and leads a lab exploring tumorigenesis.

Eleni Adamopoulou undertook her PhD at the University of Tuebingen under Profs. Rammensee and Topp, focused on antigen presenting cells and T cell responses in infection and autoimmunity. During her postdoctoral training in Tuebingen and Oxford, she made key contributions to describing presentation of MHC ligands in the human thymus responsible for deletion of autoreactive T cells. Her current research centres on discovering tumour-specific antigens for vaccines and T cell therapies, employing mass spectrometry immunopeptidomics to decode the tumour microenvironment.

Eleni and Sarah will describe BRCA-vax which started as an OxCODE-funded project exploring the immunopeptidome of high grade serous ovarian cancer and revealed a unique mRNA splicing pattern, fragments of which are presented as neoantigens by HLA molecules. The current work is further exploring the biology of ovarian and breast tumorigenesis and whether aberrant splicing could be therapeutically targeted in BRCA variant carriers.

Session 2 Panel Discussion

How do you translate your cancer early detection and prevention research for patient benefit?

Hazel Beaver

Patient and Public Representative

Hazel was diagnosed with Bladder cancer in December 2018. She had chemotherapy, followed by major surgery in April 2019. Her working career was spent in quantitative market research, and she is now retired. Hazel joined the Oxford Cancer Patient and Public Involvement (PPI) team in 2019 as a way of helping others on their cancer journey. She's particularly interested in: Prevention; Early Diagnosis; Bladder Cancer; Breast cancer. The outcome of people with cancer is improving all the time and science has a huge role to play: through research comes hope.

Claire Brown

Oxford Science Enterprises

Claire is currently a Partner in the Life Science team at OSE. Her focus is building and investing in novel therapeutics & therapeutic platforms within Oxford across diverse therapy areas and modalities. Claire has spent the majority of her career in the BioPharmaceutical industry at UCB Group, Sanofi-Genzyme and AstraZeneca where she worked in a variety of roles covering R&D strategy, licensing and corporate investing.

Session 2 Panel Discussion

Anna Dowrick

Nuffield Department of Primary Care Health Sciences, University of Oxford

Anna is an interdisciplinary social scientist. Her research explores how improvements in healthcare can be implemented in ways that are equitable and sustainable. Within the Nuffield Department of Primary Care Health Sciences Cancer Group she investigates how to deliver on the promise of new tests and technologies of cancer detection, with a focus on how qualitative methods can be used to reveal how injustice in both the design and implementation of innovation can be made visible and acted upon.

Victor Velculescu

Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine

Dr Velculescu is a Professor of Oncology, Pathology, and Medicine, and Genetic Medicine and Co-Director of Cancer Genetics and Epigenetics at the Sidney Kimmel Comprehensive Cancer Center. He led the first genome-wide sequence analysis in human cancers, and more recently, his group has created AI liquid biopsy approaches for early detection and monitoring of cancer patients.

He has been a Founder and Co-CEO of Personal Genome Diagnostics and a Founder and CEO of DELFI Diagnostics. His work has been recognized by a variety of national and international awards and honors, including for his entrepreneurial activities.

Session 2 Abstracts

Whole-genome urinary DNA methylation for earlier detection of bladder cancer recurrence

Lucy Denly

Ludwig Institute for Cancer Research, University of Oxford

Up to 70% of patients with non-muscle invasive bladder cancer (NMIBC) experience tumour recurrence. Current detection methods rely on frequent cystoscopies, which are costly, invasive, and may lead to delayed diagnoses. There is a pressing need for non-invasive diagnostic tools to detect NMIBC recurrence. Urinary DNA methylation analysis is a promising approach, as urine is easy to obtain, remains in contact with any tumour present, and reflects aberrant DNA methylation changes which occur early in tumorigenesis.

We employ TET-assisted pyridine borane sequencing (TAPS) to conduct whole-genome, base-resolution methylation analysis on urinary DNA. TAPS offers advantages over bisulfite sequencing by being more cost-effective, accurate, and requiring less input DNA. We applied TAPS to DNA isolated from longitudinal urine samples collected from 8 NMIBC patients at high risk of recurrence. We observed global hypomethylation, a common phenomenon of tumorigenesis, in urine samples with a high proportion of tumour-derived DNA. These changes were enriched in the low-molecular weight DNA fraction and detectable at the time of recurrence in NMIBC patients.

Our findings demonstrate that TAPS on urinary DNA enables identification of whole-genome DNA methylation changes associated with NMIBC recurrence. This approach has potential for early, non-invasive detection of bladder cancer recurrence.

Session 2 Abstracts

Nanopore whole genome sequencing of liquid biopsies for cancer detection

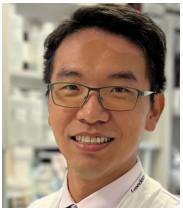
Dimitris Vavoulis

Oxford Molecular Diagnostics Centre, Department of Oncology, University of Oxford

Liquid biopsies hold significant potential for transforming Clinical Oncology by enabling easier sampling for early cancer detection and disease monitoring. We developed a multi-cancer early triage test, TriOx, using TET-Assisted Pyridine Borane Sequencing (TAPS) to sequence whole genomes at high coverage. TAPS allows simultaneous analysis of genetic and epigenetic data with minimal DNA disruption. TriOx integrates genomic and epigenomic data to detect ctDNA in plasma, achieving high sensitivity (85.2%) and over 80% classification performance at ctDNA fractions as low as 0.7% in a cohort of 61 cancer patients and 30 non-cancer controls.

However, current multi-cancer early detection tests (MCEDTs) are costly, limiting accessibility in low-resource settings. To address this, we adapted TriOx for use with shallow Oxford Nanopore Technology (ONT) sequencing, which is less expensive and preserves DNA integrity. Using ONT at 1x genome coverage, we analysed 35 non-cancer and cancer patients with common cancers, such as colorectal and pancreatic. Our method examines copy number aberrations, fragmentomics, structural variation, methylation signals, and viral infection markers, demonstrating performance comparable to deep TAPS sequencing. This cost-effective, minimally invasive triage tool shows promise for accurately identifying cancer and tissue origin in resource-limited clinical environments.

Session 2 Abstracts



Targeting c-MET for endoscopic detection of dysplastic lesions within Barrett's Esophagus using EMI-137 fluorescence imaging

Yi-Jhih Huang

Department of Oncology, University of Oxford

Objective: The goal of this study was to investigate the utility of EMI-137, a c-Met-targeted near-infrared fluorescence imaging tracer, for the detection of Barrett's oesophagus (BE), dysplasia, and oesophageal adenocarcinoma (EAC).

Methods: We conducted an analysis of c-Met expression in human oesophageal tissues using GEO datasets, tissue microarrays, and BE biopsy samples. The diagnostic capability of EMI-137 was evaluated in a dual-xenograft mouse model with c-Met high expressing (OE33) and c-Met negative (FLO-1) tumours. Additionally, in vivo fluorescence molecular endoscopy (FME) was performed in a transgenic mouse model (PL2-IL1b) which closely resembles the progression from normal squamous epithelium to BE/EAC.

Results: Analysis of GEO and microarray data confirmed c-Met is upregulated in BE, and EAC tissues compared to normal squamous epithelium. Following administration of EMI-137, OE33 tumours showed a robust fluorescent signal, while FLO-1 did not, indicating in vivo specificity. FME showed that EMI-137 uptake in the oesophagus of PL2-IL1b mice correlated with late dysplasia. Histopathological analysis revealed a correlation between the c-Met expression in BE tissue and dysplasia grade.

Conclusion: Our results indicate that EMI-137-based imaging could serve as a precise method for the detection of oesophageal dysplasia and early-stage EAC.

Session 2 Abstracts

Using Mendelian randomization to identify circulating proteins involved in multiple myeloma risk

Lucy Goudswaard

Population Health Sciences, University of Bristol

Background: Multiple myeloma (MM) is an incurable blood cancer. The aetiology is unclear; studying the role of circulating proteins may provide biological insight. Here, we investigated the causal relationship between circulating proteins and MM risk.

Methods: We performed two-sample Mendelian randomization (MR), undertaking a discovery and replication approach. GWAS data for proteins were available from two proteomic platforms: (1) SomaLogic (N=35,559 Icelanders) and (2) Olink (N=34,557 UK Biobank; UKB). GWAS data for MM were available from UKB (case=601; control = 372,012) and FinnGen (case=1,085; control=271,463). Sensitivity analyses included reverse MR and colocalization.

Results: Across analysis stages, 440 proteins were instrumentable; 302 proteins MR estimates showed consistent directions of effect. Seven proteins had 95% confidence intervals (CIs) that did not overlap the null in both forward MR analyses, e.g., dermatopontin had a positive effect on MM risk in the discovery (OR: 1.49; 95% CI 1.06-2.09) and replication (OR: 1.47; 95% CI 1.14-1.90) analyses.

Conclusion: Our results highlight seven circulating proteins which may be involved in MM risk; these proteins may be useful markers of MM risk. Future work should explore the utility of these proteins in disease prediction or prevention using proteomic data from patients with MM or precursor conditions.

Session 3 Abstracts


PPI and cancer vaccination: lessons learned so far

Catriona Gilmour Hamilton & Anna Fry

Oxford Cancer, University of Oxford & Patient and Public Representative

After an early career in cancer nursing, Catriona has spent much of the last 30 years working with people affected by cancer. She worked for a national cancer support organisation for 15 years, before embarking on an MA and PhD in Medical History. Her research considered the cancer patient voice and patient empowerment in recent British history. For the past 7 years she has worked with researchers at the University of Oxford to ensure that cancer research learns from the experiences of people affected by cancer.

Anna is one of four Patient and Public Involvement (PPI) representatives on the LynchVax project. Anna has Lynch Syndrome – a genetic predisposition to developing certain cancers. Anna is interested in the prevention of cancer for high-risk individuals and also therefore in raising awareness of the condition which affects 1 in 400 people but only 5% of those people ("Lynchies") being aware they have it. Anna works for a cancer charity but is speaking at the event as a patient representative.

In this talk, they will ask "What do people with experience of cancer think about cancer vaccinations?" "Will people at high risk of cancer be willing to participate in clinical trials?" "What do we need to know to ensure the success of cancer vaccinations in future?" This talk will report on insights gained and lessons learned during consultation meetings with patients, members of the public, and people in high-risk groups.

Session 3 Abstracts

Harnessing the power of tissue resident memory T cells (TRMs) to prevent ovarian cancer

Nancy Zaarour

MRC Weatherall Institute of Molecular Medicine, University of Oxford

Dr Nancy Zaarour is a T cell immunologist and junior research fellow in cancer translational immunology. She moved to Oxford to work on drug discovery and development aiming to identify and validate new targets in Spondylarthritis patients. In 2021, she joined the Weatherall Institute of Molecular Medicine, (Women's Reproductive Health at University of Oxford) as a Postdoc, supported by funding from Ovarian Cancer Action to work with Professor Ahmed Ahmed on enhancing T cell immune response to Ovarian cancer with the aim to identify and develop preventive therapeutic strategies. This work was recognised recently by an award of 5-year Elman Poole Fellowship from Lincoln College, Oxford.

Her research aim is to understand the immunology of the tissue of origin of High Grade Serous Ovarian Cancer, focussing on identifying specific T cells populations with potential to recognise and prevent ovarian cancer. In this talk, she will summarise her recent work on applying *ex vivo* approaches to identify tumor-targeting T cells. The overall goal of this research is to translate her findings into designing and developing immunopreventive strategies for patients. She will also cover how her recent findings had led up to undertaking preclinical testing to evaluate both immunogenicity and antitumor efficacy of a newly designed multipeptide preventive vaccine for ovarian cancer.

Session 3 Abstracts

LynchVax – a precision prevention vaccine for Lynch Syndrome

David Church

Centre for Human Genetics, University of Oxford

David Church is an Associate Professor and CRUK Advanced Clinician Scientist Fellow at the Centre for Human Genetics, University of Oxford. He is also an Honorary Consultant Medical Oncologist at the Oxford Cancer Centre, and clinical lead for Lynch Syndrome across the Central and South Genomics Medicine Service Alliance (population 10.5m). In addition to leading a research group focused on colorectal and endometrial cancers, he leads the Oxford LynchVax group, which aims to develop a vaccine to prevent cancer in this high-risk population.

This talk will present preclinical work towards a preventative vaccine for Lynch syndrome, and outline future steps towards clinical translation.

Session 4 Abstracts

Lung Cancer Screening Big Data Collection in the NHS

Fergus Gleeson

Department of Oncology, University of Oxford

Professor Fergus Gleeson is a Consultant Radiologist and Professor of Radiology in Oxford. He is the Head of Academic Radiology, the Director of the Oxford Radiology Research Unit at Oxford University Hospitals NHS Foundation Trust and the past President of the European Society of Thoracic Imaging. He is the PI for The Integration and Analysis of Data using Artificial Intelligence to Improve Patient Outcomes with Thoracic Diseases (DART), a multicentre study investigating the use of Artificial Intelligence in pulmonary nodules and lung cancer. His specialist interests are in Artificial Intelligence, Thoracic Imaging, PET-CT and Hyperpolarized xenon MRI.

This presentation will discuss the collection of large data sets in the NHS, focusing on the data collected in the DART research programme, This is a multicentre study linking the routine data collected from 16 Targeted Lung Health Centres with outcome data, and includes more than 250,000 participants and over 100,000 linked CT scans and reports, with associated digital pathology and blood samples in a subset of these.

Session 4 Abstracts

Abbreviated Magnetic Resonance Imaging vs ultrasound surveillance for liver cancer detection - The AMULET study

Michael Pavlides

Radcliffe Department of Medicine, University of Oxford

Dr Michael Pavlides is a consultant hepatologist at the John Radcliffe Hospital and lead liver imaging research at the Oxford Centre for Clinical Magnetic Resonance Research (OCMR). His research investigates how magnetic resonance imaging and other biomarkers could be used in the evaluation of people with chronic liver disease including those with liver steatosis, those with diseases of the bile ducts and those at risk of primary liver cancer.

The talk will give an overview of the AMULET study - a single-arm study comparing ultrasound and non-contrast-enhanced MRI scans as surveillance tools for people with liver cirrhosis who are at risk of developing liver cancer. In current practice, people with cirrhosis have 6 monthly ultrasound scans as surveillance for liver cancer - The AMULET study will investigate if non-contrast-enhanced MRI can improve hepatocellular carcinoma diagnosis rates.

Session 4 Keynote

New bio-engineering approaches to treat and detect cancer

Dame Molly Stevens

Kavli Institute for Nanoscience Discovery, Department of Physiology, Anatomy and Genetics, Department of Engineering Science, University of Oxford

Professor Dame Molly Stevens FREng FRS is the John Black Professor of Bionanoscience at the University of Oxford. Her multidisciplinary research spans fundamental science and technology development to tackle major healthcare challenges. A serial entrepreneur, she has founded companies in diagnostics, therapeutics, and regenerative medicine. Her substantial body of work influences research groups around the world (>450 publications, h-index 116, >53k citations, 2018, 2021, 2022 and 2023 Clarivate Analytics Highly Cited Researcher). She is a Fellow of the Royal Society and the Royal Academy of Engineering, and received the 2023 Novo Nordisk Prize.

This talk will present her group's recent advances in bioinspired materials for cancer diagnostics and therapy. They are developing microrobots for targeted drug delivery and nanoneedle arrays for intracellular biosensing at sub-cellular resolution for tumour mapping. Functionalized nanoparticles are being engineered for advanced therapeutics and in vivo diagnostics with a colourimetric readout, validated for prostate cancer detection. She will also discuss SPARTA™ technology for label-free characterization of single nanoparticles, enabling the use of extracellular vesicles as breast cancer biomarkers. She will explore how these innovations can be translated into clinical applications for transformative biomedical advances.

Session 5 Abstracts

Understanding the mechanisms of pre-leukaemic clonal selection

Asger Jacobsen

MRC Weatherall Institute of Molecular Medicine, University of Oxford

Asger studied Medicine at the University of Cambridge, before moving to Oxford Medical School where he qualified in 2014. After work as a junior doctor, he joined Prof Paresh Vyas's laboratory at the Weatherall Institute of Molecular Medicine as an MRC Clinical Research Training Fellow. During his DPhil, he established the MARCH Study, a collaboration with teams at NDORMS and the Nuffield Orthopaedic Centre, to collect bone marrow and blood samples from individuals undergoing hip replacement surgery, which enabled the study of clonal haematopoiesis in healthy older people. He recently moved to Prof Ross Chapman's lab to continue his postdoctoral research.

Clonal haematopoiesis (CH) is a pre-cancerous condition that is common in healthy older people and is associated with a risk of leukaemia. CH occurs when blood stem cells acquire mutations that confer a selective advantage, leading to the growth of an expanded clone. It is unclear how these clones expand, but understanding this is key to developing strategies that may prevent the development of leukaemia. Using single-cell techniques, he has undertaken the first detailed analysis of how CH mutations affect blood production in healthy people. This work gives clues for why mutant cells have an advantage, suggesting a role for inflammation in progression of these clones towards leukaemia.

Session 5 Abstracts

Using spatial biology to quantitively map and understand cell interactions in colorectal adenoma-carcinoma progression

Simon Leedham

Centre for Human Genetics, University of Oxford

Simon Leedham is Professor of Molecular and Population Genetics and an Honorary Consultant Gastroenterologist at the University of Oxford. His research is into the morphogenic signalling pathways that control the intestinal stem cell in homeostasis, regeneration and cancer, and he has published more than 100 peer reviewed papers in journals that include Nature, Nature Medicine, Nature Genetics, Cell Stem Cell, Gastroenterology and Gut. Simon's research has been recognised by the United European Gastroenterology Rising Star award in 2010, the British Society of Gastroenterology Francis Avery Jones research prize in 2015 and the CRUK Future Leaders prize in 2017.

Spatial biology has the potential to unlock information about the disrupted cellular ecosystems that define human disease. Quantitatively assessing cell interactions within the tissue context allows us to map cell self-organisation, to determine why cells interact differently in disease, and to use this to develop diagnostics and treatments. Spatial technologies are advancing rapidly, offering capacity to measure expression of 100s of genes and cellular markers at single cell resolution. However, analysis of these images remains a significant bottleneck, which increases the gap between our ability to generate and interpret these datasets. In this talk, Simon will discuss the development of a mathematical toolkit that can quantify non-random cell interactions in spatial biology images, across tissue organisational structures and multiple length scales, and show how they have applied it to identify changing cell interactions as a colorectal cancer emerges from a benign adenoma precursor.

Session 5 Keynote

Pre-invasive lung cancer progression

Sam Janes

University College London

Sam is the Director of Medicine at University College London. Major contributions include defining that normal airway homeostasis is governed by stochastic division of basal cell; showing that airways genetically damaged by smoking can resolve on quitting; mapping the molecular architecture of pre-cancerous Squamous cell lesions, and identifying the immunological abnormalities that allow precancerous lesions to progress to cancer. These achievements were recognised with his election to the Academy of Medical Sciences in 2021. He is the chief investigator of several trials ranging first-in-man trials of cell and gene therapies emanating from his own lab, to SUMMIT, the largest lung cancer screening trial in Europe recruiting over 13000 people. He works across the University, UCL Hospitals, the UCLH Biomedical Research Centre and interacts closely with industry, again ranging from trial delivery through to venture capital funded drug discovery programmes. He works as a respiratory consultant at UCLH with a particular interest in lung cancer, mesothelioma, interventional and diagnostic bronchoscopy and early lung cancer detection.

Session 6 Abstracts

Chronic pathogen infections and risk of cancers

Ling Yang

Nuffield Department of Population Health, University of Oxford

Associate Professor Ling Yang is a senior epidemiologist at the Nuffield Department of Population Health at the University of Oxford, and coordinates the long-term follow-up working group in the China Kadoorie Biobank study (CKB). Her main research focuses on Women's reproductive health, Chronic infections and environmental causes of chronic diseases and Cancer research based on large-scale cohort studies, and also evidence-based medicine using large national disease surveillance and risk factors survey data to provide strategies for chronic disease prevention and control in developing countries.

Based on the large-scale China Kadoorie Biobank study, this talk will summarise what we have conducted over last years on the aetiological role of multiple chronic pathogen infections in different cancers development, through using conventional test and high-throughput multiplex serology assay measured data and applying conventional, genetic epidemiology and multi-omics approaches.

Session 6 Abstracts

Blood test trends for cancer detection in patients presenting with unexpected weight loss in primary care: a diagnostic accuracy, longitudinal cohort study

Pradeep Virdee

Nuffield Department of Primary Care Health Sciences, University of Oxford

Pradeep is a statistician in the Cancer Theme at the Nuffield Department of Primary Care Health Sciences, University of Oxford. His expertise primarily include the acquisition and use of linked electronic health records data for large-scale cancer diagnostic and prediction modelling studies. His interests lie in the use of repeated measures data for earlier detection of cancer.

Unexpected weight loss (UWL) is a non-specific symptom of cancer. Combining presence of UWL with co-occurring blood test abnormality enhances patient selection for cancer referral. Their recent work found that monitoring trends over repeated blood tests may further improve risk stratification. They compared the diagnostic accuracy of blood test trend to abnormality in 275,234 primary care patients with UWL. Blood test trend gave a higher area under the curve (95% CI) than abnormality for 20 (77% of 26) blood tests. The positive predictive value (95% CI) favoured trend for 18 (69% of 26) blood tests, highest for C-reactive protein (trend 11.9% (10.4-13.5); high 8.2% (7.9%-8.4%)).

Session 6 Abstracts

Proteogenomic and observational evidence implicate ANGPTL4 as a therapeutic target for colorectal cancer prevention

James Yarmolinsky

Department of Epidemiology and Biostatistics, Imperial College London

Background: The role of lipid-perturbing medications in cancer risk is unclear.

Methods: We employed cis-MR and colocalisation to evaluate the roles of ANGPTL4 and 4 other lipid-perturbing drug targets in risk of 5 cancers (breast, colorectal, head and neck, ovarian, prostate). We then triangulated findings using pre-diagnostic protein measures in the EPIC study. To gain mechanistic insight into carcinogenic effects of ANGPTL4, we examined the impact of ANGPTL4 loss-of-function on gene expression in normal colon tissue in BarcUVa-Seq. Finally, we evaluated the association of ANGPTL4 expression in colon tumour tissue with all-cause mortality in TCGA.

Results: Genetically-proxied circulating ANGPTL4 inhibition was associated with reduced colorectal cancer (CRC) risk (OR:0.76, 95% CI:0.66-0.89, P=5.52x10-4, PPcolocalisation=0.83). This association was replicated using pre-diagnostic ANGPTL4 concentrations (HR:0.92, 95% CI:0.85-0.99, P=0.02). In gene set enrichment analysis of differential gene expression in colon tissue, ANGPTL4 loss-of-function was associated (FDR P<0.05) with down-regulation of cellular proliferation, epithelial-to-mesenchymal transition, among other pathways. Lower tumour ANGPTL4 expression was associated with reduced all-cause mortality risk (HR:0.85, 95%CI:0.73-0.99; P=0.04).

Conclusion: Our integrative analyses suggesting a protective role of lower ANGPTL4 concentrations in CRC risk support further evaluation of ANGPTL4, an emerging drug target for hypertriglyceridemia, as a potential therapeutic target for CRC prevention.

Session 6 Abstracts

The RNA binding protein LARP1 drives tumorigenesis by promoting metabolic plasticity and resistance to oxidative stress

James Chettle

Department of Oncology, University of Oxford

Most epithelial cancers transition from precancerous dysplastic lesions to invasive, detectable cancers over several years. Examples of this progression are in high grade serous ovarian cancer which progresses from serous tubal intraepithelial carcinomas (STICs), and in invasive breast cancer which often progresses from ductal carcinoma in situ (DCIS). This 5–10 year latency provides a window of opportunity for both early detection and intervention. We have discovered that the evolutionarily conserved RNA binding protein LARP1 is strongly upregulated in precancers such as STICs and DCIS as well as in invasive cancers. We demonstrate that LARP1 allows cancer cells to dynamically reprogram their metabolism to maintain sufficient supplies of ATP even under nutrient stress. LARP1 acts at a nexus of phosphorylation by multiple kinases including CK2, MEK and mTORC1, whereupon it binds and coordinates the expression of thousands of mRNAs (the “LARP1-regulon”) encoding enzymes within the glycolytic, OXPHOS and ROS homeostasis pathways. This enables LARP1 to transduce growth factor signalling to modulate metabolic plasticity whilst simultaneously protecting the cell from oxidative damage. As pre-cancers frequently display high levels of oxidative stress, our findings underscore the importance of LARP1 during tumorigenesis, as well as in established cancer.

Session 6 Abstracts

Excess galectin-1 in myeloproliferative neoplasms induces platelet activation and pro-fibrotic megakaryocytes

Natalie Jooss

MRC Weatherall Institute of Molecular Medicine, Radcliffe Department of Medicine, University of Oxford

Introduction: Myeloproliferative neoplasms (MPNs) are blood cancers affecting ~40,000 individuals in the UK. Patients present with increased risk of vascular events, including heart attacks or strokes, and 1 in 3 progress to a severe form of MPN called myelofibrosis. Our recent work identified Galectin-1 (Gal1) as novel biomarker of myelofibrosis, further functional inhibition of Gal1 ameliorated progression1.

Hypothesis/Aims: We aimed to interrogate the role of Gal1 on megakaryocyte and platelet phenotypes. Specifically, we hypothesised that increased Gal1 levels in MPNs may induce thrombotic phenotype in platelets and pro-fibrotic megakaryocytes.

Results: In healthy donors Gal1 dose-dependently induced platelet spreading as well as showed αIIbβ3 activation ($P<0.0023$ at 10µg/ml Gal1). However, it did not affect other platelet activation markers, P-selectin or CD63 expression (α/dense granule secretion). Further, additive effects of Gal1 to low dose thrombin were observed. Human iPSC-derived megakaryocytes increased TGFb-secretion in presence of Gal1 (1.5fold increase, $P=0.1595$ at 10µg/ml Gal1). We are now testing whether Gal1 neutralisation may mitigate the prothrombotic phenotype using MPN patient samples in a whole blood thrombus formation assay.

Conclusions: This study uncovers the mechanisms by which Gal1 contributes to MPN disease features, and further highlights Gal1 as an attractive novel target in this setting.

Session 7 Panel Discussion

How do you get grant funding for your cancer early detection/prevention research?

Françoise Howe

Oxford Centre for Cancer Early Detection and Prevention

Françoise Howe is the Scientific Coordinator for OxCODE. A large part of her role is to provide writing support for Oxford-based researchers applying for external funding for cancer early detection and/or prevention research programmes, contributing directly towards >£38m successful grants and industry partnerships to date. Previously she undertook a PhD and her post-doctoral research in Oxford's Department of Biochemistry on the regulation of transcription in yeast.

Talisia Quallo

Cancer Research UK

Talisia Quallo is a Research Programme Manager for Early Detection and Diagnosis research at Cancer Research UK where she oversees CRUK's research portfolio and strategic initiatives for early detection/ diagnosis marker discovery and validation, data science for early detection and early detection/diagnosis technology development. She is also responsible for creating opportunities for industry-academia collaboration.

Session 7 Panel Discussion

Janette Rawlinson

Patient and Public Representative

Involved in cancer research since 2013, Janette is an active patient representative involved with funding panels, co-applicant in several studies, governance committees and groups including cancer alliance, CTUs and various cancer organisations in the UK and Europe. She entered this world oblivious that it existed but immersed herself! Having lived experience of a lifestyle condition without the lifestyle, not treated in a specialist centre and living in a highly diverse area helped her suggest different perspectives to researchers and policy makers as part of CRUK's JING, NIHR, NCRI, EORTC, ERS and other expert advisory groups or screening committees.

Florence Theberge

MRC/UKRI (Translation Research)

Florence Theberge is a Programme Manager within the MRC/UKRI Translation Research Team where she oversees the vaccine, antibody, and protein/peptide therapeutics research portfolio. She is also the MRC representative for the MRC/NIHR Efficacy and Mechanism Evaluation Programme. With a PhD in Experimental Psychology/Neuroscience from the University of Cambridge and over 10 years of research management experience in the UK HEI sector and NIHR, Florence is dedicated to translating fundamental discoveries into interventions that benefit patients and enhance the return on investment in research.

Session 8 Abstracts


Cancer, serious disease diagnoses, and clinically significant incidental findings in the first six years of the Oxford Suspected CANcer (SCAN) pathway

Fergus Gleeson & Claire Friedemann Smith

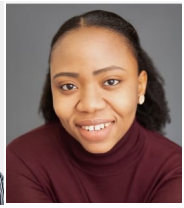
Department of Oncology & Nuffield Department of Primary Care Health Sciences, University of Oxford

Professor Fergus Gleeson is a Consultant Radiologist and Professor of Radiology in Oxford. He is the Head of Academic Radiology, the Director of the Oxford Radiology Research Unit at Oxford University Hospitals NHS Foundation Trust and the past President of the European Society of Thoracic Imaging.

Dr Claire Friedemann Smith is a senior mixed methods researcher at the Nuffield Department of Primary Care Sciences, University of Oxford. Claire has an MSc in Health Psychology from the University of Surrey and a DPhil in Primary Care Research from the University of Oxford. She joined the SCAN Pathway team in 2017 as the SCAN Researcher and has worked on the prospective cohort study of the Pathway since its launch. Her research interests include routes to diagnosis for cancer, clinician-patient communication, and clinical decision making.

The Oxford SCAN Pathway opened in 2017 as one of five pilot rapid diagnostic centre (RDC) based pathways in England, providing a route to diagnosis for patients with non-specific symptoms. The SCAN Pathway accepts patients referred by their GP with at least one of the SCAN criteria, and provides all patients with a low-dose, contrast enhanced computed tomography (CT) scan, panel of blood tests, and follow-up in a multi-disciplinary clinic if no diagnosis is made from the CT scan. Fergus and Claire present the pathway and patient outcomes of the first six years of the SCAN Pathway and discuss what can be learnt for the future of RDC pathways.

Session 8 Abstracts

Understanding barriers to research participation alongside the SCAN pathway

Julie-Ann Moreland & Aduke Onafowokan

Oxford University Hospitals NHS Foundation Trust & Inclusivitii

Julie-Ann Moreland is an academic and clinical diagnostic radiographer working clinically in the Suspected CANcer (SCAN) Pathway at the Churchill Hospital, Oxford. Her research interests are in the evidence base of Non-Specific Symptom cancer pathways and early diagnostic techniques, particularly the equitable access of testing and support services for patients and the patient experience of these pathways and how pathways can be redesigned to best support patients.

Aduke Onafowokan is the Founder, CEO, and Principal Consultant of Inclusivitii, a leading diversity, equity, and inclusion (DEI) consultancy. Since 2018, she has driven transformative change in workplaces and communities by collaborating with employees, suppliers, and public bodies to design global and regional initiatives focused on equity, inclusive cultures, and belonging. She leads bias mitigation, allyship, and inclusive hiring programmes, and has worked with major organisations like NHS England and the University of Oxford, while also leading Horizon Collective, empowering >10,000 women worldwide.

The Suspected CANcer (SCAN) Pathway has an optional research arm, involving blood sample donation. Fewer than half of patients consent to research. Demographics and ethnicity of the research cohort are not representative of the SCAN cohort. The aim was to understand what barriers are for participation in research. A prospective audit began in April 2024, collating patient's demographics, socioeconomic status, if they were approached for consent, reasons for no approach and reasons for refusal. Audit data was reviewed with Inclusivitii to help identify short-, medium- and long-term changes in consent process and patient engagement, ensuring that the approach is inclusive.

Session 8 Keynote

Doing “detective work”: how are non-specific symptom pathways for cancer investigation organised, and what are the implications for safety and quality of care?

Georgia Black

Wolfson Institute of Population Health, Queen Mary University of London

Dr Georgia Black is an applied psychologist and health services researcher with a focus on diagnostic safety in primary care and cancer pathways, healthcare exclusion and socioeconomic inequalities. In 2019, she was awarded a prestigious Postdoctoral Fellowship by THIS Institute to study diagnostic safety culture in non-specific symptom pathways for cancer. Georgia leads a multidisciplinary team with expertise in human factors, digital inclusion, and implementation science in a programme of work including pathways to diagnostic testing, referral behaviours, cancer diagnosis for patients with a learning disability and the delivery and uptake of interpreters in primary care.

Over the past two decades, the UK has prioritised early cancer diagnosis, particularly for patients with non-specific symptoms. In 2015, NSS pathways were introduced to reduce delays in referral and diagnosis. This talk examines the 'detective work' of clinical teams who investigate these cases, where symptoms offer few clear clues. She will discuss how teams gather and connect diagnostic information, focusing on tasks performed to ensure patient safety. She will also explore the roles, skills, and clinical backgrounds that shape activities, highlighting the value of generalist-specialist expertise in guiding decisions.

Poster Presentations

	Presenter	Title
1	Shalin Abraham	Exploratory preliminary analysis of cohort recruited to the Pearl study in the DeLIVER-HCC programme
2	Haige An	Diurnal variation in the human blood proteome: a cross-sectional study in the UK Biobank
3	Thineskrishna Anbarasan	Integrating multiparametric MRI with spatial transcriptomics to identify “Radio-Spatial Genomic” features of prostate cancer using artificial intelligence
4	Stephanie Chan	Prospective and genetic analyses implicate immunosurveillance in the aetiology of prostate cancer
5	Yiquan Chen	Investigating the role for elevated 2-hydroxyglutarate (2-HG) in IDH1 mutant glioblastoma cells using 13C5 2-HG as a metabolic tracer
6	Jingfei Cheng	A methylation and hydroxymethylation atlas of normal and tumour tissues
7	James Chettle	The RNA binding protein LARP1 drives tumorigenesis by promoting metabolic plasticity and resistance to oxidative stress
8	Lucy Denly	Whole-genome urinary DNA methylation for earlier detection of bladder cancer recurrence
9	Alison Dillman	The circulating proteome and cancer risk: A systematic literature review and meta-analysis of prospective cohorts

Poster Presentations

	Presenter	Title
10	Helene Dreau	Oxford Molecular Diagnostics Centre - Driving innovation and collaboration in genomics and molecular pathology testing
11	Aleksandra Dzhoneva	Uncovering the cell type-specific antigenic landscape in colorectal cancer
12	Joe Gilbody	Using reverse Mendelian randomization to discover novel circulating biomarkers for early detection of ovarian and pancreatic cancer
13	Victoria Goss	MODERNISED Trial design: Cost-effective multi-cancer early detection by measuring patient plasma amino acid cross sections with the Enlighten test
14	Lisa Hobson	Using human genetic data to identify circulating protein level changes that are the causal consequence of cancer processes.
15	Yi-Jhih Huang	Targeting c-MET for endoscopic detection of dysplastic lesions within Barrett's Esophagus using
16	Zhe Huang	Proteomic risk factors for prostate cancer: a case-cohort study in EPIC
17	Natalie Jooss	Excess galectin-1 in myeloproliferative neoplasms induces platelet activation and pro-fibrotic megakaryocytes
18	Ashley Kamimae-Lanning	Endogenous formaldehyde-induced DNA damage drives stem cell attrition and pauciclonal haematopoiesis

Poster Presentations

	Presenter	Title
19	Nicole Keyworth	The NHS Cancer Vaccine Launch Pad (CVLP): expanding access to personalised cancer vaccines
20	Maira Khan	Sex differences in cancer incidence: prospective analyses in the UK Biobank
21	Joshua Moore	MuSpAn: A toolbox for multiscale spatial analysis
22	Chibuzor Ogamba	Leveraging germline genetics to predict the preventive efficacy of approved cancer therapies
23	Keren Papier	Identifying proteomic risk factors for cancer using prospective and exome analyses of 1463 circulating proteins and risk of 19 cancers in the UK Biobank
24	Sarah Pearson	Clinical trial management support for delivery of early detection and precision prevention trials, from concept to completion
25	Victoria Perletta	Prevalence of metabolic dysfunction in cancer patients in England using large-scale linked population based data
26	Anne Powell	The Integration and Analysis of Data using Artificial Intelligence to Improve Patient Outcomes with Thoracic Diseases (DART) research programme
27	Tara Seedher	The presenting signs, symptoms and tests associated with a lymphoma diagnosis within primary care settings: a systematic review
28	Dimitris Vavoulis	Nanopore whole genome sequencing of liquid biopsies for cancer detection

Poster Presentations

	Presenter	Title
29	Yanxia Wu	Unlocking the potential of omics: comprehensive research solutions with CHG-TP
30	Qian Yang	A novel bioinformatics pipeline for the identification of reliable cancer-testis antigens in colorectal cancer
31	James Yarmolinsky	Proteogenomic and observational evidence implicate ANGPTL4 as a therapeutic target for colorectal cancer prevention

Poster Abstract – 1

Exploratory preliminary analysis of cohort recruited to the Pearl study in the DeLIVER-HCC programme

Shalin Abraham[1], Hamish Innes, James Robineau, Emily Ashwin, Jennifer Benselin, Manuella Siaka Monthe, Klaudia Kowska, Tamsin Cargill, Eleanor Barnes and the DeLIVER Consortium

[1]Ludwig Institute for Cancer Research, University of Oxford

Hepatocellular carcinoma (HCC) is the commonest cause of liver cancer, with a rising incidence in the UK and globally. HCC most often occurs in patients with cirrhosis caused by chronic liver diseases. The CRUK funded DeLIVER study aims to collect patient data and samples to better understand the pre-cancerous changes in the liver to inform the development of early detection technologies. The Pearl study (Prospective Cohort for Early Detection of Liver Cancer, NCT05541601), within DeLIVER, is a prospective multicentre longitudinal cohort study, which aims to recruit 3000 patients with liver cirrhosis in the UK who will be followed up over 3-4 years. We performed an exploratory analysis of the 1955 patients recruited into Pearl. Patients are distributed across 43 centres, with the highest proportion (19%) from the South-East region. The majority of patients are male (64%) and ethnically White (91%), with a mean AMAP risk score that predicts a 4.8% risk of HCC development over 3 years. The most common liver disease aetiology were alcohol (48%) and metabolic associated steatotic liver disease (34%). 42 patients having developed HCC since recruitment (incidence 1.7 per 100 people/year). We will present a description of our cohort, with a preliminary analysis of the characteristics associated with HCC surveillance and the development of HCC.

Poster Abstract – 2

Diurnal variation in the human blood proteome: a cross-sectional study in the UK Biobank

Haige An, Mahboubeh Parsaeian, Karl Smith-Byrne, Ruth C Travis

Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford

Blood collection time is an important pre-analytical factor in protein biomarker research. This study investigates how blood protein levels vary throughout the day, using data from the UK Biobank Pharma Proteomics Project. We examined plasma levels of 2,923 proteins measured by the Olink Explore platform in samples from 53,015 UK Biobank participants collected at initial recruitment centre visit. ANCOVA models assessed protein levels across six time intervals (<10 am, 10 am–12 pm, 12 pm–2 pm, 2 pm–4 pm, 4 pm–6 pm, and >6 pm), adjusting for potential confounders. Bonferroni correction was applied for multiple testing, and linear regression evaluated trends in protein levels by time of day. After adjustments, levels of 1,813 proteins varied significantly by blood collection time, with many linked to energy metabolism. Levels of 379 proteins were higher later in the day, while 1,151 were lower. The most time-sensitive proteins included PPY, GCG, and SULT1A1. This is the largest study of its kind, in terms of sample size and the number of proteins analysed. Findings emphasise the impact of blood collection time on protein levels, underscoring the need for standardised collection times to improve biomarker accuracy and patient outcomes.

Poster Abstract – 3

Integrating multiparametric MRI with spatial transcriptomics to identify "Radio-Spatial Genomic" features of prostate cancer using artificial intelligence

Thineskrishna Anbarasan[1], Sandy Figiel, Sophia Abusamra, Nikita Sushentsev, Wencheng Yin, Nithesh Ranasinha, James T Girst, Dan Woodcock, Richard J Bryant, Ruth McPherson, Freddie C Hamdy, Tristan Barrett, Bartlomiej Papiez, Ian G Mills, Alastair Lamb

Nuffield Department of Surgical Sciences, University of Oxford

Background: Precisely identifying the subgroup of men at highest risk of progressing from localised to metastatic prostate cancer (PCa) remains a challenge. By integrating clinical parameters, multiparametric MRI (mpMRI) radiomics and spatial transcriptomics (ST), this novel "Radio-Spatial Genomics" platform may identify radiomic features associated with important biological aspects of PCa.

Methods: Spatial transcriptomics was performed formalin-fixed paraffin embedded prostatectomy sections in men with Gleason 4+4 PCa. Using a proportional size algorithm and a convolutional neural network, MRI slices were aligned and registered to histopathology sections.

Results: Prostate-wide histopathology sections from a patient were registered to T2-axial MRI slices. In total 114688 sequenced ST spots were co-registered to 30485 pixels on MRI. A median DICE correlation score of 0.942, 0.738 and 0.756 was achieved for capsule, tumour and BPH nodules respectively. AMACR (marker for PCa) expression inversely correlated with T2 MRI intensity ($r = -0.793$), consistent with tumour being hypointense. Differential gene expression analysis between peri-tumoural and tumour regions revealed enrichment for genes in mucosal immune response.

Conclusion: We report a novel approach to identify genotypic changes based on radiomic features. With further validation, this "Radio- Spatial Genomics" model may allow detection of aggressive PCa genotypic features from diagnostic mpMRI imaging.

Poster Abstract – 4

Prospective and genetic analyses implicate immunosurveillance in the aetiology of prostate cancer

Mahboubeh Parsaeian*, Stephanie Chan*, Joshua R Atkins*, Keren Papier, Trishna Desai, Zhe Huang, David Conti, Konstantinos K Tsilidis, James Yarmolinsky, Sabina Rinaldi, Rudolf Kaaks, Verena Katzke, Matthias Schulze, Catarina Schiborn, Saverio Caini, Lorenzo Milani, Raul Zamora-Ros, Marcela Guevara, Maria-Jose Sánchez, The PRACTICAL Consortium, Ian G Mills, Christopher Haiman, Tim J Key, Karl Smith-Byrne, Ruth C Travis

Nuffield Department of Population Health, University of Oxford

Background: There is limited prospective evidence for the role of specific inflammation pathways and related protein markers in the development of prostate cancer.

Methods: We examined the associations of 368 inflammation and immune-related circulating proteins with prostate cancer risk, using a nested case-control study in the European Prospective Investigation into Cancer and Nutrition (EPIC). Proteins were measured using the Olink Explore Inflammation panel amongst 1,434 prostate cancer cases (158 high-grade, 273 advanced-stage, 488 clinically-aggressive) and 1,434 matched controls. We meta-analysed these estimates with results from our previous prospective analyses in UK Biobank (UKB). Mendelian randomisation, colocalization, and exome protein score analyses were also conducted.

Results: In the EPIC-UKB meta-analysis, after correcting for multiple testing, FLT3LG and CNTNAP2 were significantly associated with prostate cancer risk overall (HR: 0.88 [95% CI: 0.84-0.92] and 1.10 [1.05-1.16], respectively), while six proteins (IL15, FLT3LG, BCL2L11, PGF, CKAP4, and TNFRSF11A) were associated with risk of prostate cancer diagnosed >7 years after blood draw (HR for IL15: 0.86 [95% CI: 0.81-0.93]). IL15 and FLT3LG also had complementary evidence from exome analyses.

Conclusions: Our findings suggest that proteins involved in immunosurveillance pathways (recruitment and activation of natural killer and T cells) may be linked to prostate cancer risk.

Poster Abstract – 5

Investigating the role for elevated 2-hydroxyglutarate (2-HG) in IDH1 mutant glioblastoma cells using 13C5 2-HG as a metabolic tracer

Yiquan Chen, Ingvild C Hvinden and James SO McCullagh

Department of Chemistry, University of Oxford

Mutations in IDH1 and IDH2 are prevalent in over 70% of grade II and III gliomas, resulting in elevated levels of 2-hydroxyglutrate (2-HG). Despite its association with IDH1 mutant cells, the specific role of 2-HG in tumorigenesis remains unclear. This study aimed to elucidate the metabolic interactions of 2-HG using 13C-labelled 2-HG as an isotope tracer, comparing IDH1 mutant and wild-type LN18 glioblastoma cell extracts.

Mutant and wild-type cells, were cultured with U13C5 2-HG. Analysis was performed using untargeted anion-exchange chromatography-mass spectrometry (IC-MS) and reversed-phase liquid chromatography-mass spectrometry (RPLC-MS). Labelled 2-HG was confirmed in both cell types by matching isotope patterns and retention times to authentic standards.

A database of 458 metabolite standards was used to identify isotope abundance patterns in cell extracts. No significant 13C incorporation was observed into these metabolites. One compound-feature was identified using untargeted metabolomics analysis, with an m/z 226.9963, which showed evidence of five 13C atoms enrichment.

To conclude, utilisation of fully 13C labelled 2-HG provided insights into cellular processes. For example, we found no evidence for the conversion of 2-HG back to 2-oxoglutarate. But 2-HG derived carbon atoms were found in a single compound in intracellular suggesting a metabolic product of 2-HG.

Poster Abstract – 6

A methylation and hydroxymethylation atlas of normal and tumour tissues

Masato Inoue, Jingfei Cheng[1], Felix Jackson, Jinfeng Chen, Haiqi Xu, Beibei Wang, Yanchun Peng, Natalie J Jooss, Bob Amess, Yibin Liu, Benjamin Schuster-Böckler, Bethan Psaila, Tao Dong, Chun-Xiao Song

[1]Ludwig Institute for Cancer Research, University of Oxford

DNA cytosine modifications, 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC), are key epigenetic regulators. Their distribution across the genome helps shape tissue-specific expression in normal development, and aberrations in this distribution are linked to cancer. Accurate tissue references of 5mC and 5hmC are valuable for understanding epigenetic mechanisms and developing clinical applications. Current DNA methylation atlases rely on bisulfite sequencing, which cannot separate 5mC from 5hmC. Additionally, whole-genome methylome atlases for tumours and quantitative 5hmC are currently unavailable. Here, we present the first human atlas containing matched 5mC and 5hmC signatures for 13 normal tissue types, 9 blood cell types, 2 pre-cancerous tissue types, and 10 types of common solid tumours, using our TAPSβ and CAPS+ techniques. This atlas contains whole-genome, base-resolution, quantitative 5mC and 5hmC information for 116 samples, at a mean coverage of 30×. Harnessing this rich sequencing data, we identify spatially distinct 5mC and 5hmC markers that are tissue and tumour informative. By combining these markers, we built a prediction model that accurately predicts gene expression in a tissue-specific manner. This atlas sheds light on the emerging role of 5hmC as a distinct epigenetic regulator and provides a high-resolution resource of tissue and tumour epigenetic signatures for further investigation.

Poster Abstract – 7

The RNA binding protein LARP1 drives tumorigenesis by promoting metabolic plasticity and resistance to oxidative stress

James Chettle[1], Zinaida Dedeic, Kendra Perez-Smith, Molly Browne, Leticia Campo, Iolanda Vendrell, Roman Fischer, James McCullagh, Sarah Blagden

[1]*Department of Oncology, University of Oxford*

Most epithelial cancers transition from precancerous dysplastic lesions to invasive, detectable cancers over several years. Examples of this progression are in high grade serous ovarian cancer which progresses from serous tubal intraepithelial carcinomas (STICs), and in invasive breast cancer which often progresses from ductal carcinoma in situ (DCIS). This 5–10 year latency provides a window of opportunity for both early detection and intervention. We have discovered that the evolutionarily conserved RNA binding protein LARP1 is strongly upregulated in precancers such as STICs and DCIS as well as in invasive cancers. We demonstrate that LARP1 allows cancer cells to dynamically reprogram their metabolism to maintain sufficient supplies of ATP even under nutrient stress. LARP1 acts at a nexus of phosphorylation by multiple kinases including CK2, MEK and mTORC1, whereupon it binds and coordinates the expression of thousands of mRNAs (the "LARP1-regulon") encoding enzymes within the glycolytic, OXPHOS and ROS homeostasis pathways. This enables LARP1 to transduce growth factor signalling to modulate metabolic plasticity whilst simultaneously protecting the cell from oxidative damage. As pre-cancers frequently display high levels of oxidative stress, our findings underscore the importance of LARP1 during tumorigenesis, as well as in established cancer.

Poster Abstract – 8

Whole-genome urinary DNA methylation for earlier detection of bladder cancer recurrence

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Up to 70% of patients with non-muscle invasive bladder cancer (NMIBC) experience tumour recurrence. Current detection methods rely on frequent cystoscopies, which are costly, invasive, and may lead to delayed diagnoses. There is a pressing need for non-invasive diagnostic tools to detect NMIBC recurrence. Urinary DNA methylation analysis is a promising approach, as urine is easy to obtain, remains in contact with any tumour present, and reflects aberrant DNA methylation changes which occur early in tumorigenesis.

We employ TET-assisted pyridine borane sequencing (TAPS) to conduct whole-genome, base-resolution methylation analysis on urinary DNA. TAPS offers advantages over bisulfite sequencing by being more cost-effective, accurate, and requiring less input DNA. We applied TAPS to DNA isolated from longitudinal urine samples collected from 8 NMIBC patients at high risk of recurrence. We observed global hypomethylation, a common phenomenon of tumorigenesis, in urine samples with a high proportion of tumour-derived DNA. These changes were enriched in the low-molecular weight DNA fraction and detectable at the time of recurrence in NMIBC patients.

Our findings demonstrate that TAPS on urinary DNA enables identification of whole-genome DNA methylation changes associated with NMIBC recurrence. This approach has potential for early, non-invasive detection of bladder cancer recurrence.

Poster Abstract – 9

The circulating proteome and cancer risk: A systematic literature review and meta-analysis of prospective cohorts

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Background: Proteins have an integral role in cancer etiology and inform cancer detection, treatment, and prognosis. However, the landscape of proteomic evidence remains unclear.

Methods: We conducted a systematic review and meta-analysis. We searched Embase and Medline up to December 2023 with reference-list screening and hand-searching up to January 2024. Prospective cohort studies were eligible if they used multiplex panels, included adults without cancer diagnosis at baseline, and reported the association between circulating proteins at baseline and risk of ten cancers.

Findings: Of 4,949 articles, we included 26 unique studies comprising 84,129 participants and 14,326 cancer cases. The studies profiled 2,434 unique proteins and reported 19,130 protein-cancer associations. We conducted 3,448 meta-analyses and detected 216 associations that passed false discovery rate correction for breast (n=14), lung (n=172), colorectal (n=27), prostate (n=1), and stomach (n=2) cancer. Meta-analyses were not possible for liver, esophagus, thyroid, or cervix uteri cancer, due to limited data. No significant associations were observed for bladder cancer.

Interpretation: We identified protein-cancer associations with strong evidence. Our findings highlight the need for large, diverse, and mature prospective cohorts with high throughput proteomic methods to facilitate robust replication and better elucidate the association between circulating proteins and risk of cancer.

Poster Abstract – 10

Oxford Molecular Diagnostics Centre - Driving innovation and collaboration in genomics and molecular pathology testing

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The Oxford Molecular Diagnostics Centre (OMDC), a collaboration between Oxford University Hospitals and the University of Oxford, is pioneering advancements in genomics and molecular pathology testing with a focus on oncology. The OMDC integrates cutting-edge technology and clinical expertise to support Phase I-III clinical trials, enabling personalised approaches to diagnostics and therapeutic strategies. With robust capabilities in sample collection, processing, and molecular pathology expertise, the centre ensures high-quality, clinical-grade molecular & genomic data to inform decision-making.

Key highlights include tailored Next-Generation Sequencing (NGS) assays for tumour profiling, measurable residual disease detection, and biomarker identification. Leveraging both long-read and short-read platforms, OMDC provides flexible sequencing solutions for diverse research and clinical needs. Complementing its technical prowess, the centre employs advanced bioinformatics infrastructure, ensuring rigorous data analysis and interpretation to maximise insights from large genomic datasets.

Currently on a path to full accreditation against ISO:15189 (2022) the OMDC maintains stringent quality assurance practices, reinforcing its commitment to excellence. Current projects span the use of liquid biopsies for cancer monitoring and the development of multi-omics assays for early detection. By fostering innovation and collaboration, the OMDC is committed to driving forward precision medicine, enhancing patient outcomes and shaping the future of clinical genomics.

Poster Abstract – 11

Uncovering the cell type-specific antigenic landscape in colorectal cancer

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Colorectal cancer (CRC) is the third most prevalent malignancy and second leading cause of cancer-related mortality worldwide, highlighting an urgent need for better understanding of the neoplasm for the development of more efficient immunotherapies. Here, we employed a mass-spectrometry based immunopeptidomics approach to characterise the intra- and inter-tumoral antigenic landscape of five CRC patients, each represented by multiple tumour macro-regions from the same mass and paired non-malignant colon tissue. Immuno-affinity purified HLA Class-I peptides were sequenced using liquid chromatography with tandem mass spectrometry (LC-MS/MS). A total of 172,447 HLA Class-I restricted peptides were identified, of which 121,993 were predicted to bind to the respective patient HLA alleles. Using a novel pipeline that integrates publicly available transcriptomics, proteomics and immunopeptidomics data we aimed to deconvolute the identified HLA ligands from our discovery cohort to generate cell type-specific antigen presentation profiles, allowing for the characterisation of inter- and intra- patient tumour heterogeneity and levels of immune infiltration. Paired single-cell RNA sequencing (scRNA-seq) data from the discovery CRC cohort were used to validate our approach. Overall, we present an approach that provides a comprehensive, in-depth view of the CRC immunopeptidome in a cell-type-specific manner and reveals tumour-/immune-associated peptides with therapeutic potential.

Poster Abstract – 12

Using reverse Mendelian randomization to discover novel circulating biomarkers for early detection of ovarian and pancreatic cancer

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Cancer is the leading cause of death in the UK. Despite important advances in treatment in recent decades, the prognosis for many cancers remains poor because individuals typically present with advanced disease at which point curative treatment is no longer an option. Improvements in early detection of cancer could reduce the burden from this disease. We have used a novel approach ("reverse Mendelian randomization") to identify novel circulating biomarkers of early cancer onset to improve early detection of pancreatic, and ovarian cancer. Genetic risk scores were constructed using PRS- Continuous shrinkage (PRS-CS) and were used to estimate the association between genetic instruments and concentrations of 2,941 highly abundant proteins in the UK Biobank PPP study (N= 54,219). We performed forward Mendelian randomization analysis to distinguish proteins that are a cause of cancer as opposed to a causal consequence. In our initial reverse MR analyses we identified 221 proteins at a false discovery threshold (0.05) for ovarian cancer, of which 11 were identified as potentially causal in the forwards MR analyses. We plan on repeating these analyses with pancreatic cancer and following up our findings with colocalization analyses to further elucidate the causal relationship.

Poster Abstract – 13

MODERNISED Trial design: Cost-effective multi-cancer early detection by measuring patient plasma amino acid cross sections with the Enlighten test

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Cancer remains the leading cause of death in the UK. If found earlier there are more treatment options and patients are more likely to survive 5 years post diagnosis. The Enlighten test has been developed to quickly detect cancers as a measure of amino acid composition in the blood with results returnable within 48 hours from blood draw. Data indicates that the Enlighten test is well placed for improving cancer outcomes as it is particularly sensitive for detecting early-stage cancers.

The NIHR funded MODERNISED study is a prospective, observational, multicenter study that aims to recruit 1350 individuals (1000 cases and 350 controls) with cancer symptoms from 10 solid tumour cancer types (Bladder, Breast, Colorectal, Lung, Melanoma, Oesophageal, Ovarian, Pancreatic, Prostate, Renal). The study will collect a single 4mL blood sample which will be analysed at the Wessex Investigational Sciences Hub (WISH) laboratory.

The primary aim of MODERNISED is to evaluate sensitivity and specificity for the Enlighten test in detecting 10 solid tumour cancer types with deprivation associated gradients in mortality outcomes. Results from this trial will guide the design of a larger, randomised trial to generate evidence for evaluation as a diagnostic test as part of standard of care.

Poster Abstract – 14

Using human genetic data to identify circulating protein level changes that are the causal consequence of cancer processes

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Colorectal cancer and lung cancer 5-year survival drops from 9 in 10 and 6 in 10 when diagnosed at stage 1 to around 1 in 10 when diagnosed at stage 4. Detecting cancer at the earliest stage presents challenges; one of the challenges facing improving cancer screening is identifying specific biomarkers for the cancers of interest. This project aims to utilise genetic epidemiological approaches to identify novel proteins altered by lung and colorectal cancer. We hypothesise that protein level changes resulting from cancer onset can be identified via an individual's polygenic risk score (PRS) for the disease, representing their genetic liability to develop that cancer. Development of PRS of lung and colorectal cancer in UK Biobank (UKB) participants with Olink protein measures has been carried out using GWAS summary statistics from the International Lung Cancer Consortium & The Genetics and Epidemiology of Colorectal Cancer Consortium. Association between the proteins and PRS has been assess and bidirectional Mendelian randomisation will be performed to identify circulating proteins that are downstream of the cancer liability pathway. Proteins that change in concentration close to cancer onset and are causally downstream of cancer liability could represent novel biomarkers for early detection of cancer.

Poster Abstract – 15

Targeting c-MET for endoscopic detection of dysplastic lesions within Barrett's Esophagus using EMI-137 fluorescence imaging

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Objective: The goal of this study was to investigate the utility of EMI-137, a c-Met-targeted near-infrared fluorescence imaging tracer, for the detection of Barrett's oesophagus (BE), dysplasia, and oesophageal adenocarcinoma (EAC).

Methods: We conducted an analysis of c-Met expression in human oesophageal tissues using GEO datasets, tissue microarrays, and BE biopsy samples. The diagnostic capability of EMI-137 was evaluated in a dual-xenograft mouse model with c-Met high expressing (OE33) and c-Met negative (FLO-1) tumours. Additionally, in vivo fluorescence molecular endoscopy (FME) was performed in a transgenic mouse model (PL2-IL1b) which closely resembles the progression from normal squamous epithelium to BE/EAC.

Results: Analysis of GEO and microarray data confirmed c-Met is upregulated in BE, and EAC tissues compared to normal squamous epithelium. Following administration of EMI-137, OE33 tumours showed a robust fluorescent signal, while FLO-1 did not, indicating in vivo specificity. FME showed that EMI-137 uptake in the oesophagus of PL2-IL1b mice correlated with late dysplasia. Histopathological analysis revealed a correlation between the c-Met expression in BE tissue and dysplasia grade.

Conclusion: Our results indicate that EMI-137-based imaging could serve as a precise method for the detection of oesophageal dysplasia and early-stage EAC.

Poster Abstract – 16

Proteomic risk factors for prostate cancer: a case-cohort study in EPIC

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Background: Prostate cancer (PCa) is the most common cancer in men, yet its causes are poorly understood. Plasma proteins are central to several biological processes, including those that lead to cancer development.

Methods: We conducted a case-cohort study within the EPIC cohort, analysing plasma samples from 1,573 sub-cohort members and 982 incident PCa cases (290 aggressive cases) using the SomaLogic-7k assay. Associations between proteins and PCa risk were assessed using Prentice-weighted Cox regression models, with subgroup analyses by disease aggressiveness. Findings passing corrections for multiple testing were compared with evidence from Mendelian randomization and an independent study using Olink-3k assay.

Results: After a median of 16.2 years of follow-up, ACP3, FLT4, and KLK3 were significantly associated with overall PCa risk [HRs (95% CI) per SD increment: 1.20 (1.10, 1.31), 1.26 (1.13, 1.40), and 2.28 (1.96, 2.65), respectively]. In subgroup analyses,12 proteins were associated with high-grade disease, nine to advanced stage, and seven to aggressive PCa. ANKRD1 was associated with the risk of all three aggressive subtypes by approximately 25% per SD increase. Additionally, 12 proteins were associated with PCa diagnosed >15 years post-blood draw, with some showing concordant genetic evidence.

Conclusion: Novel circulating proteins are associated with PCa risk, particularly aggressive subtypes, which may lead to better understanding of underlying aetiological mechanisms.

Poster Abstract – 17

Excess galectin-1 in myeloproliferative neoplasms induces platelet activation and pro-fibrotic megakaryocytes

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Introduction: Myeloproliferative neoplasms (MPNs) are blood cancers affecting ~40,000 individuals in the UK. Patients present with increased risk of vascular events, including heart attacks or strokes, and 1 in 3 progress to a severe form of MPN called myelofibrosis. Our recent work identified Galectin-1 (Gal1) as novel biomarker of myelofibrosis, further functional inhibition of Gal1 ameliorated progression1.

Hypothesis/Aims: We aimed to interrogate the role of Gal1 on megakaryocyte and platelet phenotypes. Specifically, we hypothesised that increased Gal1 levels in MPNs may induce thrombotic phenotype in platelets and pro-fibrotic megakaryocytes.

Results: In healthy donors Gal1 dose-dependently induced platelet spreading as well as showed αIIbβ3 activation ($P<0.0023$ at 10µg/ml Gal1). However, it did not affect other platelet activation markers, P-selectin or CD63 expression (α/dense granule secretion). Further, additive effects of Gal1 to low dose thrombin were observed. Human iPSC-derived megakaryocytes increased TGFb-secretion in presence of Gal1 (1.5fold increase, $P=0.1595$ at 10µg/ml Gal1). We are now testing whether Gal1 neutralisation may mitigate the prothrombotic phenotype using MPN patient samples in a whole blood thrombus formation assay.

Conclusions: This study uncovers the mechanisms by which Gal1 contributes to MPN disease features, and further highlights Gal1 as an attractive novel target in this setting.

Poster Abstract – 18

Endogenous formaldehyde-induced DNA damage drives stem cell attrition and pauciclonal haematopoiesis

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Formaldehyde is a genotoxic molecule which our cells encounter daily from endogenous sources. Two tiers of protection guard genome integrity: ADH5, which enzymatically clears formaldehyde, and the Fanconi anaemia (FA) DNA repair pathway. Without these defences, DNA damage, mutagenesis, stem cell attrition, and tumorigenesis can occur. In haematopoietic stem cells (HSCs), this leads to bone marrow failure or leukaemia. However, it is unclear when and where ADH5 is required to protect blood production. We conditionally inactivated ADH5 in blood of FA-deficient mice and found they exhibit early loss of HSCs which are often undetectable and almost completely incapable of reconstitution activity. However, many mice sustain blood production for several months; to understand how, we turned to deep sequencing of short-lived granulocytes to gain insight into current blood-producing cells, followed by mathematical modelling. This approach revealed that these animals produce blood in a pauciclonal manner, often from a single ancestor. Applying this to CD34+ cells from FA patients, we observed monoclonality in one out of four patients. This technique offers unparalleled insight into when clonal blood production arises and could provide an affordable way in future to detect variant alleles and clone formation in blood decades before the onset of disease.

Poster Abstract – 19

The NHS Cancer Vaccine Launch Pad (CVLP): expanding access to personalised cancer vaccines

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The NHS Cancer Vaccine Launch Pad (CVLP) is a study designed to establish the feasibility of broadening access to vaccine trials through referral from a network of patient identification sites and in parallel, processes to streamline tissue handling and genomic analysis to prepare the NHS for wider implementation.

Since opening in September 2023, the CVLP has been supporting recruitment of colorectal cancer patients to BNT122-01, a personalised vaccine trial. To date >2000 patients have been screened with 328 participants recruited to the CVLP. UK sites are now screening over double the number of patients for BNT122-01 compared to sites in other countries and contribution from CVLP reached 61% of participants screened for BNT122-01 in July 2024. CVLP sites have demonstrated fast activation and activity with sites now recruiting and referring their first patient on average 26 days and 33 days respectively from site activation. Through involving the CVLP site network of 46 hospitals, geographical reach and inclusivity of the trial has increased. We estimate that BNT122-01 is now accessible to over 50% of resected colorectal cancer patients in England.

The study will expand in 2025 to support further industry sponsors with cancer vaccines across a broad range of cancer types.

Poster Abstract – 20

Sex differences in cancer incidence: prospective analyses in the UK Biobank

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Background: We examined differences in cancer incidence between women and men in the UK and the extent to which these persisted after accounting for established risk factors.

Methods: Prospective analyses in UK Biobank to examine associations between sex and risk of 15 cancers (and 13 subtypes) using minimal and multivariable-adjusted Cox proportional hazards regression models. Multivariable models were stratified for age, deprivation index, and region, and adjusted for ethnicity, qualifications, height, BMI, smoking status, alcohol, and site-specific risk factors.

Results: Over an average of 10.5 (SD 2.2) years of follow-up, 32,315 incident cancers (58.1% in women) were identified in 470,771 individuals (53.8% women). Some differences in cancer risk between the sexes attenuated to the null in the multivariable-adjusted models, but men remained at greater risk than women for cancers at eight sites: oesophageal adenocarcinoma (hazard ratio 5.45; 95% confidence interval, 4.18-7.12), gastric cardia (3.65; 2.48-5.38), bladder (3.47; 2.85-4.24), oral cavity (2.06; 1.69-2.51), liver (1.91; 1.48-2.47), kidney (1.77; 1.51-2.09), rectum (1.70; 1.47-1.96), and leukaemia (1.43; 1.21-1.69). Men had lower risks for cancers of the breast, thyroid (0.36; 0.26-0.49), anus (0.41; 0.26-0.64), and lung adenocarcinoma (0.72; 0.62-0.84).

Conclusion: Further research on these sex differences in risk may provide insights into cancer aetiology.

Poster Abstract – 21

MuSpAn: A toolbox for multiscale spatial analysis

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Spatial biology offers critical insights into the disrupted cellular ecosystems that define human disease. By mapping spatially-resolved cell interactions, researchers can study tissue self-organization and uncover differences in cellular behaviour between healthy and pathological states. However, the multiscale complexity of mammalian tissues poses significant challenges, limiting the interpretation of spatial data and creating inconsistencies across analytical approaches. Existing pipelines integrate image processing, cell annotation, and spatial analysis, but their varied methodologies hinder cross-compatibility and standardisation.

To overcome these challenges, we present MuSpAn, a Python-based toolbox for Multiscale Spatial Analysis of multiplex imaging data. MuSpAn provides an imaging platform-agnostic framework to analyse spatial data across scales, from subcellular to tissue-level interactions. Unlike rigid pipeline-based tools, MuSpAn offers flexible exploratory tools for interactive data evaluation, alongside customisable high-throughput pipelines tailored to users' preferred methodologies. Its methods span diverse fields, including spatial statistics, network theory, topological data analysis, and morphology, enabling robust and versatile analysis.

MuSpAn also simplifies querying of spatial elements, such as point-like data (e.g., cells) and polygon-like regions (e.g., neighbourhoods), facilitating the exploration of complex biological questions with minimal computational barriers. This open-access tool empowers researchers to advance our understanding of disease progression and improve clinical applications.

Poster Abstract – 22

Leveraging germline genetics to predict the preventive efficacy of approved cancer therapies

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Introduction: The high costs and failure rates in drug development have hindered progress in new cancer therapies. Genetic evidence has been shown to increase the likelihood of drug development success. We investigated the potential yield of germline genetics in recapitulating the efficacy of approved cancer therapeutics for prevention.

Methods: We mapped 3,080 plasma protein cis-pQTLs from UK Biobank Olink and Iceland SomaLogic data to approved cancer drugs and their indications via the Open Targets Platform. Cancer indications were mapped to 39 cancer GWAS summary statistics. Mendelian randomisation analyses estimated the association between target protein concentrations and cancer risk at $p<0.05$. We then calculated the probability, R(G), that an approved target-indication pair would have genetic support for prevention and tested its sensitivity by cancer type.

Results: Among 298 protein-cancer pairs available for analysis, 49 significant associations were found, with 36 showing a congruent direction of effect with the drug's action on the protein. These represented 20/72 unique targets of 54/139 drugs across 19 cancer subtypes. We estimated R(G) for all cancers to be 1.95 (Katz 95% CI:1.46 –2.60), varying by cancer type.

Conclusion: Our findings support the utility of genetics in identifying potential therapies that can be repurposed for cancer prevention.

Poster Abstract – 23

Identifying proteomic risk factors for cancer using prospective and exome analyses of 1463 circulating proteins and risk of 19 cancers in the UK Biobank

Keren Papier[1], Joshua R Atkins, Tammy YN Tong, Kezia Gaitskell, Trishna Desai, Chibuzor F Ogamba, Mahboubeh Parsaeian, Gillian K Reeves, Ian G Mills, Tim J Key, Karl Smith-Byrne, Ruth C Travis

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The availability of protein measurements and whole exome sequence data in the UK Biobank enables investigation of potential observational and genetic protein-cancer risk associations. We investigated associations of 1463 plasma proteins with incidence of 19 cancers and 9 cancer subsites in UK Biobank participants (average 12 years follow-up). Emerging protein-cancer associations were further explored using two genetic approaches, cis-pQTL and exome-wide protein genetic scores (exGS). We identify 618 protein-cancer associations, of which 107 persist for cases diagnosed more than seven years after blood draw, 29 of 618 were associated in genetic analyses, and four had support from long time-to-diagnosis (> 7 years) and both cis-pQTL and exGS analyses: CD74 and TNFRSF1B with NHL, ADAM8 with leukemia, and SFTPA2 with lung cancer. We present multiple blood protein-cancer risk associations, including many detectable more than seven years before cancer diagnosis and that had concordant evidence from genetic analyses, suggesting a possible role in cancer development.

Poster Abstract – 24

Clinical trial management support for delivery of early detection and precision prevention trials, from concept to completion

Sarah Pearson

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The Oncology Clinical Trials Office (OCTO) provides clinical trial management support to investigators across the CRUK Oxford Centre to manage trials from concept to completion. When you work with us you'll be working with a CTU with the professional expertise you require for the development and delivery of your clinical trial in an academic research environment.

The poster includes:

- Details about OCTO and its leadership
- How OCTO can support investigators in running trials, and what sort of trials we seek for our portfolio.
- The process for approaching OCTO with a trial
- An overview of the types of trials we are currently have in the OCTO portfolio

Poster Abstract – 25

Prevalence of metabolic dysfunction in cancer patients in England using large-scale linked population based data

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Background: Metabolic dysfunction, while variably defined, has been linked to an increased risk of developing obesity-related cancer. Population-based data can be used to explore the onset, timing, trajectories and cumulative effect of various metabolic risk factors, such as insulin resistance, inflammation, dyslipideamia and hypertension, which can be targeted in the prevention of cancer.

Objectives: Our study investigates the relationship between metabolic dysfunction, obesity and incident cancer using longitudinal databases in England. Specific objectives are to: (1) describe history of metabolic dysfunction in cancer patients across tumour and treatment types; (2) explore prevalence of metabolic risk factors in obese vs. leaner patients; and (3) understand whether metabolic dysfunction has implications on cancer treatments.

Methods: Data are linked from the Systemic Anti-Cancer Therapy (SACT) database, holding >839,000 cancer patient records; QResearch, a database of 35M primary care records; and Hospital Episode Statistics (HES), recording hospital admissions. Descriptive analyses and time-to-event models will leverage demographic, lifestyle, biomarker and comorbidity data from QResearch and HES, together with cancer type, stage and grade, and systemic treatments captured in SACT.

Impact: Understanding further the interplay between metabolic risk factors, obesity and cancer may inform preventative strategies, as well as a more precise definition for metabolic dysfunction.

Poster Abstract – 26

The Integration and Analysis of Data using Artificial Intelligence to Improve Patient Outcomes with Thoracic Diseases (DART) research programme

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Introduction: DART is a multi-collaborator research programme aiming to improve multiple facets of Lung Cancer Screening and provide a data set for future. It collects clinical metadata, CT scans, and pathology from participants in NHS England's Targeted Lung Health Checks (TLHC) programme.

Materials and Methods: DART has Health Research Authority and Confidentiality Advisory Group approvals and has uniquely linked the data collected to Health Episode Statistics data, to enable long term outcome data to be collected. The collection of this data has involved linking TLHCs and their associated Hospitals, Radiology and Pathology departments, and transferring the data into the Oxford University Hospital's Secure Data Environment and to academic and commercial collaborators.

Results: DART is now linked to 13 TLHCs, and 4 further sites are in the process of linking. It has curated 245,160 participants post opt-out, and has currently, 114,598 CT scans, and 1,434 digital pathology samples and is increasing weekly.

Conclusion: The DART dataset is enabling development, testing and validation of Artificial Intelligence algorithms that improve the selection of participants for LCS, detection of pulmonary nodules and lung cancers on CT scans, diagnosis of lung cancer and subtyping on digital pathology images, and prognostic algorithms to determine the need for neoadjuvant or adjuvant treatment post resection.

Poster Abstract – 27

The presenting signs, symptoms and tests associated with a lymphoma diagnosis within primary care settings: a systematic review

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Background: Lymphoma, subtypes Hodgkin (HL) and Non-Hodgkin (NHL), is the fifth most common cancer but challenging to diagnose in primary care. Symptoms typically mimic benign conditions and routine investigative tests are lacking. This systematic review sought to determine the accuracy of signs, symptoms and tests of incident lymphoma in primary care.

Methods: Studies were identified through MEDLINE, Embase and Cochrane Database Syst. Rev. . Data were extracted to estimate diagnostic accuracy of clinical features for HL, NHL, and Lymphoma not otherwise specified (NOS). Risk of bias was assessed using QUADAS-2.

Results: From eight eligible studies, 15 symptoms and 18 tests were identified. Most frequently reported features included head/neck swelling, lymphadenopathy, and inflammatory marker tests. Lymphadenopathy was the strongest associated feature, odds ratios ranging from 184.5 (40.7,837.1) for lymphoma NOS and 263.0 (133.0, 519.0) for NHL. The highest positive predictive values (PPVs) were for lymphadenopathy, 5.6% and 13% for HL and NHL respectively. The remaining PPVs were below 3%. Combining features often increased the PPVs. No feature provided sufficient evidence to rule out lymphoma. 6/8 studies had high bias risk.

Conclusions: Lymphadenopathy is the best predictive feature for lymphoma. Future research should report a broader range and combinations of features to better stratify lymphoma risk.

Poster Abstract – 28

Nanopore whole genome sequencing of liquid biopsies for cancer detection

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Liquid biopsies hold significant potential for transforming Clinical Oncology by enabling easier sampling for early cancer detection and disease monitoring. We developed a multi-cancer early triage test, TriOx, using TET-Assisted Pyridine Borane Sequencing (TAPS) to sequence whole genomes at high coverage. TAPS allows simultaneous analysis of genetic and epigenetic data with minimal DNA disruption. TriOx integrates genomic and epigenomic data to detect ctDNA in plasma, achieving high sensitivity (85.2%) and over 80% classification performance at ctDNA fractions as low as 0.7% in a cohort of 61 cancer patients and 30 non-cancer controls.

However, current multi-cancer early detection tests (MCEDTs) are costly, limiting accessibility in low-resource settings. To address this, we adapted TriOx for use with shallow Oxford Nanopore Technology (ONT) sequencing, which is less expensive and preserves DNA integrity. Using ONT at 1x genome coverage, we analysed 35 non-cancer and cancer patients with common cancers, such as colorectal and pancreatic. Our method examines copy number aberrations, fragmentomics, structural variation, methylation signals, and viral infection markers, demonstrating performance comparable to deep TAPS sequencing. This cost-effective, minimally invasive triage tool shows promise for accurately identifying cancer and tissue origin in resource-limited clinical environments.

Poster Abstract – 29

Unlocking the potential of omics: comprehensive research solutions with CHG-TP

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The Centre for Human Genetics Technology Platforms Hub (CHG-TP), nestled within the vibrant academic ecosystem of University of Oxford, we are your gateway to cutting-edge research and innovation in the dynamic world of omics technologies. Dissecting complex biological functions can be achieved by applying one or multiple omics technologies and capture a holistic view of multiple markers simultaneously. By integrating Single Cell (10X) and Spatial omics (Xenium) with targeted Proteomics (Olink and Alamar), CHG-TP is committed to provide access and expert advise on the latest, proven, "omics" solution. We have been the first in UK to implement and offer the newest version of the Proximity Extension Assay (PEA) technology by Olink. With Explore, a high-throughput protein profiling, PEA is coupled with NGS to vastly increase the number of detectable proteins from small volumes of samples. In addition, the portfolio has been expanded to precision proteomics by Alamar, which leverages NULISA to achieve attomolar-level limit of detection and a 10-log dynamic range. The multidisciplinary team forming CHG-TP allows great technical and scientific support and access to state-of-the-art equipment. We also embrace a collaborative approach towards training in molecular biology techniques, co-develop methods and customise automation protocols on our liquid handler instruments.

Poster Abstract – 30

A novel bioinformatics pipeline for the identification of reliable cancer-testis antigens in colorectal cancer

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Background: Cancer-testis antigens (CTAs) are proteins normally expressed immune-privileged organs, such as testis and ovary, but are often re-expressed in tumours. Colorectal cancer (CRC) is among the most life-threatening cancer types worldwide, in which CTA expression profile has been greatly overlooked. Here, we present a bioinformatics pipeline to thoroughly investigate CTA expression in CRC.

Methods: Multiple colon tumour regions derived from the same tumour and paired non-malignant adjacent colon tissues from five treatment-naive CRC patients were subjected to single-cell RNA sequencing (scRNA-seq) and mass-spectrometry-based HLA-I immunopeptidomics (ImP).

Results: We developed a 3-step CTA discovery pipeline, incorporating gene expression profiles from TCGA-COAD/READ, GTEx (normal tissue), and a curated list of CTAs. This approach identified 92 CRC-specific CTAs. Interrogation of the ImP data from CRC cohort demonstrated that all shortlisted candidates were presented and tumour exclusive. We identified a subset of epithelial cells highly expressing the shortlisted CTAs from the paired scRNAseq data, further reinforcing their tumour specificity.

Conclusions: Our unbiased CTA discovery pipeline offers a platform workflow that can be implemented to any cancer type of interest. The biological relevance of the CRC-specific CTA candidates was cross-validated using multiomics, highlighting their potential as targets for cancer vaccination strategies.

Poster Abstract – 31

Proteogenomic and observational evidence implicate ANGPTL4 as a therapeutic target for colorectal cancer prevention

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Background: The role of lipid-perturbing medications in cancer risk is unclear.

Methods: We employed cis-MR and colocalisation to evaluate the roles of ANGPTL4 and 4 other lipid-perturbing drug targets in risk of 5 cancers (breast, colorectal, head and neck, ovarian, prostate). We then triangulated findings using pre-diagnostic protein measures in the EPIC study. To gain mechanistic insight into carcinogenic effects of ANGPTL4, we examined the impact of ANGPTL4 loss-of-function on gene expression in normal colon tissue in BarcUVa-Seq. Finally, we evaluated the association of ANGPTL4 expression in colon tumour tissue with all-cause mortality in TCGA.

Results: Genetically-proxied circulating ANGPTL4 inhibition was associated with reduced colorectal cancer (CRC) risk (OR:0.76, 95% CI:0.66-0.89, P=5.52x10-4, PPcolocalisation=0.83). This association was replicated using pre-diagnostic ANGPTL4 concentrations (HR:0.92, 95% CI:0.85-0.99, P=0.02). In gene set enrichment analysis of differential gene expression in colon tissue, ANGPTL4 loss-of-function was associated (FDR P<0.05) with down-regulation of cellular proliferation, epithelial-to-mesenchymal transition, among other pathways. Lower tumour ANGPTL4 expression was associated with reduced all-cause mortality risk (HR:0.85, 95%CI:0.73-0.99; P=0.04).

Conclusion: Our integrative analyses suggesting a protective role of lower ANGPTL4 concentrations in CRC risk support further evaluation of ANGPTL4, an emerging drug target for hypertriglyceridemia, as a potential therapeutic target for CRC prevention.

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