CANCER RESEARCH UK | Oxford Centre

OXFORD CANCER

UNIVERSITY OF OXFORD

# Annual Symposium

## Tuesday 18th March 2025

### Mathematical Institute, Woodstock Road, Oxford

# Oxford Cancer Annual Symposium 2025 Programme

| | | | |
|---|---|---|---|
| | 8.30 | **Registration Open** | |
| | 9.15-9.30 | **Welcome** | **Tim Elliott**<br>Co Director - Oxford Cancer |
| **Session 1: Early Detection & Immno-Oncology**<br>Chair: Tim Elliott | 9.30-9.45 | Circulating Blood Platelets as Cancer Sentinels | **Bethan Psaila**<br>Radcliffe Department of Medicine |
| | 9.45-9.50 | Nanopore Whole-Genome Sequencing of cfDNA for Cancer Detection | **Dimitris Vavoulis**<br>Department of Oncology |
| | 9.50-10.05 | Translating GDF15 into Cancer Immunotherapy | **Ignacio Melero**<br>Nuffield Department of Medicine |
| | 10.05-10.20 | Exploring the Role of B Cells in Patients with Bowel Cancer: A Global Perspective | **Isabela Pedroza-Pacheco**<br>Nuffield Department of Medicine |
| | 10.20-10.25 | Spatial Exploration of B-Cell-Centric Immune Hubs in Colorectal Cancer | **Fengyun Zhong**<br>Nuffield Department of Medicine |
| | 10.25-10.30 | Unravelling the Evolutionary Landscape of MSS Colorectal Cancer: Insights from Single-Cell Transcriptomics and Immunopeptidomics | **Qian Yang**<br>Nuffield Department of Medicine |
| | 10.30-11.15 | **Coffee Break and Poster Viewing (odd numbers), Information Stalls** | |
| **Session 2: New to Oxford**<br>Chair: Mark Middleton | 11.15-11.30 | Shedding Light on How Immune Cells Become Dysfunctional in Tumours | **David Withers**<br>Nuffield Department of Medicine |
| | 11.30-11.45 | Activation of Bivalent Genes in Cancer by De Novo DNA Methylation | **Marketa Tomkova**<br>Nuffield Department of Medicine |
| | 11.45-12.00 | Treg Targeting Reprograms the Innate and Adaptive Immune Microenvironment in Brain Cancer | **Felipe Galvez-Cancino**<br>Nuffield Department of Medicine |
| | 12.00-12.15 | Melanoma Cell Fate - From the Inside and the Outside | **Richard White**<br>Nuffield Department of Medicine |
| | 12.15-13.20 | **Lunch, Poster Viewing (even numbers), Information Stalls** | |
| **Session 3: PPI**<br>Chair: Catriona Gilmour Hamilton | 13.20-14.00 | PPI Panel Discussion<br>Experiences of Involvement - Funding, Feelings, Publishing and Diversity | **Julliet Lwiindi**<br>**Patrick McGuire**<br>**Bep Dhaliwal**<br>Oxford Cancer PPI Group |
| **Session 4:Digitally-Enabled Research**<br>Chair: Michael Youdell | 14.05-14.30 | Building the Thames Valley and Surrey Secure Data Environment for Research | **Kerrie Woods**<br>NHS, R&D clinical informatics |
| | 14.30-14.45 | Oxford Precision Oncology for Sarcoma (Oxpos), A Prospective Observational and Data Integration Cohort for Sarcoma Care Innovation | **Bass Hassan**<br>Sir William Dunn School of Pathology |
| | 14.45-15.00 | Harnessing The Value of Routinely Collected NHS Data to Develop Deep, Multi-Modal Real-World Datasets to Support Cancer Research | **Christie Brooks**<br>Arcturis Data Limited |
| | 15.00-15.15 | Investigating T-Cell Exclusion Through Perfusion of Human Hemi-Liver Specimens | **Alex Gordon-Weeks**<br>Nuffield Department of Surgical Sciences |
| | 15.15-15.30 | Artificial Intelligence, its Development and Use in Imaging in Clinical Practice | **Fergus Gleeson**<br>Department of Oncology |
| | 15.30-15.45 | Domain-Specific Foundation Models for Better Cancer Care: Development of The Trustedmdt Copilot for Cancer Mdts | **Andrew Soltan**<br>Department of Oncology |
| | 15.45-16.00 | Predicting Cancer After Unexplained Weight Loss Using Blood Test Time Trends: A Machine Learning Approach | **Andres Tamm**<br>Nuffield Department of Primary Care Health Sciences |
| | 16.00-16.30 | **Coffee Break** | |
| **Session 5: Keynote & Centre Announcements**<br>Chair: Simon Leedham | 16.35-17.15 | The Maths of Cancer Evolution | **Trevor Graham**<br>The Institute of Cancer Research (ICR)<br>Keynote Speaker |
| | 17.15-17.25 | **Awards and closing remarks** | **Mark Middleton**<br>Co Director - Oxford Cancer |
| | 17.25 | **Networking Reception** | |

# Welcome from the Oxford Cancer Directors

**Tim Elliott**

**Mark Middleton**

## It is our great pleasure to welcome you to the 12th Annual Oxford Cancer Symposium, supported by the CRUK Oxford Centre

We are proud to present a program that highlights some of the cutting-edge cancer research taking place across Oxford. Our sessions this year will explore research within the themes of Early Detection and Immuno-Oncology, New to Oxford, and Digitally-Enabled Research. We are also honoured to welcome Professor Trevor Graham, Director of the Centre for Evolution and Cancer at The Institute of Cancer Research, as our keynote speaker. His interdisciplinary lab combines mathematical modelling and molecular biology to study cancer evolution, with a translational focus spanning early detection to treatment of metastases, particularly in colorectal cancer.

Reflecting on the past year, we take immense pride in the progress made by Oxford's cancer research community and the role that Oxford Cancer has played in facilitating your impactful and headline-grabbing research. Among this year's achievements: the MyMelanoma trial became the largest study of its kind through partnership with NHS Digitrials; we launched two new Centres of Research Excellence focused on Liver and Oesophagogastric cancers to accelerate research in two cancers of unmet need; and securing external funding for precision prevention programmes in colorectal, ovarian, lung and cervical cancers.

Another major milestone to note is the recent launch of our £50 million partnership with GSK to explore the potential of cancer prevention through immunotherapy. The GSK-Oxford Cancer Immuno-Prevention Programme, led by Professor Sarah Blagden, unites expertise from four University departments and builds on Oxford's exceptional track record in vaccine development. As Professor Irene Tracey, Vice-Chancellor of the University of Oxford, stated: 'This partnership represents a step forward in cancer research.'

Critical to all this success is putting patients at the heart of what we do. Providing them with meaningful decision-making roles in all our programmes not only improves the quality and impact of research across the city, but motivates us to continue to be ever more ambitious.

It is hugely reassuring to see many of the projects we launched as part of our 2022 scientific strategy achieve their potential. At the same time, with one eye to the future, the next 2 years will be critical as many of the underpinning grants that enable and catalyse cancer research across the city are renewed. Building on our community's success and in light of these forthcoming funding renewals, there has never been a better time for researchers to develop and grow new teams to tackle the challenges of cancer at every stage of the translational pathway. Days like today provide a fantastic opportunity to do this.

# About Oxford Cancer and the CRUK Oxford Centre

## Oxford Cancer

Oxford Cancer is a city-wide network and partnership between Oxford University and Oxford University Hospitals NHS Trust, based on the University's Translational Biomedical Research Campus.

It currently comprises over 1000 members from around 90 different Departments, Units, and Institutes of the University, as well as the NHS Trust, which invests over £55m each year into translational cancer research.

Oxford Cancer is an inclusive network of organisations in Oxford for whom cancer research is a priority focus. We support and connect people working across a range of disciplines and aim to facilitate research collaboration on a local, national and international scale to speed up translation from scientific discovery to treatments in patients.

Any faculty member, student or employee of the University of Oxford interested in cancer research, and any clinician, nurse, or employee of the Oxford University Hospitals NHS Trust interested in cancer research can join our membership. To become a member, visit our website.

## The CRUK Oxford Centre

The CRUK Oxford Centre harnesses Oxford's world-leading cancer research with the core aim of facilitating collaboration to ensure rapid translation from scientific discovery to treatments for patients. The Centre is run as part of the Oxford Cancer network, with a focus on funding Cancer Research UK strategic priorities.

# Support and Services

Oxford Cancer is here to support your research by coordinating expertise, lowering barriers and helping you to access key research facilities.

We have access to a range of services that can help your research to reach its translational potential. These are available to any University of Oxford or Oxford University Hospitals staff member belonging our Oxford Cancer community. More details on the tools, teams and resources available can be found on our website.

Funding support

Translational histopathology lab

Clinical positioning network

Patient sample access

Clinical trial support

PPI

Molecular diagnostics centre

Comms & event support

Translational data platform

# Get in touch

We are always happy to hear from our members!

Get in touch...

E: cancer@medsci.ox.ac.uk

T: +44 (0)1865 617043

Bluesky: @oxfordcancer.bsky.social

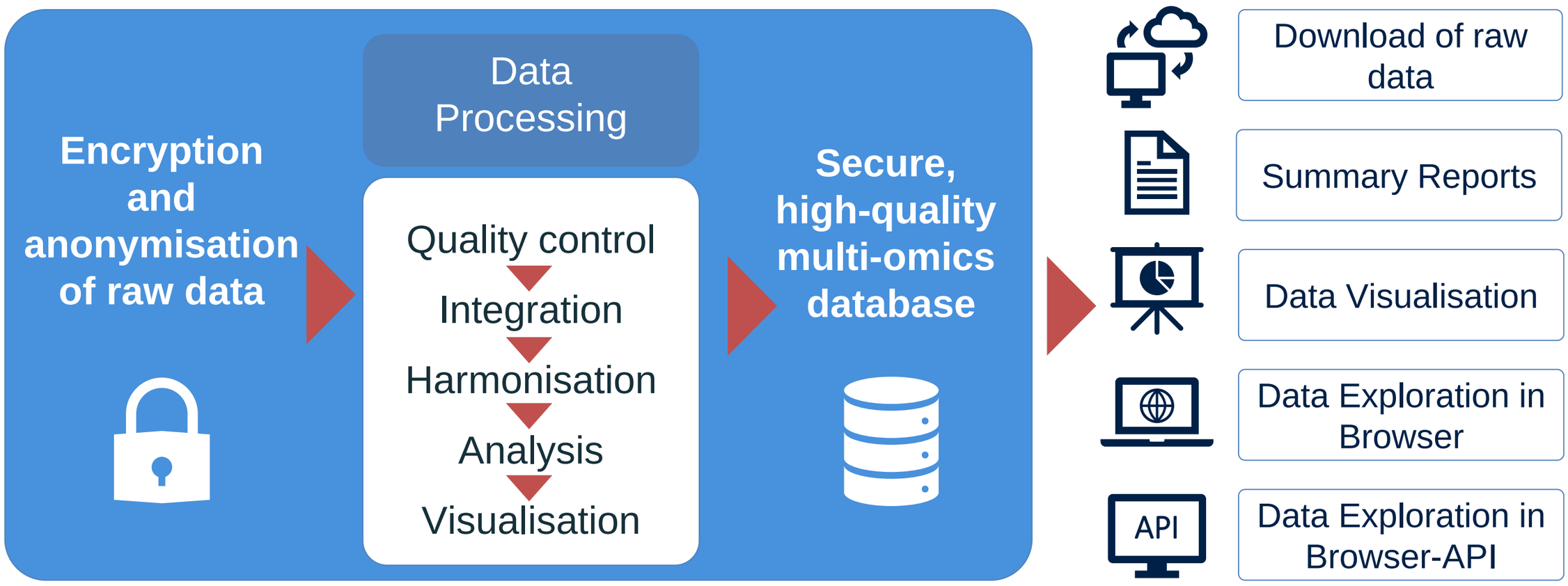
W: cancer.ox.ac.uk

# Translational Data Platform

***"We enable Oxford researchers to fully capitalise on clinical, imaging and molecular data generated during clinical studies."***

The platform can accommodate single cell and bulk RNASeq expression data, WGS mutations, SNPs, copy number variation, methylation, proteomics, IHC, H&E images, spatial transcriptomics, MRI and other scans, and clinical data.

Data are combined into a single, secure, user-friendly, data platform: **cBioportal**




To request access to our data or if you would like help with managing yours please email **sara.danielli@medsci.ox.ac.uk**

**TRIALS ON THE PLATFORM**

**S:CORT**
2000 colorectal cancer patients

**METFORMIN**
41 breast cancer patients

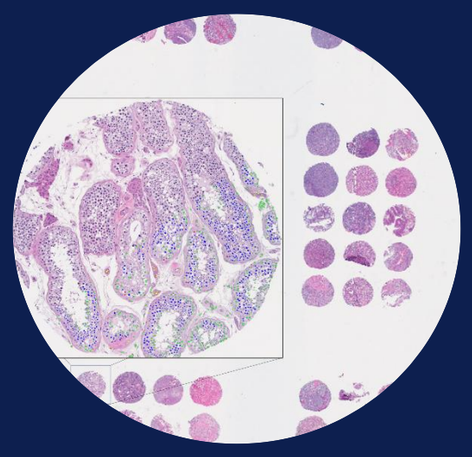
**WINGMEN**
pancreatic cancer
TBA

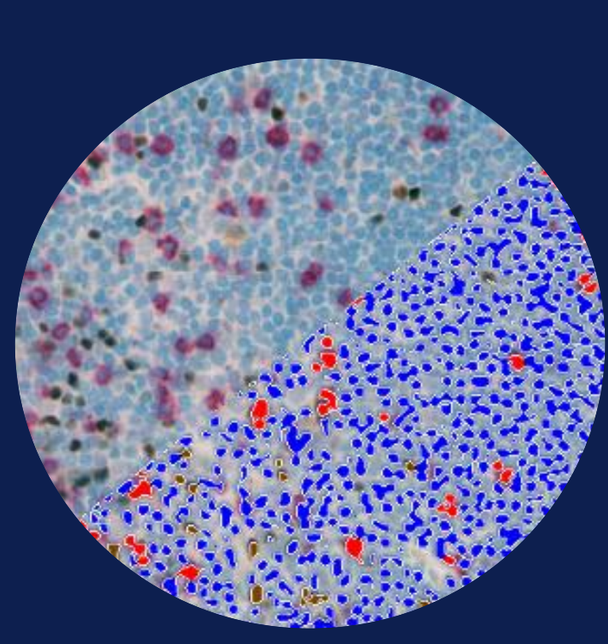
**FRONTIER**
40 breast cancer patients

**SCOPE**
250 oesophageal cancer patients

# Translational Histopathology Laboratory

thlenquiries@oncology.ox.ac.uk





## Services

**Tissue processing, embedding and sectioning**

**Tinctorial histochemical staining (H&E).**

**Multiplex immunofluorescence with panel optimisation and imaging**

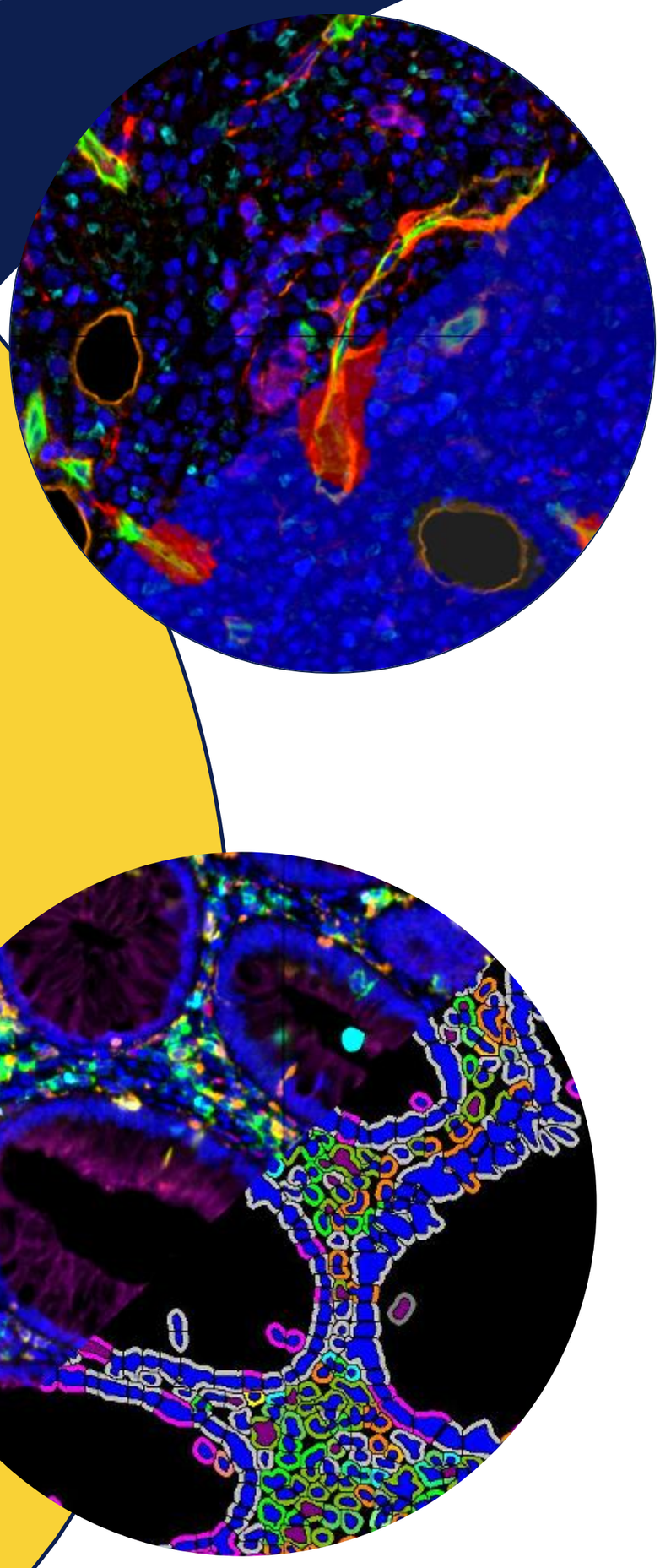
**Bespoke Tissue Micro Array (TMA) creation**

**Oesophageal Cancer TMA available**

**Indica's HALO image analysis software**

**Pathologist-led, computer-aided, analysis**

**Digital slide scanning**



UNIVERSITY OF OXFORD

OXFORD CANCER

ecmc

CANCER RESEARCH UK | Oxford Centre

# Halo® – Image Analysis Platform

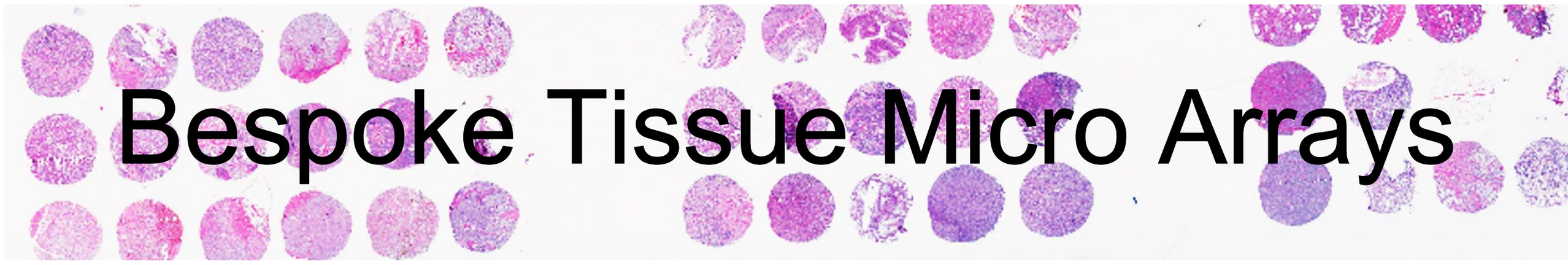
HALO® can separate **up to five stains simultaneously** within any cellular compartment.

HALO is capable of **automated tissue classification** thanks to machine learning.

The software can perform **infiltration analysis, nearest neighbour/proximity analysis and density hotspot** analysis.

HALO allows automated batch analysis of whole slides and TMAs.

We offer software training, pathology and pathology-assisted analysis or unassisted use of HALO.
To Join our **Pathology Clinics** please email thlenquiries@oncology.ox.ac.uk.



# Bespoke Tissue Micro Arrays

Tissue Micro Arrays (TMAs) are multi-tumour tissue blocks that allow standardised staining of up to **120 samples**

Using TMAs reduces IHC cost and staining variations

The THL has access to diagnostic archive samples and **pathology expertise** to choose the most interesting regions to study

We offer:

- **pan-tumour and healthy tissue** TMAs for antibody optimisation
- **Oesophageal cancer** TMA

And **bespoke TMA** creation with pathology aid

We offer bespoke TMA creation for any type of cancer as well as access to existing ones. For enquires please email thlenquiries@oncology.ox.ac.uk.

# Patient and Public Involvement

Successful cancer research can only happen in partnership with those affected by cancer: people who live with cancer; people who have recovered from it; friends and family members; and those who are at risk of getting cancer in future. At Oxford Cancer, we strive to ensure that our work learns from and responds to the experience of people like these.

## What is PPI?

Patient and Public Involvement (PPI) refers to the many ways in which people with lived experience can work in partnership with cancer researchers as colleagues, advisors and collaborators. It is about ensuring that the culture of cancer research seeks out, cultivates and welcomes multiple voices to challenge and co-design.

## Examples of PPI in action:

### What matters most to the people who might benefit from your work?

Do you know if your research is important to patients? Do you know what questions patients want answers to? We work with groups of patients to identify priorities and shape our Centres of Excellence in response.

### Building capacity in cancer researchers of the future.

We ensure that students on our DPhil programme have the opportunity to meet and learn from our PPI contributors from the outset of their studies.

### Ensuring diversity in PPI contributors.

We are working with community groups locally and nationally to build greater diversity in our panel of consultees. This ensures that our work includes perspectives from the many different communities we serve.

### Building relationships between the lab and "real world" experience.

Our 'buddy' programme allows people with cancer to see the science in action, and allows people working in labs to fully understand why their work really matters.

**To find out more - visit our stand at the symposium, or contact us at: oxfordcancerppi@medsci.ox.ac.uk.**

# OCION

Oxford Cancer Immuno-Oncology Network

## The Oxford Cancer Immuno-Oncology Network

OCION was established in June 2023 to bring together scientists from different disciplines, cutting-edge technologies and patient samples to progress our immuno-oncology understanding to the next level.

By applying Oxford's leading expertise in fundamental immunology, we hope to enable more patients, with a wide range of cancer types, to benefit safely from tailored immunotherapy use. The network is directed by Professor Tim Elliott and managed day-to-day by Beth Mann (elizabeth.mann@medsci.ox.ac.uk).

Alongside our annual symposium (pictured), our offering includes a seminar series with networking drinks, pump prime funding, a monthly newsletter, an immuno-oncology directory and support with grant writing, sample/data access and helping to foster industry relationships.

The 2025 OCION Annual Symposium will be hosted at the Mathematical Institute in Oxford on **13th June** when we will launch our next round of pump prime applications. The day will provide ample opportunities for people from different disciplines to come together to share their research.

All University of Oxford or OUHFT researchers with an interest in immunology are welcome to join. If you wish become a member and to be added the mailing list to hear about future events and funding opportunities, please email:

**cancer@medsci.ox.ac.uk**

# OxCODE

OXFORD CENTRE FOR CANCER EARLY DETECTION AND PREVENTION

## The Oxford Centre for Early Cancer Detection and Prevention

The Oxford Centre for Early Cancer Detection (OxCODE) 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 (next annual symposium in December 2025) 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).

# DPhil in Cancer Science

Launched in 2020, the DPhil in Cancer Science Programme provides research-based doctoral training for cancer researchers from clinical, biological, engineering, mathematics, and statistics backgrounds.

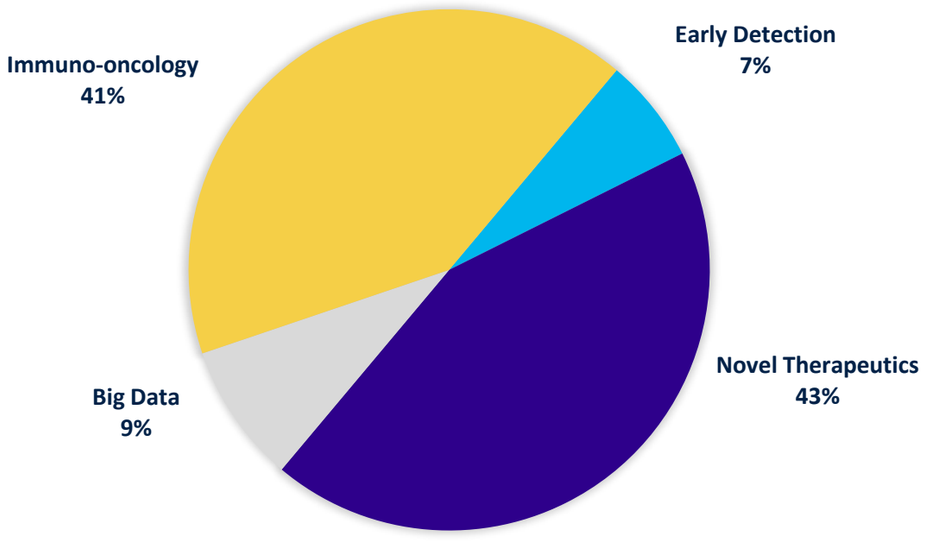
## STUDENTS

The CRUK Oxford Centre funds around 12 full-time studentships each year, and currently has 46 on-course students spread across 18 Departments. We are looking forward to welcoming an additional 18 students in October 2025. Our current cohorts consist of:

- 28% Clinical trainees
- 26% Medical Undergraduates
- 31% Fundamental scientists (biological/chemical science)
- 15% Fundamental scientists (engineering/mathematics/stats)

The programme attracts students on an international scale, with over 24 different nationalities currently enrolled.

Our students receive a world-leading research training experience that incorporates advanced level seminars; mentorship; and a subject-specific training programme tailored to individual research needs.




Main theme of current student projects

## PROJECT THEMES

The programme is distinctive in offering integrated training across the following themes: Immuno-Oncology; Cancer Big Data; Novel Therapeutics; Early Cancer Detection.

It builds on Oxford's outstanding research record in these areas, spanning both the University and Hospital Trust.

## NEW FROM 2025

Fundamental science students successfully enrolled onto our programme from October 2025 will take on two 6-month rotations within their first year, before deciding on a final 3-year project for the remainder of their DPhil. If you are interested in submitting a DPhil project for 2026, we will be opening to submissions in late-March 2025, date to be announced in the Oxford Cancer Newsletter.

To find out more about the DPhil in Cancer Science programme, view our current student profiles, or join the mailing list, scan the QR code.

# CRUK Oxford Centre Development Fund

Development Fund

## Scheme Overview

The Development Fund is a scheme that was initiated at the very inception of the Centre back in 2010.

It aims to provide short-term, pump-priming funds to support innovative, high-risk, proof-of-concept cancer research.
Priority is given to projects with a clear translational trajectory, to early career researchers, for new collaborations between investigators, and those that map onto both CRUK Oxford Centre's & Oxford Cancer's Strategic Framework.

There are two types of awards: small -up to £7,500 and main - up to £15,000. Awards are for 12 months, typically starting on 1st April and ending on 31st March.

Each project is reviewed by three scientific reviewers who score it on a scale of 1-5, based on the scientific strengths and weaknesses of the application. Additionally, applicants are required to submit a 300-word lay summary, which is reviewed by two Patient and Public Involvement (PPI) members. The summary is scored on a scale of 1-4, based on its context, patient impact, relevance, presentation, and readability.

Development Fund recipients from the past year are highlighted in the next few pages. We look forward to being able to share the successes of some of these projects at the Centre symposium in 2026.

# CRUK Oxford Centre Development Fund

## January 2024 Awards

**Pawel Swietach**
Department of Physiology, Anatomy and Genetics -£7,500.00
Title: Do mutations in SLC4A3 expose a druggable vulnerability in the adaptation of endometrial cancer to hypoxia?

**Valentine Macaulay & Jinseon (Selena) Kim**
Nuffield Department of Surgical Sciences-£7,130.00
Title: The WINGMEN trial: investigating effects of IGF blockade on the tumour immune microenvironment of localised prostate cancer

**Anna Rose**
Department of Peadiatricts/WIMM-£15,000
Title: Exploiting FAM111A protease to selectively target ALT cancers

**Berna Bou Tayeh & Yang Shi**
Ludwig Institute for Cancer Research - £14,954
Title: Unveiling the epigenetic regulators of Natural Killer cell exhaustion and their use for cancer immuntherapy

**Eileen Parkes**
Department of Oncology - £15,000
Title: Immunosuppression in oesophageal adenocarcinoma

**Keaton Jones**
Nuffield Department of Surgical Sciences - £13,408.00
Title: High Intensity Focused Ultrasound (HIFU) as an immune primer in pancreatic cancer

**Olaf Ansorge**
Nuffield Department of Clinical Neurosciences Department of Neuropathology- £15,000.00
Title: Novel Analytical Technologies for Precision Medicine in Rare Sarcomas – A Pilot Study on Mesenchymal Chondrosarcoma

**Adam Wilkinson & Yavor Bozhilov**
MRC Weatherall Institute of Molecular Medicine, Radcliffe Department of Medicine- £15,000.00
Title: Investigating the functional consequences of gaining chromosomes in human blood stem cells

**Lennard Lee, Rob Watson, David Anaya, Miles Weatherseed & Tim Elliott**
CIO, Immoncology, NDM - £15,000.00
Title: The Oxford Cancer Vaccine Project Mouse POEM pioneer study

# CRUK Oxford Centre Development Fund

## January 2023 Awards

**Simeio Go & Eric O'Neil**
Department of Oncology - £14,960.00
Title: Infiltrating NK cells as immunoregulators in pancreatic cancer?

**Oni Chowdhury**
Weatherall Institute of Molecular Medicine - £15,000.00
Title: Applying single cell genomics to clinical diagnostics - detection of TP53 mutant clones and collaborating genetic aberrations in myeloid neoplasms

**Gemma Hancock**
NDWRH and Wellcome Trust - £7,450.00
Title: Deep phenotyping of CD4+ T-cells in high-risk human papillomavirus (hrHPV) infection

**Luis Alberto Baena Lopes**
Sir William Dunn School of Pathology - £14,997.98
Title: Paired identification of gene targets and pharmacological drugs with anti-oncogenic potential

**Ejung Moon**
Department of Oncology – £7,500.00
Title: Characterisation of the role of MAFF in bone metastatic breast cancer

**Matthew Bottomley**
CAMS Oxford Institute, Nuffield Department of Medicine – £13,000.00
Title: Single-cell spatial transcriptomic profiling to delineate changes in tumour-associated macrophage behaviour in cutaneous squamous cell carcinoma with immunosuppression

**Grigore-Aristide Gafencu**
Dept of Oncology, Oxford Molecular Diagnostic Centre - £13,148.00 Title: Comprehensive multi-modal assessment of peripheral bloodfrom healthy elderly males: a key component in the interpretation of the data from the pilot collaboration between OXPLORED and CARTOGRAPHY

**Nikolaos Kanellakis**
China Oxford Institute, NDM - £7,500.00
Title: Phenotype and characterisation of the immunosuppressive mechanisms of malignant pleural effusion

**Adam Cribbs & Jianfeng Sun**
NDORMS, Botnar Research Centre - £7,500.00
Title: Single-cell spliceosome map establishment of immune cells

**Jane McKeating**
Nuffield Department of Medicine - £14,768.00
Title: Targeting the acidic microenvironment in hepatocellular carcinoma to overcome resistance to immunotherapy

**Carol Leung**
Ludwig Cancer Research - £15,000.00
Title: Developing T-cell engager bispecific antibodies targeting the Epstein-Barr virus latent membrane proteins

**Chung Ying Chan**
Department of Oncology - £15,000.00
Title: Stratifying treatment for MYC amplified prostate cancer

**Eleni Adamopoulou & Isabela Pedroza-Pacheco**
NDM Immuno-Oncology - £14,733.55
Title: Immune-profiling of malignant ascites from ovarian cancer patients as a route to sampling the tumour microenvironment

**Margarida Rei**
Ludwig Cancer Research - £7,500.00
Title: Discovery of T cell antigen targets in glioblastoma

**Valentine Macaulay**
Department of Oncology/ Nuffield Department of Surgical Sciences - £7,400.00
Title: Investigating immunosuppressive effects of IGF-1 as a growth factor for regulatory T-cells in prostate cancer

**George Adigbli**
Nuffield Dept of Surgical Sciences – £15,000.00
Title: Early Risk Stratification by Lymph Liquid Biopsy In Melanoma

**Adam Cribbs & Jianfeng Sun**
NDORMS, Botnar Research Centre - £7,500.00
Title: Single-cell spliceosome map establishment of immune cells

**Jane McKeating**
Nuffield Department of Medicine - £14,768.00
Title: Targeting the acidic microenvironment in hepatocellular carcinoma to overcome resistance to immunotherapy'

**Carol Leung**
Ludwig Cancer Research - £15,000.00
Title: Developing T-cell engager bispecific antibodies targeting the Epstein-Barr virus latent membrane proteins

**Chung Ying Chan**
Department of Oncology - £15,000.00
Title: Stratifying treatment for MYC amplified prostate cancer

**Eleni Adamopoulou & Isabela Pedroza-Pacheco**
NDM Immuno-Oncology - £14,733.55
Title: Immune-profiling of malignant ascites from ovarian cancer patients as a route to sampling the tumour microenvironment

**Margarida Rei**
Ludwig Cancer Research - £7,500.00
Title: Discovery of T cell antigen targets in glioblastoma

**Valentine Macaulay**
Department of Oncology/ Nuffield Department of Surgical Sciences - £7,400.00
Title: Investigating immunosuppressive effects of IGF-1 as a growth factor for regulatory T-cells in prostate cancer

**George Adigbli**
Nuffield Dept of Surgical Sciences – £15,000.00
Title: Early Risk Stratification by Lymph Liquid

The next Development Fund call for projects opens in the Autumn of 2026!

# Clinical Trial Management

**OCTO is the first CTU in the UK specialising in Early Detection (ED) and Cancer Precision Prevention (PP) Studies working in partnership with the Oxford Primary Care CTU. Our portfolio also continues to include early phase trials (FIH-PhaseII) of novel cancer therapies as monotherapies or combinations, working in collaboration with biotech/pharma and academics.**

**Prof. Sarah Blagden**

**OCTO Director & Precision Prevention Lead**

**Sarah Pearson**

**OCTO Trial Management Director**

**Dr. Brian Nicholson**

**Early Detection Lead**

**Prof. Ly-Mee Yu**

**Statistical Lead**

**OCTO's priorities are prevention, detection and treatment, with cross-cutting themes including:**

- Fully integrated patient and public involvement
- Equality, diversity and inclusivity
- Embedded translation
- Sustainability
- Digitally enabled trials
- Data for real-time decision making

## Work With Us:

If you would like to have an initial discussion about bringing your trial to OCTO please email:

octo-trialdev@oncology.ox.ac.uk

When you work with OCTO you will 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.

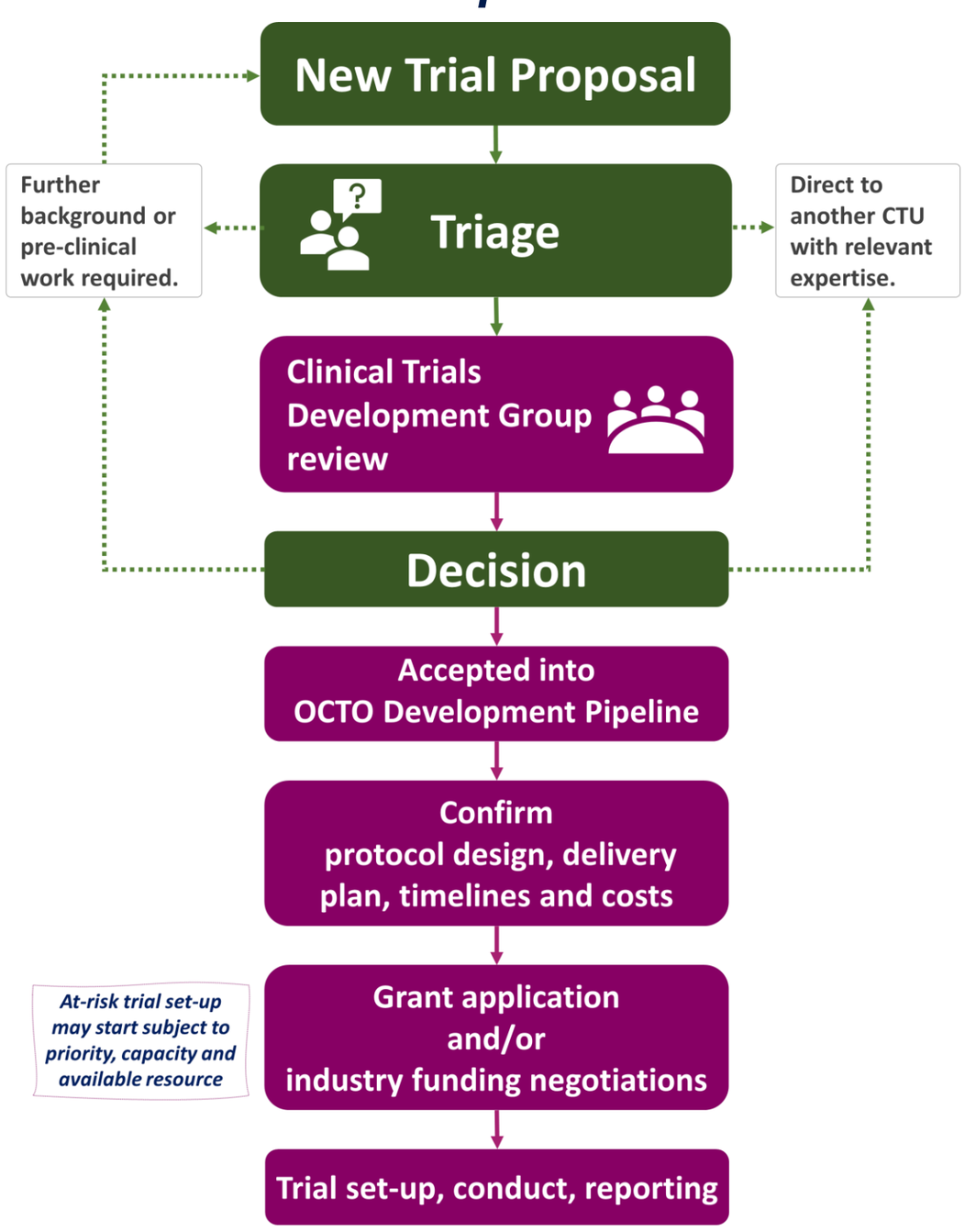
**How we can support your trial:**

- Trial Development & Planning
- Funding Application Support
- Regulatory Approvals
- Statistics
- Site Feasibility & Set Up
- Site Management
- Data Management
- IMP & Supplies Management
- PPIE Input
- Safety Reporting
- Sample Management
- Results Reporting & Dissemination

*For more information: https://www.oncology.ox.ac.uk/octo*

## A trial's journey:

***from first approach to decision, and on to set up:***




***Prevention, detection, treatment. Transforming the future of cancer.***

OXFORD CANCER

# YOUR PARTNERS IN PHILANTHROPY

**The Development and Alumni Engagement Office is proud to partner with Oxford Cancer.**

**Together we can achieve our shared vision to advance cancer research and care across the city of Oxford.**

**Please get in touch:**


**Tannis Walker,** CFRE
Head of Development
Medical Sciences
tannis.walker@dae.ox.ac.uk



**Georgie Coutts**
Development Executive
Medical Sciences
georgie.coutts@dae.ox.ac.uk


www.medsci.ox.ac.uk/for-staff/resources/development-office

# 2025 Innovation and Entrepreneurship Awards

Presented by Cancer Research Horizons, the innovation arm of Cancer Research UK, these Awards are a unique opportunity to showcase your work, receive funding, expand your industry connections and gain sector-wide recognition at the Award ceremony this summer.

You can nominate yourself or a colleague for one or more of the following categories:

- **Early Career Entrepreneur of the Year**
- **Entrepreneurial Group Leader of the Year**
- **Woman Entrepreneur of the Year**
- **New Start-Up of the Year**
- **Further, Faster, Together (Industry-Academia Collaboration)**


Raise the profile of your discoveries with the Innovation and Entrepreneurship Awards

You could access:

- ☑ £5,000-£15,000 to boost your research
- ☑ A network of like-minded entrepreneurs, industry connections and investors
- ☑ A chance to showcase your work at our Awards ceremony on 10 July

Scan to submit a nomination for yourself or a colleague

CANCER RESEARCH HORIZONS

FURTHER FASTER TOGETHER

# HAVE AN IDEA THAT COULD HELP WITH THE DIAGNOSIS, MONITORING AND TREATMENT OF CANCER?

## EXPLORE OPPORTUNITIES TO TRANSLATE YOUR RESEARCH WITH CANCER RESEARCH HORIZONS

Get in touch with Ruth Barrett, our Oxford representative

Translation Manager

Ruth.Barrett@cancer.org.uk

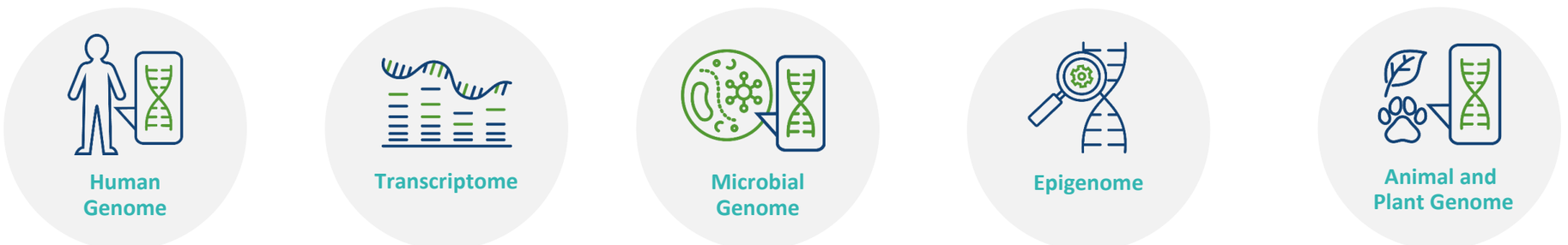
Scan to learn about how we can help you to translate your research(incl. funding opportunities and entrepreneurial programmes.

# Our Symposium Sponsors

Novogene

Novogene is a leading provider of genomic services and solutions with cutting edge Next Generation Sequencing and bioinformatics expertise. With one of the leading sequencing capacities in the world, Novogene utilises scientific excellence, a commitment to customer service and unsurpassed data quality to help our clients realise their research goals in the rapidly evolving world of genomics. With almost 2,000 employees, multiple locations around the world, 66 NGS related patents, and over 22,000 publications in top tier journals such as Nature and Science, the company has become a world-leader in NGS services and a trusted genomics partner. Our services are supported by the latest platforms from Illumina, PacBio and Oxford Nanopore Technology.

## Full-Service Next-Generation Sequencing




**Reliable Results**

Illumina NovaSeq Q30 ≥ 85% guarantee

**Large Capacity**

Unmatched automation and throughput

**Latest Technology**

Illumina, PacBio, Oxford Nanopore

**Fast Turnaround**

Faster than local cores and the vast majority of service providers

**Expert Analysis**

“Publication-ready” data provided by expert bioinformaticians

**info@novogene-europe.com | www.novogene.com**

# Our Symposium Sponsors

## Environmental Sustainability Team

**From 2025, Cancer Research UK (CRUK) will require all new wet-lab grant applications to have sustainability accreditation. Join the Laboratory Efficiency Assessment Framework (LEAF).**

**Sustainable labs: what you need to know?**

Laboratories are among the most resource-intensive spaces in the University, consuming over 60% of the University's energy and associated carbon emissions and is one of the five top contributors to scop 3 carbon emissions, accounting for 9% of the indirect emissions from the supply chain. The Laboratory Efficiency Assessment Framework (LEAF) provides a structured approach to improving sustainability in lab spaces while also saving an average of £3,700 and 3 tonnes of $CO_2e$ per lab per year.

**Get on top of new funding requirements**

From 2025, Cancer Research UK (CRUK) will require all new wet-lab grant applications to have sustainability accreditation. Labs must achieve Silver-level LEAF certification or higher to maintain eligibility for new and continued funding. Certification can be obtained at a research group or building level and involves practical steps to improve efficiency in equipment use, ventilation, procurement, waste, and more.

**Supporting your transition to LEAF**

LEAF has already been successfully implemented at Oxford on a voluntary basis, and the University's Environmental Sustainability (ES) Team is scaling up support to help researchers meet these new requirements. While many labs already follow good sustainability practices, certification will formalize these efforts and drive further improvements.

**Find us at the Oxford Cancer Symposium**

**To learn more about how LEAF impacts your research, visit the Environmental Sustainability team in the atrium from 8:30 AM. We'll be available to answer questions, provide resources and guide you through the certification process.**
**For more details, visit our Sustainable Labs webpage.**

**LEAF readiness to meet funder requirements | Sustainability**

# Speaker Abstracts & Summaries

# Speaker Abstracts & Summaries

## Session1: Early Detection and Immuno-Oncology

### Circulating Blood Platelets as Cancer Sentinels

Blood platelets are the smallest and second most frequent blood cell type in the human body. In mammals, platelets lack a cell nucleus, and have previously been assumed to be devoid of nuclear DNA. We recently discovered that platelets do indeed contain a repertoire of DNA fragments that map over the entire human nuclear genome. These are partly inherited from their parent megakaryocyte, and in part sequestered during their circulation in the peripheral blood. We have shown the presence of Y-chromosome DNA fragments in maternal platelets, and detected cancer cell-derived DNA in patients with both overt cancer and pre-malignant lesions. In blood cancer, platelets provide a window into the genome of megakaryocyte-biased blood stem cells. This study establishes a new biological role for platelets in the sequestration of cell free DNA from plasma and demonstrates clinical utility of this for liquid biopsies – including in the early detection of cancer.

Beth is a Cancer Research UK Senior Fellow and Associate Member of the Ludwig Cancer Research Institute. She leads a research group at the MRC Weatherall Institute of Molecular Medicine whose broad focus is to understand the role of the bone marrow microenvironment in cancer progression and therapy resistance, and the cell biology of megakaryocytes and platelets, and their roles in cancer. Their research is highly translational, based on deep interrogation of clinical samples and aiming to discover novel targets for therapies that may improve outcomes for patients. She is also an honorary haematology consultant and specialist in the care of patients with myeloproloferative neoplasms, and leads a portfolio of clinical trials with a focus on emerging immunotherapies.

09:30

Beth Psaila

Associate Professor of Heamatology

Radcliffe Department of Medicine

# Speaker Abstracts & Summaries

## Session1: Early Detection and Immuno - Oncology

### Flash Talk: Nanopore Whole-Genome Sequencing of cfDNA for Cancer Detection

**Background**

Liquid biopsies can potentially transform Clinical Oncology by simplifying early cancer detection and disease monitoring. We recently developed TriOx, a multi-cancer early triage test using TET-Assisted Pyridine Borane Sequencing (TAPS), which enables whole-genome sequencing with minimal DNA disruption (Figure 1; Vavoulis et al. *Nat Comms* 2025). TriOx combines genomic and epigenomic data to detect plasma ctDNA with 94.9% sensitivity and at least 86% classification accuracy at ctDNA fractions as low as 0.7% of the total cfDNA. However, the high cost of current multi-cancer early detection tests (MCEDTs) remains a significant barrier to their widespread use, especially in low-resource clinical settings.

**Methods**

We present a precise, affordable, and minimally invasive initial triage tool for use in resource-restricted environments, by adapting TriOx to run on shallow Oxford Nanopore Technology (ONT) sequencing data. Like TAPS, ONT sequencing makes possible the genome-wide extraction of genetic and epigenetic information from liquid biopsies using the same sample, but without any build-in chemistry that may have a detrimental effect on the DNA, and at significantly reduced cost. To assess the feasibility of this approach, we used ONT to sequence at 1x the genomes of 13 non-cancer controls recruited at the Oxford University Hospitals (**S**uspected **CAN**cer Pathway, SCAN) and at Cambridge Biosciences, and 22 cancer patients recruited by the Oxford Biomedical Research Centre Cancer Pilot and the Oracle Cancer Trust covering a range of common diseases, including colorectal, pancreatic, and head & neck cancers. We examined multiple data modalities, including copy number aberrations, fragmentomics, structural variation, methylation signals, and viral infection markers.

**Results**

We demonstrate comparable performance to deep TAPS sequencing, as well as tissue-of-origin detection based on methylation signatures. For specificity pre-fixed at 100%, we can correctly identify as positive 19 cancer cases (sensitivity 86.4%), of which 6 are early stage (I/II) cancers. Across all data modalities, methylation signals are the most sensitive (81%), followed by copy number aberrations (45.5%), fragmentomics and translocations (27.3% each).

**Conclusions**

This cost-effective, minimally invasive triage tool shows promise for accurately identifying cancer and tissue origin, particularly in resource-limited clinical environments. We are currently aiming to expand the above analysis to hundreds of samples for a more precise characterisation of its cancer detection performance.

09:45

Dimitris Vavoulis

Department of Oncology

# Speaker Abstracts & Summaries

## Session 1: Early Detection and Immuno – Oncology

### Translating GDF15 into cancer Immunotherapy

Cancer immunotherapies with antibodies blocking immune checkpoint molecules are clinically active across multiple cancer entities and have markedly improved cancer treatment. Yet, response rates are still limited, and tumour progression commonly occurs. Soluble and cell-bound factors in the tumour microenvironment negatively affect cancer immunity. Recently, growth differentiation factor 15 (GDF-15), a cytokine that is abundantly produced by many cancer types, was shown to interfere with antitumour immune response in cancer mouse models as a result in part of downregulating the function of the LFA-1 integrin on T cells. In such preclinical cancer models, GDF-15 blockade synergistically enhanced the efficacy of anti-PD-1-mediated checkpoint inhibition. However, regardless of exhaustive quests, no receptor for GDF-15 on leukocytes has been identified yet. GDF-15 has also been incriminated in the pathogenesis of cancer-associated cachexia acting on the GFRAL receptor in the central nervous system.

In a first-in-human phase 1-2a study (GDFATHER-1/2a trial, NCT04725474 ), patients with advanced cancers refractory to anti-PD-1 or anti-PD-L1 therapy (termed generally as anti-PD-1/PD-L1 refractoriness) were treated with the neutralizing anti-GDF-15 antibody visugromab (CTL-002) in combination with the anti-PD-1 antibody nivolumab.

A multitumor dose escalation part of visugromb with fixed doses of nivolumab part and subsequently specified expansions were conducted at the recommended dose.  Here we observed that durable and deep responses were achieved in some patients with non-squamous non-small cell lung cancer, urothelial cancer and hepatocellular carcinoma, three cancer entities identified as frequently immunosuppressed by GDF-15 in an in silico screening of approximately 10,000 tumour samples in the TCGA database. Increased levels of tumour infiltration, proliferation, interferon-γ-related signalling and granzyme B expression by cytotoxic T cells were observed in response to treatment in a fraction of patients. In conclusion, neutralizing GDF-15 holds promise in overcoming resistance to immune checkpoint inhibition in cancer. Other groups have reported amelioration of cancer associated cachexia upon GDF-15 blockade.

Professor Melero's  MD PhD main areas of expertise are tumor immunology and immunotherapy. Ignacio Melero serves a full Professor of Immunology at the Universidad de Navarra and as a professor of cancer immunotherapy at the University of Oxford. Dr Melero earned his medical degree from the Universidad de Navarra and completed his residency training at Hospital Universitario de la Princesa, Madrid. In his doctoral thesis he made seminal discoveries regarding human Natural killer receptors (KIRs and NKG2A/CD94) under the supervision of Miguel Lopez-Botet. In 1994, Dr Melero joined Bristol-Myers Squibb, Seattle, USA, as a researcher in cancer immunotherapy, where he contributed to pioneering publications in the field of co-stimulation of antitumour immune responses and the use of agonist immunostimulatory monoclonal antibodies such as anti 4-1BB (CD137). Besides CD137-based immunotherapies his main contributions over the years include the preclinical and transformative clinical development of immunotherapy for hepatocellular carcinoma, the preclinical and clinical study of the protumor inflammatory actions of TNF and IL-8, as well as the use of immunotherapy agents via intratumoral routes of administration. The implementation of synergistic combined strategies of immunotherapy treatments has been a very fruitful area of research at Melero's group. Results on biomarker discovery and validation as well as actionable targets and mechanisms have been achievements of his investigations, most recently including GDF-15 neutralization.

Dr Melero's research interests focus on translational research in cancer immunotherapy with cell, gene and monoclonal antibody-based strategies. He has served as Principal Investigator in numerous cancer immunotherapy clinical trials sponsored by pharmaceutical industry and other institutions.

Ignacio Melero has authored over 370 peer-reviewed publications and currently serves as Senior Editor for Clinical Cancer Research, Scientific Editor for Cancer Discovery, and Section Editor for the Journal for Immunotherapy of Cancer.
Member of the scientific advisory boards of institute Curie (Paris), institute the investigación Biomédica de Granada, Netherlands cancer Institute (NKI) and member of the scientific council of Institute Gustave Roussy. Dr. Ignacio Melero has just been awarded an ERC-Advanced Grant from the European Union for his investigations on mRNA-based immunotherapies.The sentence that best summarizes Dr. Melero's career is translational research in immunoncology from bench to bedside and vice versa.

09:50

Nacho Melero

Kidani Professor of Immunotherapy, Group Leader

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 1: Early Detection and Immuno-Oncology

### Exploring the Role of B Cells in Patients with Bowel Cancer: A Global Perspective

Bowel cancer is one of the most commonly diagnosed cancers worldwide. According to the World Health Organization (WHO) and the Global Cancer Observatory (GLOBOCAN 2020), approximately 1.93 million new cases were diagnosed in 2020—equivalent to one case every 16 seconds. With incidence rates rising in some regions due to lifestyle changes, diet, and ageing populations, this number is expected to increase. When detected at an advanced stage, the relapse rate is as high as 60%, highlighting the urgent need for improved prevention, early detection, and treatment strategies. For many years, B cells have been largely overlooked in cancer immuno-oncology (IO), partly due to early studies suggesting they might promote tumour progression through immunosuppressive cytokines. However, more recent research has revealed that B cell–driven immune responses can also enhance anti-tumour immunity. A recent shift in perspective came from the discovery of tertiary lymphoid structures (TLS) near tumours for their positive correlation with both survival and response to IO agents across many cancer types. These ectopic microstructures form within or adjacent to cancerous tissue resemble the follicle of secondary lymphoid organs. TLS are especially notable for their frequency of B cells and germinal centre-like structures, features that correlate even better with positive outcomes, suggesting that TLS may be engaging an active and functional antigen-specific responses that contribute to tumour immunity.

With advancements in spatial and single-cell technologies, we now have the ability to study B cells and TLS at unprecedented resolution—from gene expression to cellular function—opening exciting new possibilities for leveraging B cells in immunotherapy. By comparing two cohorts with distinct lifestyles and health behaviours—patients from the UK and Mexico—this study aims to dissect the cellular, molecular, and environmental mechanisms associated with TLS. Using a combination of genetic, cellular, and spatial techniques, we seek to harness functional TLS-derived B and T cell responses to develop novel IO strategies and cancer vaccines for prevention, diagnosis, and treatment in the near future.

Dr. Isabela Pedroza-Pacheco is an immunologist specialising in secondary and tertiary immune responses in colorectal cancer, with a focus on early detection, prevention, and immunotherapy. She leads the Laboratory for Functional Immunology at the Nuffield Department of Medicine, University of Oxford, and directs the Mexico Cancer Initiative. Her research integrates genetics, cellular immunology, and functional assays to uncover the mechanisms regulating T and B cell interactions in the tumour microenvironment and their potential as therapeutic targets.

With a background in bioengineering and a PhD in immunology, Dr. Pedroza has contributed significantly to systems functional immunology, particularly in identifying predictors of humoral immune responses in HIV vaccine development. Since 2023, she has led the Mexico Cancer Initiative, an alliance between Oxford Cancer and Mexican universities and hospitals, aimed at advancing research into immune responses in colorectal cancer within diverse populations. Her work seeks to bridge immuno-oncology research across global cohorts, with the goal of developing B and T cell–based immunotherapies and cancer vaccines. In recognition of her contributions, Dr. Pedroza was awarded the Young Faculty Award by the Consortia for HIV/AIDS Vaccine Development in 2022.

10:05

Isabela Pedroza-Pacheco

COI/CIO Career Development Fellow

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 1: Early Detection and Immuno-Oncology

### Spatial exploration of B-cell-centric immune hubs in colorectal cancer

Colorectal cancer (CRC) is a global health concern ranking top 3 among all cancer types in incidence and mortality. Previous studies have shown the prognostic role of B cells in different cancer types including CRC, however, their spatial distribution and cellular interactions in CRC remain unclear. With state-of-the-art single cell resolution spatial transcriptomic and proteomic platforms, we identified B-cell-rich tertiary lymphoid structures (TLS) in CRC tumour tissues. These hubs harbour heterogeneous B cell subsets, indicating potential interconnection and trajectory of TLS in the tumour microenvironment. We further observed $IgG^+$ plasma cells populating matrix cancer-associated fibroblast (mCAF) tracks and positioning near tumor cells and macrophages, suggesting possible anti-tumour role of IgG antibodies and underscoring the clinical relevance of harnessing TLS B cells and IgG plasma cells for tumour-specific antibody therapies.

I earned my Bachelor of Medicine degree from Peking University in 2023 before I came to Oxford topursue my DPhil degree. During my undergraduate years, I completed a clinical clerkship at PekingUniversity People's Hospital and actively participated in research at the Department of GI Surgery. Myfocus was on multidisciplinary treatment approaches, particularly neoadjuvant therapy for GI cancer. Idelved into investigating the intricate role of the immune microenvironment in treatment responses,enriching my understanding of the dynamic interplay between clinical practice and research.

As a beneficiary of the CSC-COI program and the CSC funding, I joined Dr. Pedroza-Pacheco's group under the co-supervision of Prof. Elliott in 2023. Our collective research interest revolves around tertiary lymphoid structures (TLSs) in cancer, which are characterized as structured, secondary-lymphoid-organ-like immune aggregates within tumour tissues.

In my research, I've chosen to concentrate on B cells, pivotal figures within these immune "communities". My aim is to elucidate the phenotypes, distribution, cell interactions, and functions of B cells in colorectal cancer. By doing so, I aspire to provide a novel perspective on understanding the heterogeneity of patients' treatment responses and survival, contributing to advancements in patient stratification, personalised treatment and ultimately the prognosis of patients.

10:20

Fengyun Zhong

Dphil Student

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 1: Early Detection and Immuno-Oncology

### Unravelling the Evolutionary Landscape of MSS Colorectal Cancer: Insights from Single-Cell Transcriptomics and Immunopeptidomics

Colorectal cancer (CRC) remains a leading cause of cancer-related mortality, with microsatellite stable (MSS) tumors representing over 85% of cases. This study employs multi-omics approaches, including single-cell RNA sequencing (scRNAseq) and HLA-I immunopeptidomics (ImP), to explore the evolutionary dynamics and phenotypic heterogeneity of MSS CRC. Multi-region samples from five treatment-naive MSS CRC patients revealed subclusters of epithelial cells with MSS-specific copy number alterations (e.g., 20q amplification) and identified four conserved meta-programs shared across tumors, involving pathways such as oxidative stress.

Qian is interested in using multiomics (genomics, transcriptomics and immunopeptidomics) to identify tumour specific neoantigens for vaccine strategies and immunotherapy.

10:25

Qian Yang

Postdoctoral Scientist

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 2: New to Oxford

### Shedding light on how immune cells become dysfunctional in tumours

David Withers studied for a PhD in Immunology focused on the recovery of the bursa to viral infection, at the Institute for Animal Health/University of Bristol (2000-2004). After obtaining his PhD, David continued his studies of B cell responses in the laboratory of Dr Peter Lipsky at NIAMS, NIH, Bethesda (2004-2006). He then returned to the UK to study with Professor Peter Lane at the University of Birmingham, UK, cementing his interest in how interactions within secondary lymphoid tissue control adaptive immune responses. In 2011, David was awarded a Wellcome Trust Research Career Development Fellowship investigating the role of innate lymphoid cells in regulating memory T cell responses. In 2016, he was awarded a Wellcome Trust Senior Research Fellowship, further developing his studies of how innate lymphoid cells regulate adaptive immunity.

Most recently, his research has developed to consider the regulation of anti-tumour immunity, exploiting novel in vivo models and supported by Cancer Research UK, the Cancer Research Institute, Worldwide Cancer Research and the MRC. In June 2024, David moved his lab to the NDM Centre for Immuno-Oncology at the University of Oxford. As Professor of Experimental Cancer Immunology, he leads the Tumour-Immune Cell Dynamics Group, which is focused upon understanding how immune cells behave within, and respond to, the tumour microenvironment and then what this means for enhancing anti-tumour T cell responses. The lab is currently supported by a Wellcome Discovery Award and Cancer Research UK Programme grant.

11:15

David Withers

Group Leader in Experimental Cancer Immunology

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 2: New to Oxford

### Activation of bivalent genes in cancer by de novo DNA methylation

DNA methylation is frequently altered in cancer, but it is largely unknown what roles these alterations play in cancer initiation and progression. Here, we use a combination of pan-cancer patient data analysis and CRISPR/dCas9 epigenome editing to study the role of DNA methylation in gene regulation in cancer. While promoter DNA methylation acts primarily as a repressive mark, we show that it can surprisingly *activate* expression of bivalent genes. These bivalent genes have promoters marked with both activating H3K4me3 and repressive H3K27me3 histone modifications, and they comprise many transcription factors that play important roles in the regulation of pluripotency, development, and cancer. We show that the DNA methylation-induced activation results from reduced MTF2 binding and eviction of H3K27me3, a repressive histone mark that maintains bivalent genes in a poised state. We demonstrate that bivalency is critical for this, as the presence of H3K27me3 without H3K4me3 does not overall lead to gene activation upon DNA methylation gain. We show that the mechanism is general across several cell types and operates on a large-scale. It explains why hundreds of genes become hypermethylated and upregulated in cancer, including dozens of oncogenic transcription factors that target members of the p53, PI3K-Akt, MAPK, EGFR, HIF-1, Ras, JAK-STAT, apoptosis, senescence, pluripotency, and other cancer pathways. In conclusion, our results reveal an activating role of DNA methylation in bivalent chromatin and a novel mechanism of activation of oncogenic transcription factors, with other broad implications for gene regulation, epigenome editing, developmental biology, chromatin biology, and cancer.

Marketa Tomkova is a Ludwig Leadership fellow and a Wellcome Trust fellow at the University of Oxford. She has a background in Computer Science, obtained a DPhil in cancer genomics, followed by a postdoc on gene regulation at the University of California Davis. In 2023, she obtained independent funding from the Wellcome Trust and started a group at the Ludwig Institute for Cancer Research at the University of Oxford. Her group studies the interplay between DNA mutagenesis and epigenomics in carcinogenesis, and how the knowledge can be used for cancer prevention, detection, and treatment. They use a combination of computational genomics, integration of large omics datasets, and various wet-lab approaches in collaboration with other groups in Oxford and internationally. Their current focus is on the mechanisms of epigenetic and genetic alterations in non-coding regulatory DNA sequences in driving cancer, and on the role of DNA polymerase errors in mutational signatures observed in cancer.
Recently, Marketa and her colleagues have discovered a completely new mechanism underlying generation of C>T mutations in CpG context, the most common mutational pattern in most cancers, also known as the mutational signature 1. They showed that these mutations frequently arise as errors during DNA replication. She has also contributed to the understanding of mutagenicity of 5hmC, replication strand asymmetry of mutational signatures, detection of non-coding cancer drivers, and the interplay betweendifferent epigenetic marks in gene regulation, studied using epigenome editing.

11:30

Marketa Tomkova

Leadership Fellow

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 2: New to Oxford

### Treg targeting reprograms the innate and adaptive immune microenvironment in brain cancer

Despite the success of anti-CTLA-4 and anti-PD-1 for melanoma and lung cancer, to date immunotherapy for glioblastoma (GB) has been ineffective. Although at a small frequency, effector CD8+ and CD4+ T cells (Teffs) are present in GB tumors, displaying an exhausted phenotype while regulatory CD4+ T cells (Tregs) express high levels of the high affinity alpha chain of the IL2 receptor, CD25, suggesting that these cells are actively suppressing the immune response against the tumor. However, the role of Tregs in human GB and whether its therapeutic targeting has the potential to promote tumor regression is not fully understood. Our laboratory has developed the new anti-CD25NIB that depletes Tregs via antibody dependent cell cytotoxicity and/or phagocytosis by engaging activating Fcg receptors on macrophages and NK cells, whilst preserving IL2 signalling on effector CD4+ and CD8+ Teffs. In this study we show that one dose of the anti-CD25 dose promotes effector CD8+ and CD4+ Teff activation that results in around 60% survival. This effect was accompanied by the recruitment of myeloid cells expressing high levels of activating Fcg receptors, creating a window of opportunity to combine with Fc-optimized tumor targeting antibodies. As EGFRvIII is expressed in the surface of up to a 60% of all GBs, these tumors could be therapeutically targeted with antibodies targeting this antigen. Coadministration of anti-CD25NIB together with an Fc-optimized anti-EGFRvIII antibody led to complete elimination of all GB tumors in the mice. The results suggest that therapeutic targeting of Tregs in the tumor can be used to prime both adaptive and innate compartments within GB tumors, leading to enhanced responses.

Dr. Felipe Galvez-Cancino is an immunologist with a long-standing interest in T and myeloid cell biology. He performed his doctoral studies in Chile and the USA at Fundacion Ciencia & Vida and Stanford University. Following his PhD, Felipe conducted postdoctoral training at the UCL Cancer Institute in London, UK. Since June 2024, Felipe has been a Group Leader and Kidani Fellow at the Centre for Immuno-Oncology at the University of Oxford, where he leads the Immune-Regulation and Immune-Interactions group (IRII).

Felipe’s work has led to key discoveries in the field of vaccination, identifying the role of vaccination-induced tissue-resident memory CD8+ T cells as key players in the immunity against melanoma. Felipe’s latest work has been focused on understanding the mechanisms of action of immunomodulatory agents, particularly depleting antibodies targeting regulatory $CD4^+$ T cells (Tregs) and their interaction with Fc receptors on myeloid cells. These findings have shown that Tregs control the phagocytic capacity of tumour-infiltrating macrophages, axes that could be therapeutically harnessed for drug development. Dr. Galvez-Cancio’s current interest is understanding the phagocytic compartment of liver tumours and sarcomas and developing novel therapies that engage phagocytosis.

11:45

Felipe Galvez – Cancino

Kidani Fellow, Junior Group Leader

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 2: New to Oxford

### Melanoma cell fate – from the inside and the outside

The White lab is interested in the intersection between developmental biology and cancer biology. There are many parallels in these processes, including both cell-intrinsic fate decisions as well as cell-cell interactions in the microenvironment. Using both zebrafish and human pluripotent stem cell models of melanoma, his lab has described a mechanism called “oncogenic competence” that explains why DNA mutations are only sometimes able to initiate tumors. His lab has found that the ability to initiate melanoma is strongly influence by the anatomic position of the cell along the body axis. Whereas cutaneous melanomas are enriched for BRAF mutations, acral melanomas more commonly harbor amplifications of genes such as CRKL. These specific oncogenes depend upon the positional gene program in the melanocytes, suggesting that an anatomic code could be a targetable vulnerability in melanoma. Finally, his work has more recently investigated how cells in the TME such as keratinocytes and adipocytes promote melanoma progression and metastasis, acting through signaling and epigenetic mechanisms. He has been awarded the NIH Director’s New Innovator Award, as well as awards from the Melanoma Research Alliance, the Pershing Square Foundation Award, the American Cancer Society, and the Mark Foundation ASPIRE award.

12:00

Richard White

Professor of Genetics

Nuffield Department of Medicine

# Speaker Abstracts & Summaries

## Session 3: Patient and Public Involvement Panel Discussion

### Experiences of Involvement - funding, feelings, publishing and diversity

Julliet Lwiindi, Oxford Cancer's Public Engagement and Involvement (PPI) Officer, is joined by PPI contributors Patrick Maguire and Bep Dhaliwal. Together, they will share their experiences of working with Oxford Cancer researchers, as PPI expert and patient consultants, respectively. Patrick and Bep will discuss their roles in supporting funding applications and publications, highlight diversity challenges, and explore ways to improve existing processes. Julliet will share her experience of supporting and managing public involvement in research. The session will be chaired by Catriona Gilmour Hamilton, Oxford Cancer's Patient and Public Involvement Manager.

Catriona is responsible for developing a comprehensive, embedded strategy for patient involvement in cancer research across all of the Centre's research programmes. Her focus is on enabling researchers to learn from patient experience, understanding what matters to people with cancer, and working in collaborative partnership with patient contributors.

Julliet is responsible for implementing the Oxford Cancer patient and public involvement strategy. She is interested in how organisations can develop long-term strategies and processes to support, monitor and report on public involvement in research. Bep is an established member of Oxford Cancer's PPI community.

Bep provides resilience coaching services and uses her experiences of cancer to help others thrive. She is particularly interested in promoting empathy and kindness in cancer care. She has supported the development of the Nuffield Department of Population Health's *Ethnicity in Breast Cancer* project and is a PPI contributor to the LynchVax Study.

Patrick volunteers as a member of Oxford Cancer's Patient and Public Involvement Group. With many years of experience in Patient and Public Involvement both within and beyond the University, he has been a key contributor to the centre's initiatives. His dedication to PPI work is inspired by his late wife, who passed away from bowel cancer at 52 after being misdiagnosed three times.

13:20

Catriona Gilmour Hamilton, Julliet Lwiindi, Patrick McGuire, Bep Dhaliwal

Patient and Public Involvement Manager, Public Engagement and Involvement Officer, Oxford Cancer PPI Patient Co-Lead, Ethnicity in Breast Cancer Patient Representative

Oxford Cancer

# Speaker Abstracts & Summaries

## Session 4: Digitally Enabled Research

### Building the Thames Valley and Surrey Secure Data Environment for research

This presentation sets out the development of the NHS Secure Data Environment for Thames Valley and Surrey. Alongside, the strategic context, you will hear about the key enabling activities, the technical infrastructure and how this approach will benefit cancer researchers, cancer patients and the NHS system.

Kerrie has delivered large-scale transformation programmes in the field of clinical informatics for over 15 years. With expertise in programme, project and IT service management as well as research data governance, she has established new capability for a range of initiatives within the NHS and beyond, including the 100,000 Genomes Project, NIHR DeNDRoN, the NIHR Health Informatics Collaborative and the National Consortium for Intelligent Medical Imaging. As Director for R&D Clinical Informatics at Oxford University Hospitals NHS Foundation Trust, Kerrie oversees the Trust's clinical data warehouse for research. She is also an associate director for the University of Oxford Centre for Doctoral Training in Health Data Science.

14:05

Kerrie Woods

Director

NHS, R&D Clinical Informatics

# Speaker Abstracts & Summaries

## Session 4: Digitally Enabled Research

### Oxford Precision Oncology for Sarcoma (OxPOS), a prospective observational and data integration cohort for sarcoma care innovation

The comprehensive sarcoma centres in the UK have drawn together critical mass within sarcoma teams and provided the centralisation of patient care. With this structure comes the expectation for innovation in sarcoma, with excellent recent independent examples in relation to diagnostic genome sequencing, clinical trials and imaging. There remains, however, a lack of digital integration across domains that sustains the overall innovation momentum, such as in sarcoma specific target discovery. Here, I share reflections on the Oxford Precision Oncology for sarcoma, a prospective real world observational study of 200 patients with high grade sarcoma diagnosed and treated in one centre, that attempts to bring together such innovation. The principal aim is to try and work out how to hard wire innovation in this 'sandbox'. Firstly, we wanted to integrate incremental improvements across the sarcoma domains to create an overall step change. Central to the approach is a sustainable and scalable cloud based digital solution linked to EPR through the clinical data warehouse/ secure data environment structure that acts to facilitate MDT data flows and patient care. With test solutions in place, we have taken forward germline susceptibility variant panel testing, somatic sequencing and VUS, 18FDG PET-CT radiomics, digital pathology, health economic assessments, patient and family data virtual clinics, patient and MDT communication support tools and facilitated LLM models and laboratory translation. This model may help inform a wider national sarcoma digital based care network to automate sample procurement, patient reported outcomes, economics of care, clinical trial innovation and recruitment, n=1 clinical experience reporting in a rare cancer and a dashboard for monitoring care performance.

Bass trained in clinical medicine in Oxford (Merton) in the 1980's, and completed a DPhil (Brasenose, Wellcome Fellow) at the Sir William Dunn School in 1994 in Peter Cook's laboratory. After a period in Cambridge and Southampton training in Medical Oncology, he returned to work on imprinted gene functional regulation in embryonic and cancer development with Chris Graham, Department of Zoology (Cancer Research UK Senior Clinical Research Fellow). He was appointed Professor of Oncology in Bristol in 2003 before joining the CRUK Medical Oncology Unit at the Weatherall Institute of Molecular Medicine in 2007. Bass returned to the Sir William Dunn School in 2009 to pursue further work on basic and translational aspects of cancer, mainly focusing on sarcoma. He is a Professor of Medical Oncology, Senior Research Fellow at Lincoln College, Honorary Consultant in Medical Oncology and former Clinical Director of Oncology, Haematology, Physics/Engineering and Palliative Medicine at Oxford University Hospitals NHS Trust.

14:30

Bass Hassan

Professor of Medical Oncology

Sir William Dunn School of Pathology

# Speaker Abstracts & Summaries

## Session 4: Digitally Enabled Research

### Harnessing the value of routinely collected NHS data to develop deep, multi-modal real-world datasets to support cancer research

The NHS collects vast quantities of data in its routine treatment of cancer patients in the UK. Increasingly, these Real-World Data (RWD) are being identified as important tools for supporting the clinical development, approval, and regulatory reimbursement of new therapeutics in oncology.

RWD provides insight into a patient's characteristics, treatment pathways and care experiences as they interact with their care providers. It provides much-needed contextual information where UK representation in clinical trials is lacking, and can be used to evidence the burden of disease to the patient and healthcare system. More recently, it is being used to supplement single-arm studies through the curation of external comparators, enabling assessment of treatment response and safety over the current standard of care.

As precision oncology advances, RWD provides a valuable baseline where augmentation with genetic sequencing data can allow us to curate sub-groups of patients according to how they should be treated based on their present risk of poor disease outcomes, or how they, or patients like them, could be targeted with future treatments.

However, there are well-recognised challenges in accessing NHS data. National policy, patient privacy concerns and operational capacity constraints in the NHS can present as barriers to researchers being able to encounter these data in the form, quantity and technology environment necessary to undertake meaningful research.

Navigating these hurdles requires understanding the relevance and extent of national policy when designing studies which rely on routinely collected NHS data, employing data collection strategies which minimise the resource burden on the NHS, and early engagement with patients and the public. Successful use of these data to address evidence gaps in oncology will progress digitally-enabled drug development and approvals, and ultimately improve the access to novel, effective precision-based medicines for cancer patients in the NHS.

14:45
Christie Brooks
Director
Arcturis Data Limited

# Speaker Abstracts & Summaries

## Session 4: Digitally Enabled Research

### Investigating T-cell exclusion through perfusion of human hemi-liver specimens

Colorectal liver metastasis (CRLM) occur in 50% of colorectal cancer patients and carry a poor prognosis, with 10% 5-year survival in untreated patients. Although surgical resection offers the chance of cure, recurrence is common and even in surgical candidates, 5-year survival is only 40%. Systemic treatments have improved survivorship to a small degree, but whilst immunotherapy (particularly immune checkpoint blockade, ICB) is found to be of significant benefit in some cancer types, most CRLM are insensitive. Currently, ICB is only licenced for use in patients with microsatellite instability, which account for 7-8% of patients with CRLM.

In this project, we used multiplexed immunohistochemical techniques to map the spatial biology of CRLM across whole-slide images. We identify unique features of two CRLM subtypes and demonstrate significant T-cell exclusion, with T-cells accumulating specifically within the peri-CRLM portal triads but not within the cancer itself. Using a novel hemi-liver perfusion platform containing incumbent human CRLM, we demonstrate failed T-cell extravasation within the CRLM and identify CRLM endothelial cell anergy as a potential mechanism limiting T-cell extravasation within CRLM. These findings have relevance for the development of novel immunotherapeutics such as CAR T-cells and bi-specific antibodies which our models predicts would be of limited efficacy unless failure of T-cell extravasation is overcome.

I am a consultant hepatobiliary surgeon operating on patients with cancers of the liver, bile ducts and pancreas. My research interest is in the liver cancer microenvironment and the development of human liver cancer models. I took my DPhil in 2014 under the supervision of Professor Ruth Muschel where I studies the role of myeloid cell subsets in the development of colorectal liver metastasis. Since then I have taken up a lectureship post within the Nuffield Department of Surgical Sciences and I am the Royal College of Surgeons UK lead for liver metastasis research.

15:00

Alex Gordon – Weeks
Consultant Hepatobiliary Surgeon and Clinical Lecturer
Nuffield Department of Surgical Sciences

# Speaker Abstracts & Summaries

## Session 4: Digitally Enabled Research

### Artificial Intelligence: its Development and Use in Imaging in Clinical Practice

It appears that the UK is uniquely placed to provide large data sets from the NHS to develop and test AI algorithms, and these will “save the NHS”. Unfortunately, as is usually the case, life is not so simple, and the devil is in the detail. This talk will discuss the collection of large data sets in the NHS, focusing on Lung Cancer Screening. It will also highlight why it is important to identify the gaps in data needed to develop useful applicable AI, and then discuss the complexities associated with multimodal data sets, before highlighting with examples the complexity of AI use in clinical practice

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 DART, a multicentre study investigating the use of Artificial Intelligence in pulmonary nodules and lung cancer. DART is the world’s largest Lung Cancer Screening dataset with 230,00 participants and over 120,000 CT scans, coupled with outcome data, and digital pathology specimens. His research interests are in Artificial Intelligence applied to thoracic imaging, and Hyperpolarized Xenon MRI.

15:15

Fergus Gleeson
Consultant Hepatobiliary Surgeon and Clinical Lecturer
Department of Oncology

# Speaker Abstracts & Summaries

## Session 4: Digitally Enabled Research

### Domain-specific foundation models for better cancer care: Development of the TrustedMDT copilot for Cancer MDTs

In this talk, I will explore some of the opportunities for large domain-specialised models in Oncology, starting with the cancer multidisciplinary team meeting (MDT).

Using colorectal cancer data from three University NHS Trusts, we have developed an Artificial Intelligence (AI) copilot for MDTs. TrustedMDT's functionality includes (i) summarising clinical reports with a focus on details relevant to the tumour-specific MDT, (ii) automating staging using American Joint-Committee on Cancer (AJCC) criteria, and (iii) drafting treatment plans ahead of the meeting, including identifying patients eligible for peri-operative therapies and clinical trials. TrustedMDT's personalised recommendations aim to promote best practice, improve inter-professional communication, and reduce the time from investigations-to-treatment. A prototype was developed in 2024 and clinical evaluation is planned in 2025/26.

Future opportunities would harness multi-modal capabilities, and could include patient-facing conversational components, novel predictors for treatment success, and enhancements in the uses of routinely collected data for research. Emerging capabilities, as domain-specialised models increase in specialisation and scale, may aid the discovery of new knowledge through agentic reasoning and the connection of previously unrelated facts.

I am a Specialty Registrar in Medical Oncology at Oxford University Hospitals NHS Foundation Trust and Clinical Artificial Intelligence Researcher at the University, working with Professor David Clifton (Engineering Science) and Professor Mark Middleton (Oncology). I also lead the dissertation module for the MSc in Applied Digital Health.

My research develops AI-driven clinical decision support tools for cancer care. Supported by the Microsoft Research Accelerating Foundation Models award, I use transformer-based multimodal techniques and real-world clinical data to generate personalised treatment recommendations, with a focus on privacy-enhancing approaches.

During my NIHR Academic Clinical Fellowship, I specialised in developing AI-enabled screening, diagnostic and prognostic tools using routinely collected data. Working with Professor Clifton's group, I led development and evaluation of an AI screening test for COVID-19 in emergency departments, based upon blood tests and vital signs recorded within 1h of a patient arriving in hospital. The CURIAL AI test was piloted in Oxford's John Radcliffe Hospital Emergency Department in 2021, and described in an accompanying *The Lancet Digital Health* commentary as "an elegant breakthrough to enhance the clinical decision-making process in the age of artificial intelligence".

To support confidential development of AI models within the NHS, I developed a new platform for rapidly-deployable and readily scalable federated learning, using inexpensive micro-computing devices. The CURIAL-Federated platform was piloted across 4 NHS Trusts in 2022 to train and evaluate a Covid-19 screening test, with participating hospitals retaining custody of their data at all times, and published in *The Lancet Digital Health* in February 2024.

15:30

Andrew Soltan

NIHR Academic Clinical Fellow & Dissertation Lead

Department of Oncology

# Speaker Abstracts & Summaries

## Session 4: Digitally Enabled Research

### Applying machine learning to blood test time series to predict the risk of subsequent colorectal cancer

In primary care, unexplained weight loss (UWL) is a non-specific cancer symptom, but uncertainty remains in whether GPs should refer for urgent cancer investigation. Previous research has shown that trends over repeated full blood count test over time can be predictive of subsequent colorectal cancer (Virdee et al, 2022). This study explores whether blood test trends over a 10-year period before UWL could improve patient selection for referral after UWL. The Clinical Practice Research Datalink (CPRD) database (Herrett et al, 2015) was used to extract data for patients with UWL in primary care, as part of the BLOTTED project (Virdee et al, 2023). The analysed data includes full blood count time series for 206,579 patients from GP practices across the UK, 10,325 (5%) of whom were diagnosed with cancer within 6 months after UWL. The five most common cancers were lung, colorectal, pancreas, prostate and stomach cancers. Here, we outline the initial results of a baseline machine learning (ML) strategy: extract various characteristics from each blood test time series and apply ML models with varying degrees of complexity to predict the risk of undiagnosed cancer. The models included penalised logistic regression (PLR), explainable boosting machine (EBM), and gradient-boosted decision tree (GBDT). Models were run on five sets of predictors: (1) age alone; (2) age and sex; (3) age, sex, haemoglobin; (4) age, sex, haemoglobin, platelets; (5) age, sex, haemoglobin, platelets, haemoglobin time series characteristics, and platelet time series characteristics. The data was split over time into training (80%), hyperparameter selection (10%), and held-out test sets (10%). GBDT tended to perform the best. The test-set *c*-statistics for GBDT for the five classes of predictors were (1) 0.66, (2) 0.69, (3) 0.72, (4) 0.74, (5) 0.76. Future research will include additional blood tests, a more rigorous hyperparameter search and other time series classifiers.

Andres Tamm is a health data scientist and researcher working on applying machine learning methods to electronic health records to improve the understanding of cancer and cancer care. He is supervised by Dr Brian Nicholson at the Nuffield Department of Primary Care Health Sciences and by Professor Eva Morris at the Big Data Institute at the University of Oxford. As part of the Oxford University EPSRC Centre for Doctoral Training in Health Data Science, his recently submitted thesis investigated how the faecal immunochemical test can be combined with routinely collected data to increase its precision, developed lightweight text processing tools to extract cancer staging scores from free text clinical reports to facilitate cancer research, and explored methods of automatically clustering patient pathways to study variations in treatment. Outside of research, Andres practices mindfulness and yoga. For more information about the research groups, see https://www.phc.ox.ac.uk/research/research-themes/cancer and https://www.ndph.ox.ac.uk/research/applied-health-research-unit-ahru

**References**

Herrett, E., Gallagher, A.M., Bhaskaran, K., Forbes, H., Mathur, R., Van Staa, T. and Smeeth, L., 2015. Data resource profile: clinical practice research datalink (CPRD). *International journal of epidemiology*, *44*(3), pp.827-836.

Virdee, P.S., Bankhead, C., Koshiaris, C., Drakesmith, C.W., Oke, J., Withrow, D., Swain, S., Collins, K., Chammas, L., Tamm, A. and Zhu, T., 2023. BLOod Test Trend for cancEr Detection (BLOTTED): protocol for an observational and prediction model development study using English primary care electronic health record data. *Diagnostic and Prognostic Research*, *7*(1), p.1.

Virdee, P.S., Patnick, J., Watkinson, P., Holt, T. and Birks, J., 2022. Full blood count trends for colorectal cancer detection in primary care: development and validation of a dynamic prediction model. *Cancers*, *14*(19), p.4779.

15:45

Andres Tamm

Health Data Scientist

Nuffield Department of Primary Care Health Sciences

# Speaker Abstracts & Summaries

## Session 5: Keynote Speaker

### The Maths of Cancer Evolution

How do cancers evolve? We cannot directly watch a person's cancer grow, and so to try and answer this question we have turned to the cancer genome.

Cancer genomes are complicated, containing many thousands of mutations that are the consequence of a complex and protracted evolutionary process. The most common approach to make sense of this complexity has been to first identify distinctive mutational patterns using statistical tools, and then try and work backwards to figure out the process that generated the pattern. Over the past 10 years, we have approached cancer genomics the other way around: we first use mathematical models to precisely express a hypothesis about how a cancer evolves, and then second evaluate the hypothesis by comparing the predictions of the mathematical model to the cancer genome.

Our "maths first" approach has led to lots of surprising findings:

We showed that, across cancer types, most intra-tumour mutational heterogeneity is the result of neutral evolution, not subclonal selection[1]. When subclonal selection is detectable, it is very strong[2]. Paradoxically, only moderately strong negative selection (negatives selection arises from processes such immunoediting) detectability shapes ITH; very strong negative selection (i.e. if immunoediting is very efficient) is invisible[3]. Understanding how selection shapes ITH has enabled us to test the evolutionary consequence of individual driver alterations in individual tumours: in colorectal cancer we found that many mutations thought to be drivers are not actually operating as a driver in individual cancers[4]. More recently we have been using our mathematical lens to explore non-genetic evolution and plasticity, metastasis, prognostication and drug resistance.

Simple evolutionary rules can lead to complex patterns. Maths models are very powerful tools for discovering cancer biology because they make it easy to untangle the underlying rules from the complexity.

Professor Trevor Graham is Director of the Centre for Evolution and Cancer at the Institute of Cancer Research. He leads an interdisciplinary lab that combines mathematical modelling with molecular biology to understand cancer evolution.  His translational interests that span early detection through to treatment of metastatic disease, with a particular focus on colorectal cancer. Trevor was elected Fellow of the Academy of Medical Sciences in 2022 for his work on cancer evolutionary genomics.

[1] https://www.nature.com/articles/ng.3489
[2] https://www.nature.com/articles/s41588-018-0128-6
[3] https://www.nature.com/articles/s41588-020-0687-1
[4] https://www.nature.com/articles/s41586-022-05311-x

16:35

Trevor Graham
Director of the Centre for Evolution and Cancer: Genomics and Evolutionary Dynamics
The Institute of Cancer Research (ICR)

# Poster Showcase

Posters will be presented during the following breaks:

- 10:35 - 11:15 AM (Odd-numbered posters)
- 12:15 - 13:20 PM (Even-numbered posters)

Please make sure to visit the poster displays during both the morning and afternoon coffee breaks and engage with the presenters to learn more about their work. This is an excellent opportunity to network, gain deeper insight into the research and expand your understanding of the cancer community.

The winner will be announced during last session in the awards and closing remarks, starting at 17:15.

Vote for your favourite poster by scanning the QR code below or through the Vevox App.

Poster voting will close at 16:15

Please note: you can only vote for 1 poster. You can change your poster choice at any time until the survey is closed. You must not vote for your own poster.
These votes will not be counted.

If you have any questions, please ask a Centre team member at the registration desk.

CANCER RESEARCH UK | Oxford Centre

OXFORD CANCER

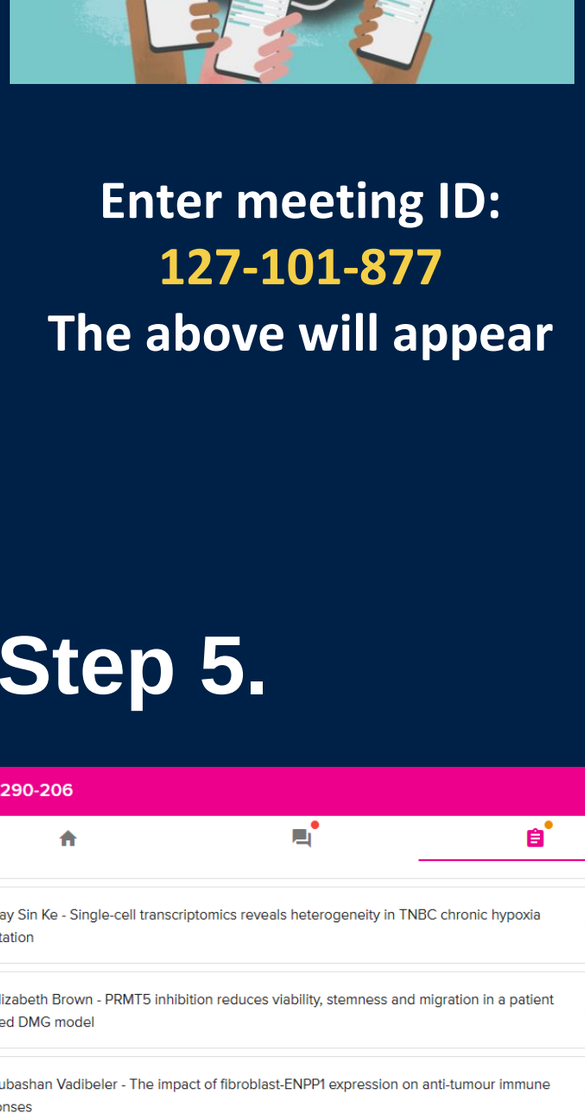
UNIVERSITY OF OXFORD

# How to vote for your favourite poster

## Step 1.

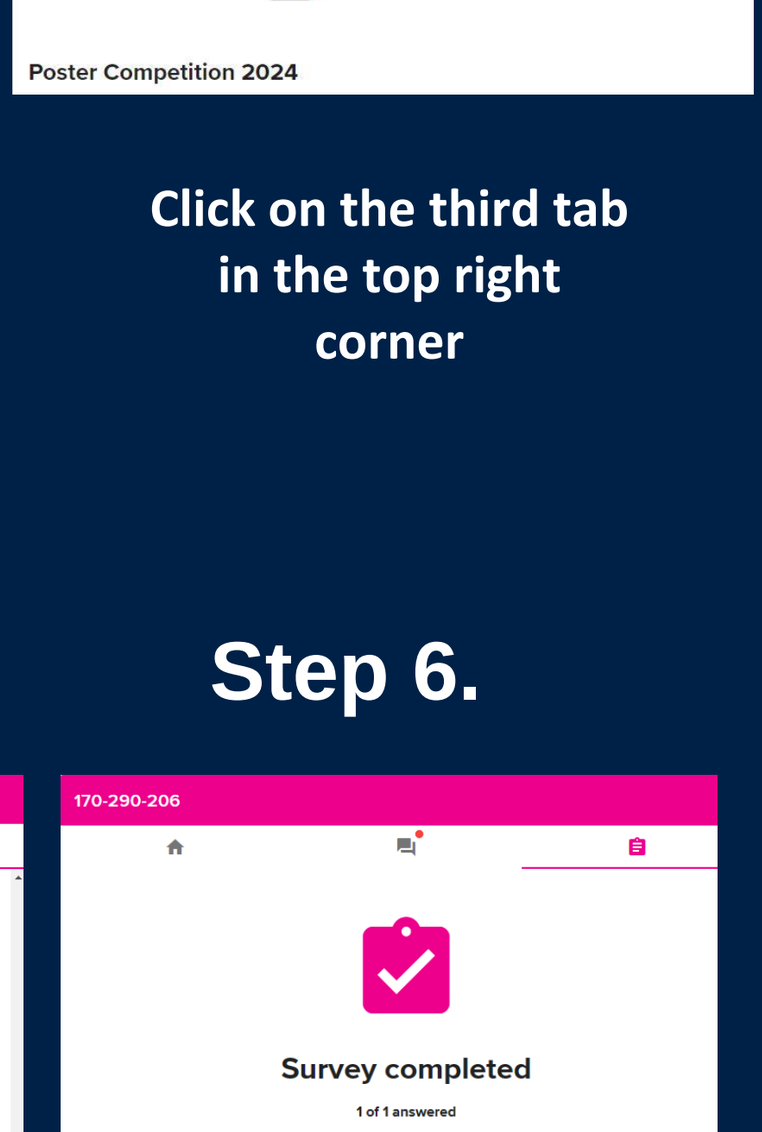
Scan this QR code

## Step 2.



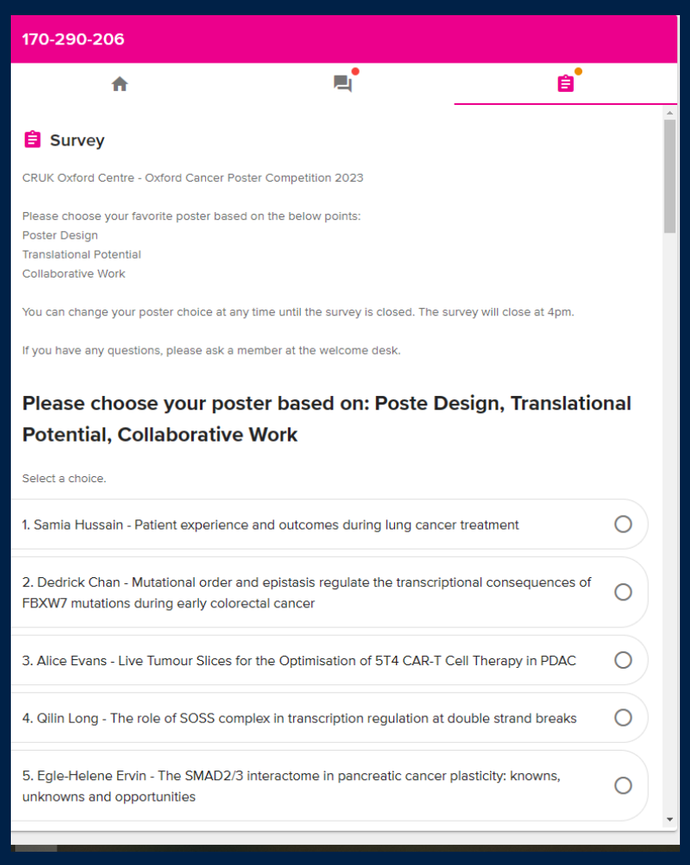

Enter meeting ID:
127-101-877
The above will appear

## Step 3.



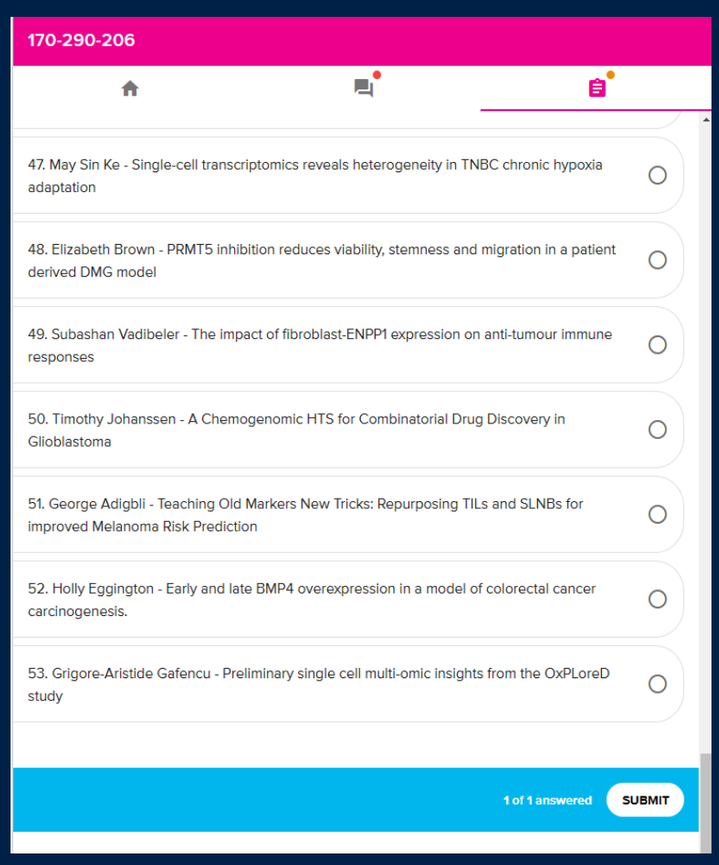

Click on the third tab in the top right corner

## Step 4.



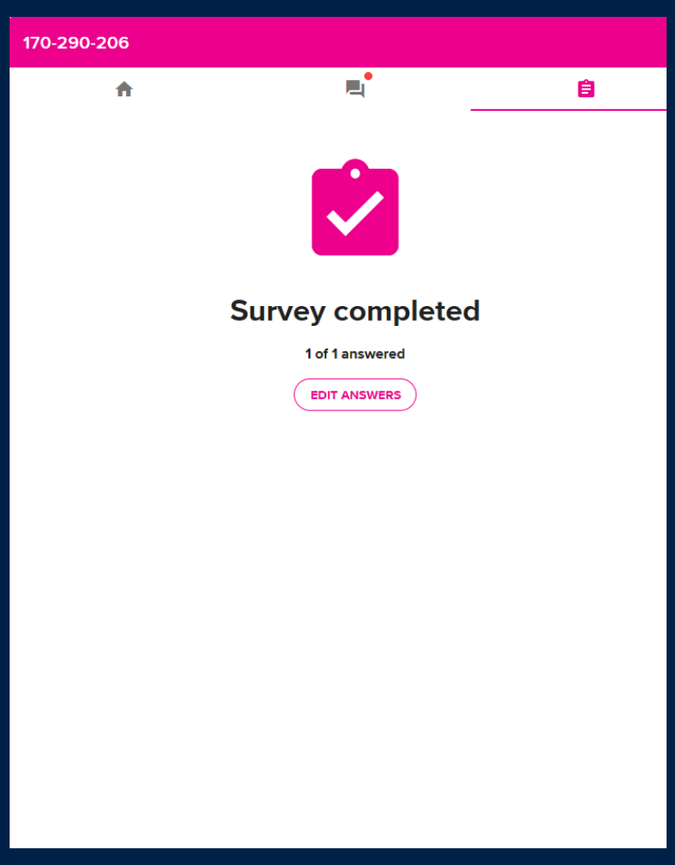

Instructions and the poster numbers will appear. Please choose your favourite poster based on: -
Poster Design
Translational Potential
Collaborative Work

## Step 5.




Once you've selected your favourite, scroll to the bottom of the page and click the submit button.

## Step 6.




Vote complete!

# Poster Abstracts

# 1

# A Preclinical Setup to Inform the Clinical Introduction of Lattice Radiotherapy

**Themed Session:** New to Oxford
**Author(s):** Jia-Ling Ruan, Iain Tullis, Geoff Higgins, Kristoffer Petersson
**Department:** Department of Oncology

## Background

Lattice radiotherapy (LRT) is a form of spatially fractionated radiotherapy (SFRT) designed to enhance tumour control by leveraging highly non-uniform dose distributions. It involves the delivery of small, high-dose regions (~20 Gy) interspersed within a low-dose background (~2 Gy) across a tumour volume. This approach aims to stimulate a robust immune response while minimising toxicity to surrounding healthy tissues. We are developing a clinical protocol to integrate LRT as a high-dose boost prior to standard palliative radiotherapy for large tumours, with the objective of improving therapeutic outcomes. To support the safe and effective clinical translation of this technique, we have established a dedicated preclinical LRT research platform using a FLASH-capable linear accelerator (LINAC).

## Method

To replicate LRT in preclinical models, we designed and fabricated collimators featuring 2 mm diameter apertures arranged in a hexagonal pattern with 5 mm centre-to-centre spacing. These collimators, constructed from 6 mm thick brass plates, allow the precise spatial modulation of dose delivery using 6 MeV electrons. The LINAC facilitates dose delivery at both conventional (~0.1 Gy/s) and ultra-high FLASH (10–$10^6$ Gy/s) dose rates, enabling the investigation of the interaction between spatial and temporal dose modulation in tumour response.
An *in vivo* study was conducted using a subcutaneous bladder cancer (UPPL1541) model in C57BL/6J mice. Tumours were treated with a single fraction of either a homogeneous 10 Gy FLASH beam, or SFRT with peak doses of 20 or 30 Gy (SFRT-FLASH 20 Gy or SFRT-FLASH 30 Gy), while maintaining the same 10 Gy average dose. To assess the impact of dose rate, SFRT at 20 Gy was also delivered conventionally (SFRT-CONV 20 Gy, ~0.1 Gy/s). Tumour growth was monitored over time to evaluate treatment efficacy.

## Results

Tumour growth delay varied significantly between treatment conditions. The control group exhibited continuous tumour progression, whereas homogeneous FLASH 10 Gy induced only moderate growth inhibition. SFRT-CONV 20 Gy and SFRT-FLASH 20 Gy both demonstrated superior tumour control compared to the homogeneous FLASH 10 Gy treatment, highlighting the added therapeutic effect of spatial dose fractionation. The most pronounced tumour growth delay was observed in the SFRT-FLASH 30 Gy group, where tumour suppression was more sustained. These results suggest that LRT elicits a dose-dependent response, with FLASH delivery further amplifying its therapeutic efficacy.

## Conclusions

This preclinical setup enables controlled investigation of lattice radiotherapy's biological effects and dose rate dependencies. The findings will inform the safe and effective clinical translation of SFRT, particularly in combination with immuno-oncology strategies for improved tumour control.

**Contact:** jia-ling.ruan@oncology.ox.ac.uk

2

# Surface glycan of small extracellular vesicles *in-vitro* and *in-vivo* increase in early -stage colon cancer to provide novel biomarkers for potential blood biopsy

**Theme:** Early Detection
**Author(s)**: Cooper, Jamie; Airstone, Bethy; Carollo, Emanuela; Brooks, Susan Ann; Pink, Ryan*, Oxford Brookes University. *corresponding author: rpink@brookes.ac.uk
**Department**: Department of Health and Life Sciences, Oxford Brookes University

## Background

Colon cancer is the 4th most commonly diagnosed cancer, accounting for 11% of all cases. The role and release of plasma small extracellular vesicles (sEVs) in cancer is well documented. Glycoproteins are commonly used in cancer diagnosis *i.e.* CEA, CA125, PSA *etc.* Here, we show that colon epithelial cancer cells and their sEVs have surface glycans that increase with cancer, this translates to plasma patient samples.

## Method

Colon cancer cell lines were probed for surface glycans using lectins and analysed by confocal microscopy and flow cytometry. Imaging-flow cytometry and single particle interferometry were used for the detection using the lectins on EVs. Total plasma EVs from 1ml whole blood from healthy, stage I-II and IV metastatic colon cancer patients were tested by imaging-flow cytometry for lectin binding.

## Results

There were increased glycan-positive cells and their EVs from metastatic and non-metastatic patient-derived colon cancer cell lines compared to immortalised healthy cells. In colon cancer patient-derived plasma sEVs, lectin binding was significantly higher in patients with stages I and II colon cancer than in healthy individuals. Highlighting the potential of glycans as a biomarker method for blood biopsy cancer detection.

## Conclusions

This pilot research suggests that sEV surface glycans could suggest potential early diagnostic utility in colon cancer for lectin-positive sEVs from 1ml blood samples.

**Contact**: rpink@brookes.ac.uk

# 3

# Conserved patterns of transcriptional dysregulation, heterogeneity and cell states in clear cell kidney cancer

**Theme:** Digitally-enabled research
**Author(s):** Olivia Lombardi[1], Ran Li[1], Faiz Jabbar[1], Hannah Evans[1], Silvia Halim[1], Joanna D.C.C. Lima[1], Lisa Browning[2], Helen Byrne[3], Peter J. Ratcliffe[1], David R. Mole[1]
**Departments:** [1]Nuffield Department of Medicine, [2]Oxford University Hospitals NHS Foundation Trust, [3] Wolfson Centre for Mathematical Biology.

**Background:** Clear cell kidney cancers are characterized both by conserved oncogenic driver events (e.g. VHL loss and constitutive activation of hypoxia pathways) and by marked intratumor genetic and phenotypic heterogeneity, which help drive tumour progression, metastasis and resistance to therapy. How these are reflected in transcriptional programs within the cancer and stromal cell components remains an important question with the potential to drive novel therapeutic approaches to treating cancer.

**Methods:** To better understand these programs, we perform single cell transcriptomics on 75 multi-regional biopsies from kidney tumours and normal kidney.

**Results:** We identify conserved patterns of transcriptional dysregulation within the tumour, driven by multiple transcription factors, and reflecting pathways modulated during kidney fibrosis and injury as well as by hypoxia. We identify receptor-ligand signaling between tumor and stromal cell types, leading to phenotypic switches within the vasculature and conserved vascular responses within the tumors. We describe the recurrent transcriptional consequences of Chr14q loss (a common chromosomal abnormality in clear cell kidney cancer that is linked to metastatic potential) within multiple subclonal cell populations. This alters the balance between different hypoxic transcriptional regulators to promote more tumorigenic responses. Finally, we identify conserved patterns of intratumor transcriptional heterogeneity that carry prognostic significance. These reflect co-existing cell states found in both cancer cells and normal kidney cells.

**Conclusions:** Since tumors are derived clonally from single founder cells, our results indicate that as well as arising from genetic heterogeneity transcriptional programmes within tumour cells are also a consequence of lineage plasticity. This ability of cancer cells to transdifferentiate between multiple co-existing states has widespread implications for tumor biology, with likely roles in tumor initiation, progression, metastasis and therapeutic resistance.

**Contact:** david.mole@ndm.ox.ac.uk

4

# High definition scRNA-seq analysis of transcriptionally quiescence dormant cancer cell revealed unexpected enrichment of proliferative gene signatures

**Theme:** Early Detection

**Author(s)**: Pakavarin Louphrasitthiphol[1, 2] and Colin R Goding[1]

**Department(s)**: 1 Ludwig Institute for Cancer Research, University of Oxford, Headington, Oxford, OX3 7DQ, UK.
2 Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki, 305-8575, Japan

**Background**
While targeted- and immune-therapies have significantly advanced patients care, these along with conventional chemotherapies are ineffective against dormant cancer cells. Dormant cancer cells are characterized by global reduction in cellular demands reflected in reduced transcription, translation and metabolism which make dormant cells intrinsically resistance to all current cancer therapies.

Although, late relapse, a hallmark of dormancy has been observed in multiple cancer types, we lack means to detect and target dormant cancer cells for eradication. The goal is to better understand how dormancy is maintained and what might trigger exit from dormancy to generate relapse.

**Method**
To circumvent reliance on specific biomarker, we use a fluorometric marker of dormancy (OSCAR) and performed high definition single-cell transcriptomic study. To mitigate potential methodological bias and to ensure translatability of the finding across different cancer types, we employed two different single-cell transcriptomic technologies on two very different cancer cell line models, skin cutaneous melanoma (SKCM) and pancreatic ductal adenocarcinoma (PDAC).

**Results**
Contrary to expectations transcriptionally quiescence and dormant cancer cells are enriched in genes associated with pro-proliferative pathways. Gene signatures associated with epithelial to mesenchymal transition and inflammatory response associated with translation reprogramming that drive cells to enter slow-cycling and invasive phenotype are reduced. Nevertheless, KRAS signalling, glycolysis, hypoxia and apoptosis gene signatures are down in dormant cells as expected.

**Conclusions**
Although gradual accumulation of mRNA content was proposed to be the key determinant of dormant cells re-entry into cell cycle, one can envisage that on entry into dormancy, cells sequester mRNA associated with proliferative processes away from the translation machinery. Upon receiving signals that trigger re-entry into cell cycle, these mRNA can be released for rapid translation and phenotype switches.

**Contact e-mail:** pakavarin.louphrasitthiphol@ludwig.ox.ac.uk (Post-doc)

5

# Prevalence of obesity in cancer patients receiving systemic therapy: a population-based study in 69,898 cancer patients across 11 cancer types

**Theme:** New to Oxford
**Authors:** Perletta V,[1] Kulkarni S,[1] Wang Z,[2] Tomlinson JW,[3] Hippisley-Cox J,[4] Collins G, [5] Clift AK,[6] Dodwell D,[2] Lord S[1]
**Departments:** [1] Department of Oncology, University of Oxford, [2] Nuffield Department of Population Health, University of Oxford, [3] Oxford Centre for Diabetes, Endocrinology & Metabolism and NIHR Oxford Biomedical Research Centre, University of Oxford, [4] Queen Mary University of London,[5] Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, [6] Department of Surgery & Cancer, Imperial College London

**Background**
Obesity increases the risk of developing multiple cancers, however the impact of obesity on cancer treatments and outcomes is not fully understood. Longitudinal body mass index (BMI) measures from population-based electronic health records (EHR) data can be leveraged to investigate the relationship between obesity, receipt of systemic anticancer treatment (SACT) and survival. Our objective was to use large-scale linked EHRs to estimate prevalence of obesity in cancer patients at time of receiving first SACT overall and across cancer types in England, 2013-2023.

**Methods**
Data are linked from five EHR sources in England: (1) QResearch primary care records, (2) hospital episode statistics (HES), (3) cancer registry, (4) SACT data set, and (5) mortality registry. Patients with a first record of cancer in 2013-2023 were observed for a consecutive first SACT treatment record. BMI was derived from heights and weights recorded on the earliest regimen start date for patients with breast, prostate, lung, bowel, melanoma, kidney, pancreas, bladder, gastroesophageal, ovarian, and hepatocellular cancers. Obesity prevalence was estimated as the number of the patients with BMI≥30 kg/m$^2$ divided by the total number of patients with a complete BMI value and reported as a percentage with 95% confidence interval (% [95%CI]).

**Results**
There were 346,954 patients with a record of cancer diagnosis in the cancer registry, QResearch and/or HES. A SACT record was observed for 69,898 patients. The median (Q1, Q3) age at regimen start date was 67.8 (58.1, 75.0), 36,635 (52.4%) patients were female and 28,478 (62.8%, N=45,322) had stage III/IV disease at diagnosis. Median (Q1, Q3) time from cancer diagnosis to first SACT date was 72 (39, 155) days. The completeness of BMI was 88.8% overall, and ranged from 69.4% (prostate) to 97.3% (bowel, pancreas) across cancer types. The observed prevalence of obesity was 25.9% [25.5-26.2%] overall, higher for breast (34.6% [33.8-35.3%]), melanoma (31.6% [29.5-33.8%]) and kidney cancer (29.2% [27.1-31.3%]) and lower for bowel (23.5% [22.8-24.2%]), gastroesophageal (19.9% [18.8-21.0%]), lung (19.8% [19.0-20.5%]) and pancreatic cancer (13.6% [12.4-14.9%]).

**Conclusions**
In our sample of cancer patients receiving SACT, we observed an obesity prevalence rate of approximately 1 in 4 patients. However, there were differences across cancers types and expectedly lower obesity prevalence rates among cancers associated with weight loss. Our future research will focus on the prognostic relevance of obesity, together with metabolic dysfunction, in relation to treatment utilisation and survival with the goal of developing a clinical outcome prediction model.

**Contact:** victoria.perletta@oncology.ox.ac.uk

# 6

# Nanopore Whole-Genome Sequencing of cfDNA for Cancer Detection

**Theme:** Early Detection/Immuno-Oncology
**Authors:** Vavoulis DV[1], Burns A, Cutts A, Halim S, Dreau H, Taylor JC, Nicholson BD, Schuh A
**Department(s):**[1]Oxford Molecular Diagnostics Centre, Department of Oncology, University of Oxford, Oxford

**Background**: Liquid biopsies can potentially transform Clinical Oncology by simplifying early cancer detection and disease monitoring. We recently developed TriOx, a multi-cancer early triage test using TET-Assisted Pyridine Borane Sequencing (TAPS), which enables whole-genome sequencing with minimal DNA disruption (Figure 1; Vavoulis et al. *Nat Comms* 2025). TriOx combines genomic and epigenomic data to detect plasma ctDNA with 94.9% sensitivity and at least 86% classification accuracy at ctDNA fractions as low as 0.7% of the total cfDNA. However, the high cost of current multi-cancer early detection tests (MCEDTs) remains a significant barrier to their widespread use, especially in low-resource clinical settings.

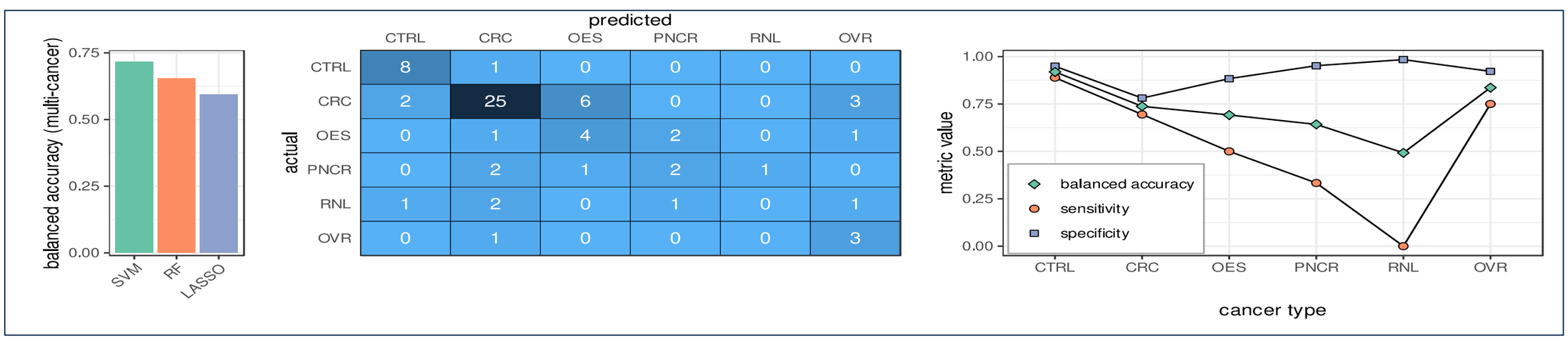



***Figure 1:*** *Overview of TriOx cancer detection performance.*
***CTRL:*** *controls,* ***CRC:*** *colorectal,* ***OES:*** *oesophageal,* ***PNCR:*** *pancreatic,* ***RNL:*** *renal,* ***OVR:*** *ovarian*

## Methods

We present a precise, affordable, and minimally invasive initial triage tool for use in resource-restricted environments, by adapting TriOx to run on shallow Oxford Nanopore Technology (ONT) sequencing data. Like TAPS, ONT sequencing makes possible the genome-wide extraction of genetic and epigenetic information from liquid biopsies using the same sample, but without any build-in chemistry that may have a detrimental effect on the DNA, and at significantly reduced cost. To assess the feasibility of this approach, we used ONT to sequence at 1x the genomes of 13 non-cancer controls recruited at the Oxford University Hospitals (**S**uspected **CAN**cer Pathway, SCAN) and at Cambridge Biosciences, and 22 cancer patients recruited by the Oxford Biomedical Research Centre Cancer Pilot and the Oracle Cancer Trust covering a range of common diseases, including colorectal, pancreatic, and head & neck cancers. We examined multiple data modalities, including copy number aberrations, fragmentomics, structural variation, methylation signals, and viral infection markers.

## Results

We demonstrate comparable performance to deep TAPS sequencing, as well as tissue-of-origin detection based on methylation signatures. For specificity pre-fixed at 100%, we can correctly identify as positive 19 cancer cases (sensitivity 86.4%), of which 6 are early stage (I/II) cancers. Across all data modalities, methylation signals are the most sensitive (81%), followed by copy number aberrations (45.5%), fragmentomics and translocations (27.3% each).

## Conclusions

This cost-effective, minimally invasive triage tool shows promise for accurately identifying cancer and tissue origin, particularly in resource-limited clinical environments. We are currently aiming to expand the above analysis to hundreds of samples for a more precise characterisation of its cancer detection performance.

**Contact:** dimitris.vavoulis@oncology.ox.ac.uk

7

# Developing a tractable *ex vivo* model of human haematopoiesis

**Theme:** Early detection/immune-oncology
**Authors:** Elizabeth J Brown*, Yavor K Bozhilov, Ian Hsu, Adam C Wilkinson
*presenting author
**Department:** Weatherall Institute for Molecular Medicine, Radcliffe Department of Medicine, University of Oxford

## Background

Self-renewing multipotent haematopoietic stem cells (HSCs) are a rare but indispensable cell population for the life-long maintenance of the haematopoietic system. The loss or dysfunction of haematopoiesis underlies a wide range of disorders which collectively contribute to an estimated 70,000 deaths per year in the US. HSCs are also important therapeutically because they are used in stem cell transplantation and associated gene therapies for various blood diseases. A major hurdle in studying the haematopoietic system has been the availability of tractable ex vivo models of human haematopoiesis that supports deep experimental interrogation. This has at least in part been due to a lack of culture conditions that stably maintain and expand HSCs *ex vivo*.

## Method

Building on recent advances in polymer-based expansion of functional human HSCs, we have optimised *ex vivo* culture conditions for human HSC expansion and the directed differentiation of expanded HSCs into 6 major blood lineages – erythroid, megakaryocytic, monocytic, granulocytic, and the B and T lymphoid lineages. To enhance reproducibility and tractability of this model, we have focused on generating serum-free, feeder-free protocols that are amenable to genetic modification.

## Results

We have validated these *ex vivo* culture-derived cell types using flow cytometry, imaging, RNA-sequencing, and functional assays. Using our *ex vivo* model of myelopoiesis I have performed a large scale CRISPR screen of epigenetic regulators (2,500 sgRNAs total) and identified a series of genes that regulate differentiation towards specific myeloid progenitor populations.

## Conclusions

Our model systems can now support in-depth study of human haematopoiesis which was not previously possible. We hope that this *ex vivo* human model system will support investigations into the molecular regulation of healthy and diseased haematopoiesis, and facilitate the development of new HSC-based therapies.

**Contact:** elizabeth.brown@ndcls.ox.ac.uk

8

# Impact of Extracellular Matrix Physical Properties on Colorectal Cancer Liver Metastasis Organoids

**Theme**: New to Oxford
**Author(S)**: Jasmine (Jue) Ban
**Department**: Nuffield Department of Surgical Sciences, University of Oxford

**Background**
The extracellular matrix (ECM) provides essential structural support, bioactive signalling, and morphological guidance to cellular clusters, playing a pivotal role in tumour progression. In organoid-based cancer research, the culture of patient-derived organoids predominantly relies on basement membrane extract (BME) derived from Engelbreth-Holm-Swarm tumours. However, BME presents significant limitations, including high cost, batch-to-batch variability, and an undefined protein composition, introducing substantial biological variability that complicates experimental reproducibility and precise control over physical and biochemical properties.

**Methods**
To explore alternative ECM environments, we cultured patient-derived colorectal cancer liver metastasis organoids in alginate hydrogel, a naturally derived, non-adhesive hydrogel with tuneable and well-defined mechanical properties upon ionic crosslinking. We assessed morphological changes, differentiation status, and stem cell marker expression in organoids cultured in alginate, RGD-functionalized alginate (to enable integrin-mediated adhesion), and standard BME.

**Results**
Here, we demonstrate that organoids cultured in alginate exhibited a novel differentiation phenotype, characterized by the transition from cystic to intestine-like morphology with lumen formation and reduced stem cell population. This effect was partially reversed upon incorporation of the RGD peptide, a common cell adhesion motif, into the alginate matrix. Parallel experiments across multiple patient-derived organoid lines confirmed that the absence of integrin-mediated adhesion drives tumour organoids toward a differentiation trajectory.

**Conclusions**
Our findings highlight the critical role of ECM composition in modulating tumour cell fate and suggest that alginate-based hydrogels provide a defined and tuneable platform for organoid research and therapeutic applications.

**Contact**: jasmine.ban@nds.ox.ac.uk

9

# Bivalent Gene Regulation in Cancer: Paradoxical Upregulation and Promoter Hypermethylation Revealed by Pan-Cancer Analysis

**Theme:** Digitally-Enabled Research
**Author(s):** Alina Mihalovits[1], Henriette O'Geen[2], David J. Segal[2,3], Marketa Tomkova[1,2]
**Departments:** [1]Ludwig Institute for Cancer Research, Nuffield Department of Medicine, University of Oxford, Oxford, UK , [2]Genome Center, University of California, Davis, CA 95616, USA, [3]Department of Biochemistry and Molecular Medicine, University of California, Davis, CA 95616, USA

**Background:**
DNA methylation at promoter regions is generally associated with gene silencing.
**Method:**
We conducted an integrated analysis of The Cancer Genome Atlas (TCGA) data across seven cancer types to examine promoter methylation patterns.
**Results:**
Our analysis revealed a paradoxical phenomenon where promoter hypermethylation is linked to upregulation of many genes (HyperUp) in cancer. This pattern is especially prominent in genes with bivalent chromatin marks (combinations of H3K27me3 and H3K4me3) on their promoters in healthy tissue. Many of these HyperUp genes encode transcription factors involved in key cellular processes, including development and cancer, such as members of the ZIC, FOX, and WNT families. Additionally, their targets are significantly enriched in cancer-associated pathways like p53, MAPK, Wnt, and JAK-STAT.
**Conclusions:**
Our data suggest that bivalent chromatin marks are strong predictors of promoter hypermethylation and subsequent gene activation in cancer. This finding reveals a paradoxical positive correlation between promoter methylation and gene expression at bivalent genes, challenging the conventional view of DNA methylation and highlighting its complex role in cancer biology.
**Email:** alina.mihalovits@reuben.ox.ac.uk

**Position:** DPhil Clinical Medicine

# 10

# Common Genetic Dependencies of Sonic Hedgehog Medulloblastoma (SHH-MB) variants are Regulated by the Non-Malignant Microenvironment

**Theme**: Digitally-Enabled Research

**Author**: John Jacob

**Department**: Nuffield Dept. of Clinical Neurosciences

## Background

Medulloblastoma, of which SHH-MB is a major subtype, is the commonest malignant childhood brain tumour (1). Intensive analysis of the genetic landscape of these tumours has uncovered further subdivisions of SHH-MB, which has led to the view that their optimal treatment will require uniquely tailored therapies (2). Superimposed on this classification scheme are key oncogenic mutations, for example affecting TP53 which have a profound effect on prognosis. We recently showed that SHH-MB cell states can mirror in vivo tumour cell states in a manner that is determined by the cerebellar microenvironment (3). To determine whether there are shared cell-intrinsic determinants across SHH-MB variants, we sought to identify the key upstream regulators in the gene regulatory network and their direct targets using a digitally-enabled approach.

## Method

The SHH-MB cell line, DAOY which harbours a mutation in TP53, was grown as monocultures or in co-culture with non-malignant human iPSC-derived cerebellar organoids for 25 days. Cells were then processed for single cell RNA-seq on the 10X Chromium platform yielding thousands of sequenced transcriptomes, which were analysed using the three-step SCENIC computational pipeline (4). First, candidate regulatory modules are inferred from gene co-expression patterns. Next, co-expression modules are pruned by eliminating indirect targets using transcription factor motif discovery, to define ‘regulons’ for each transcription factor. Last, the activity of these regulons is measured in individual cells and used for clustering.

## Results

There was a striking shift in the combinatorial pattern of regulons expressed by tumour cells in co-culture. Indeed, one of the top regulons, ELK1 in co-cultured tumour cells matched the second highest ranked regulon in a batch of four single cell sequenced TP53 wild-type (n=2) and mutant (n=2) patient tumours. Furthermore, another top regulon in DAOY cells in co-culture, CREB5 was a homologue of the highest ranked factor, ATF4 (also called CREB2) in these patient tumours. Unexpectedly, high-risk TP53 mutant tumours shared identical top ranked regulons with TP53 wild-type tumours.

## Conclusions

This in silico analysis suggests common genetic dependencies across distinct SHH-MB tumour subtypes which is regulated by the cerebellar microenvironment, and that could be exploited therapeutically.

**Contact:** john.jacob@ndcn.ox.ac.uk

### References

1.J. Garcia-Lopez, R. Kumar, K. S. Smith, P. A. Northcott, Deconstructing Sonic Hedgehog Medulloblastoma: Molecular Subtypes, Drivers, and Beyond. Trends Genet 37, 235-250 (2021).

2.F. M. G. Cavalli et al., Intertumoral Heterogeneity within Medulloblastoma Subgroups. Cancer Cell 31, 737-754 e736 (2017).

3.M. J. van Essen, A. Nicheperovich, B. Schuster-Böckler, E. B. E. Becker, J. Jacob, Sonic hedgehog medulloblastoma cells in co-culture with cerebellar organoids converge towards in vivo malignant cell states. Neuro-Oncology Advances,  (2024).

4.B. Van de Sande et al., A scalable SCENIC workflow for single-cell gene regulatory network analysis. Nature Protocols 15, 2247-2276 (2020).

# 11

# Comprehensive characterization of tumor-specific CD8 T cells in HR+ breast cancer patients reveal an impaired antitumoral response in patients with lymph node metastasis

**Author(s)**: Mariana Pereira Pinho[1,2], Elie Antoun[2], Balraj Sandhar[1,2], Ting Shu[2], Fei Gao[1,2], Xiaobao Yang[2], Lucia Cerundolo[3], David Maldonado-Perez[3], Renuka Teague[3], Adam Bates[1,2], Megat H. B. A. Hamid[2], Eve Warner[3], Lucinda Winter[4], Nasullah Khalid Alham[5,6], Clare Verrill[3,6], Simon Lord[7], Timothy Rostron[1], Sally-Ann Clark[1], Craig Waugh[1], Paul Sopp[1], Chris Conlon[2,] Ricardo A. Fernandes[2], Adrian L. Harris[7], Yanchun Peng[1,2,], Asha Adwani[8], Tao Dong[1,2]

**Department(s):** [1] MRC Translational Immune Discovery Unit, Weatherall Institute of Molecular Medicine (WIMM), Radcliffe Department of Medicine, University of Oxford, UK; [2] CAMS Oxford Institute (COI), Nuffield Department of Medicine, University of Oxford, UK; [3] Nuffield Department of Surgical Sciences, University of Oxford, John Radcliffe Hospital, UK; [4] Department of Cellular Pathology, Oxford University NHS Foundation Trust, UK; [5] Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford, UK; [6] Oxford NIHR Biomedical Research Centre, John Radcliffe Hospital, UK; [7] Department of Oncology, University of Oxford, UK; [8] Department of Breast Surgery, Oxford University Hospitals NHS Foundation Trust, UK.

**Background**
Most breast cancers express hormone receptors, but the antitumor immune response of these hormone receptor-positive ($HR^+$) breast cancer remains poorly characterized.

**Method**
Dendritic cells loaded with tumor lysate were used to identify tumor-reactive CD8 T cells in HR+ breast cancer patients. These cells were sorted and their specificity were confirmed by culture with tumor cell lines and tumor-associated antigens. The antitumor TCR repertoire was analyzed by sequencing the TCR of the tumor-specific CD8 T cells.

**Results**
Tumor-reactive CD8 T cells were detected in most $HR^+$ breast cancer patients, especially those with early-stage tumors. When present, the circulating antitumor CD8 response contained cytotoxic T cells with diverse specificity and TCR repertoire. Additionally, patients with circulating cancer-specific T cells had significantly more CD8 tumor-infiltrating lymphocytes (TILs). Moreover, tumor-specific TCR sequences were found in the tumor, but at a significantly lower proportion in patients with lymph node involvement.

**Conclusions**
Our data suggest that $HR^+$ breast cancer patients with lymph node metastasis lack tumor-specific CD8 T cells with capacity to infiltrate the tumor at significant levels. However, early-stage patients have a diverse antitumor CD8 response that could be harnessed to develop immunotherapeutic approaches for late-stage $HR^+$ patients.

**Contact:** mariana.pereirapinho@rdm.ox.ac.uk

12

# Identification of novel regulators of IFN-I in cancer

**Theme:** Immuno-Oncology
**Author(s):** Alice Beard[1], Sneha Anand[2], Ilknur Sur Erdem[1], Simeon Draganov[1], Beatrice Salerno[1], Elena Navarro-Guerrero[2], Daniel Ebner[2], and Adán Pinto-Fernández[1]
**Department(s):** [1]Chinese Academy of Medical Sciences Oxford Institute, Nuffield Department of Medicine, University of Oxford, Oxford, UK
[2] Centre for Medicines Discovery, Nuffield Department of Medicine, University of Oxford, Oxford, UK

## Background

Immune checkpoint blockade therapy (ICB), has become a powerful tool to treat cancer, however, response rates to ICB remain low for most cancers, and patients can develop resistance. Response is highly dependent on tumour mutational burden, expression of target ligands, and interferon (IFN) signalling. Type I IFN signalling can upregulate tumour antigen presentation, limit tumour growth, and enhance apoptosis. Targeting negative regulators of the IFN-I signalling pathway, is therefore a potentially powerful approach to combat immune evasion and resistance to immunotherapy.

## Methods

A genome-wide CRISPR-Cas9 screen was performed to identify targets that sensitise cells to IFN-I, in a chronic myeloid leukaemia (CML)-derived cell line. This generated several potential hits, two of which were selected for further validation using commercial CML knockout cell lines.

## Results

Knockout (KO) cell lines for the selected genes showed no augmentation in IFNa2 response or increase in sensitivity relative to wild-type (WT) cells. However, both KO cell lines displayed enhanced sensitivity to ionising radiation and nucleic acid treatment. In response to nucleic acid treatment, changes in expression of IFN-I pathway components and modulators, including pSTAT1, pTBK1, USP18 and ISG15, were observed in KO cells relative to WT.

## Conclusions

By using a genome-wide CRISPR screen we have identified genes involved in innate ligand sensing and radiosensitivity in cancer, strongly suggesting a role in response to stimuli such as infection and cell damage, and are therefore potential targets to bolster responses to cancer therapies.

**Contact:** alice.beard@ndm.ox.ac.uk

# 13

# Single-Cell Functional Biology in the Tumour-Bone Microenvironment: identification of individual prostate cancer cells with high metastatic potential

**Theme:** Digitally-Enabled Research.
**Author(s)**: Daniele T. Cotton[1], Joseph A. E. Morgan[2], Sophia M. Abusamra[3], James R. Edwards[1], Srinivasa R. Rao[1,3], Edmond J. Walsh[2], Claire M. Edwards[1,3].
**Department(s):** [1] Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, [2] Department of Engineering Science, University of Oxford, [3] Nuffield Department of Surgical Sciences, University of Oxford.

**Background**
Prostate cancer (PCa) is the second leading cause of cancer death in men. Bone is a clinically important site of PCa metastasis, indicating progression to incurable disease. Though clonally derived, somatic mutation facilitates tumour evolution, resulting in metastasis-competent subclones. Identifying these cells and their unique characteristics offers an opportunity to develop targeted therapeutics to combat the fatal outcome of PCa bone metastasis.
**Methods**
We deployed microfluidic technology (IotaSciences) to (1) design miniaturised multiplexed assays to identify and retrieve rare but functionally significant subclonal populations, (2) probe individual cell metastatic potential by picking cells into bone microenvironment models and (3) adapt this workflow for human blood spike-recovered PCa cells, providing the foundation to apply the model to patient-circulating tumour cells.

**Results**
Miniaturised assays revealed subpopulations of highly migratory ‘super-spreader’ cells (SSCs) in the PC3 PCa line, with a subset possessing polyaneuploid cancer cell state characteristics (a transient state implicated in treatment resistance), including senescence markers (β-galactosidase, γH2Ax foci) and characteristic increases in cell and nuclear size and perinuclear granularity. We developed a workflow to isolate individual SSCs and deposit them into microplates for downstream analysis. Though initially non-proliferative, an LNCaP feeder bed restored proliferation in SSCs after a 3-7 day quiescent period, reminiscent of the metastatic cascade. Single-cell picking demonstrated heterogeneity in individual LNCaP PCa cell survival and proliferation in bone stromal cell lines (HS-5, HS-27A) and whole-murine marrow models. Microenvironment cells attenuated heterogeneity in survival and proliferation relative to controls, suggesting a combination of microenvironment and clone drives differential cell fate. Higher proliferation was observed in aged murine marrow relative to young, recapitulating orthoptic xenograft tumour burden trends. Average LNCaP colony size was greater for cells picked into LNCaP than media, HS-5 ($p<0.0001$), and HS-27A ($p<0.001$) conditions.

**Conclusion**
This study leveraged cutting-edge microfluidic assays to interrogate single-cell-level diversity in bone metastatic potential in PCa cell lines. Together, our results identify distinct PCa cells with high metastatic potential and demonstrate the impact of the bone microenvironment on tumour cell heterogeneity.

**Contact**: daniele.cotton@seh.ox.ac.uk.

# 14

# Type I interferon regulation by USP18 is a key vulnerability in cancer*

**Theme:** Immuno-Oncology
**Author(s):** Veronica Jové [1], Heather Wheeler [2], Chiachin Wilson Lee [2], David R Healy [2], Kymberly Levine [1], Erik C Ralph [2], Masaya Yamaguchi [2], Ziyue Karen Jiang [3], Edward Cabral [3], Yingrong Xu [2], Jeffrey Stock [2], Bing Yang [3], Anand Giddabasappa [3], Paula Loria [2], Agustin Casimiro-Garcia [4], Benedikt M Kessler [5 6], Adán Pinto-Fernández [5 6], Véronique Frattini [1], Paul D Wes [1], Feng Wang [2]
**Department(s):** [1]Centers for Therapeutic Innovation, Pfizer, New York City, NY 10016, USA,[2]Discovery Sciences, Medicine Design, Pfizer, Groton, CT 06340, USA, [3]Comparative Medicine, Pfizer, La Jolla, CA 92121, USA, [4]Medicine Design, Pfizer, Cambridge, MA 02139, USA, [5]Chinese Academy for Medical Sciences Oxford Institute, Nuffield Department of Medicine, University of Oxford, Oxford OX3 7BN, UK, [6]Target Discovery Institute, Centre for Medicines Discovery, Nuffield Department of Medicine, University of Oxford, Oxford OX3 7FZ, UK.

**Background**
Precise regulation of Type I interferon signaling is crucial for combating infection and cancer while avoiding autoimmunity. Type I interferon signaling is negatively regulated by USP18. USP18 cleaves ISG15, an interferon-induced ubiquitin-like modification, via its canonical catalytic function, and inhibits Type I interferon receptor activity through its scaffold role. USP18 loss-of-function dramatically impacts immune regulation, pathogen susceptibility, and tumor growth. However, prior studies have reached conflicting conclusions regarding the relative importance of catalytic versus scaffold function.

**Method**
Here, we develop biochemical and cellular methods to systematically define the physiological role of USP18.

**Results**
By comparing a patient-derived mutation impairing scaffold function (I60N) to a mutation disrupting catalytic activity (C64S), we demonstrate that scaffold function is critical for cancer cell vulnerability to Type I interferon. Surprisingly, we discovered that human USP18 exhibits minimal catalytic activity, in stark contrast to mouse USP18.

**Conclusions**
These findings resolve human USP18's mechanism-of-action and enable USP18-targeted therapeutics.

***References***
*Jové V, Wheeler H, Lee CW, Healy DR, Levine K, Ralph EC, Yamaguchi M, Jiang ZK, Cabral E, Xu Y, Stock J, Yang B, Giddabasappa A, Loria P, Casimiro-Garcia A, Kessler BM, Pinto-Fernández A, Frattini V, Wes PD, Wang F. Type I interferon regulation by USP18 is a key vulnerability in cancer. iScience. 2024 Mar 27;27(4):109593. doi: 10.1016/j.isci.2024.109593. PMID: 38632987; PMCID: PMC11022047.*

15

# Investigating the Therapeutic Potential of ROS Elevation in ALT-positive Cancers

**Theme:** New to Oxford
**Authors:** N. Mattis, T. Goncalves, Kanggeon Kim, R. Gibbons, D. Clynes, E. Hammond, A.M. Rose
**Department(s):** Department of Paediatrics

## Background

Telomere maintenance mechanisms (TMMs) are critical for cancer cell immortality, with the Alternative Lengthening of Telomeres (ALT) pathway serving as a telomerase-independent mechanism in aggressive cancers such as high-grade gliomas (HGG) and osteosarcomas (OS). ALT is frequently associated with *ATRX* deficiency, but additional factors are required for its activation. Recent findings suggest that reactive oxygen species (ROS) play a key in initiating and sustaining the ALT pathway (Goncalves *et al.,* 2025). This study aims to characterise TMMs and molecular profiles in cancer cell lines to guide the development of targeted therapies while also investigating whether elevated ROS levels can induce hyper-ALT and sensitise ALT-positive cells to chemotherapy.

## Method

To test our hypothesis, we silenced *SOD1* using lentiviral transduction to increase ROS levels and treated cells with camptothecin (CPT), a DNA-protein crosslinking agent. ALT activity was assessed through using C-circle assays and immunofluorescence imaging of ALT-associated PML bodies (APBs), both of which are key hallmarks of ALT. Genomic instability was evaluated through immunofluorescence imaging of DNA-protein crosslinks, while cell viability assays were performed to determine the cytotoxic effects of the treatments.
Ongoing work aims to characterise TMMs in a panel of HGG and OS cell lines using telomere length assays (TRF and qPCR) and assess TERT expression through TRAP assays and sequencing data analysis. Additionally, efforts are underway to generate an isogenic high-grade glioma cell line to evaluate whether ROS elevation enhances the sensitivity of currently licensed drugs.

## Results

Initial data revealed that *SOD1* silencing effectively increased ROS levels, leading to elevated ALT activity in *ATRX*-null cells, as evidenced by increased C-circle formation and APB accumulation. Dual treatment with *SOD1* silencing and CPT induced significant genomic instability, resulting in a synergistic reduction in cell viability compared to individual treatments. Notably, *SOD1* silencing pre-sensitised *ATRX*-null cells to CPT, reducing the required drug dose to achieve cytotoxicity (lower IC50). These effects were more pronounced in *ATRX*-null cells compared to their *ATRX*-wildtype counterparts.

## Conclusion

This study highlights the potential of ROS modulation via *SOD1* inhibition to induce hyper-ALT and enhance the sensitivity of ALT-positive cancers to chemotherapy. Characterising TMMs in cancer cell lines is essential for informing therapeutic strategies targeting ALT-positive malignancies, particularly those with aggressive clinical phenotypes. These findings provide foundational data for developing innovative treatment approaches aimed at improving outcomes for patients with ALT-driven cancers, especially in paediatric and young adult populations, where these cancers are most prevalent.

**Contact:** natalie.mattis@paediatrics.ox.ac.uk

16

# Unravelling the Evolutionary Landscape of MSS Colorectal Cancer: Insights from Single-Cell Transcriptomics and Immunopeptidomics

**Theme:** Early Detection/Immuno-Oncology
**Author(s):** Qian Yang[1], Aleksandra Dzhoneva[1], Philip Carter[2], Dan Woodcock[2], COMBATCancer consortium, Timothy Elliott[1], Nicola Ternette[3], Eleni Adamopoulou[1].
**Department(s):** [1]NDM Centre for Immuno-Oncology, University of Oxford, [2]UK, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK, [3]University of Dundee, Dundee, UK.

**Background**
Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide, with microsatellite stable (MSS) tumours representing over 85% of cases. MSS CRC is resistant to immunotherapy and classified as immunologically "cold," posing significant treatment challenges. This study investigates the evolutionary dynamics and phenotypic heterogeneity of MSS CRC using multi-omics approaches.

**Methods**
Multi-region samples from primary tumours and paired adjacent non-malignant tissues were collected from five treatment-naive MSS CRC patients. Single-cell RNA sequencing (scRNAseq) was performed to profile tumour cell populations, and mass spectrometry-based HLA-I immunopeptidomics (ImP) was used to identify tumour-specific antigens. Copy number alterations (CNAs) were inferred from scRNAseq data using normal epithelial cells as a reference.

**Results**
Tumour evolution analysis revealed subclusters of epithelial cells harbouring MSS CRC-specific CNAs, such as 20q amplification. On exploring intra-tumour expression heterogeneity in the tumour cell population, we identified four conserved meta-programs, shared across at least three tumours, encompassing genes involved in oxidative stress and goblet cell specific markers. ImP data validated the presence of peptides derived from meta-program genes in the tumour immunopeptidome.

**Conclusions**
We integrate scRNAseq and ImP to delineate the evolutionary landscape and phenotypic diversity of MSS CRC tumour cells. The identification of conserved meta-programs and their validation through ImP underscores their potential as targets for cancer vaccination strategies.

**Contact:** qian.yang@immonc.ox.ac.uk

17

# MuSpAn: A Toolbox for Multiscale Spatial Analysis

**Theme:** Digitally-enabled research
**Author(s):** Joshua Moore[1], Joshua Bull[1], Eoghan Mulholland[2], Simon Leedham[2] & Helen Byrne[1,3]
**Department(s):** [1]Wolfson Centre for Mathematical Biology, Mathematical Institute, University of Oxford, UK, [2]Centre for Human Genetics, University of Oxford, UK, [3]Ludwig Centre for Cancer Research, University of Oxford, UK.

## Background

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-organisation 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.

## Method

To overcome these challenges, we present **MuSpAn**, a Python-based toolbox for **Mu**ltiscale **Sp**atial **An**alysis of biomedical imaging data.

## Results

MuSpAn provides an imaging technology-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. Critically, MuSpAn is supplemented with a rich set of documentation, tutorials and exemplar analysis from existing studies (found at www.muspan.co.uk), to support the community with their analysis of spatial data.

## Conclusion

MuSpAn is an open-access tool that empowers researchers to use quantitative spatial biology to advance our understanding of disease progression and improve clinical applications.

**Contact:** Joshua.moore@maths.ox.ac.uk

18

# TMEM33: A Putative Intracellular Checkpoint Modulating T Cell-Mediated Anti-Tumour Immunity

**Theme**: Immuno-Oncology
**Authors:** Matthew Jackson[1,]Tianming Zhao, Gusztav Milotay, Isabela Pedroza-Pacheco, Jan Rehwinkel, David Withers, Benjamin Fairfax, OxCITE, John Christianson, Eileen Parkes.
**Department:** Department of Oncology

## Background

The Endoplasmic Reticulum (ER) is a critical immunomodulatory hub governing multiple processes relating to anti-tumour immunity. TMEM33 is an ER-resident membrane protein implicated in various ER-associated functions including cholesterol metabolism and calcium homeostasis. We have previously described TMEM33 as a negative modulator of the innate immune signalling protein STING (STimulator of INterferon Genes). Here we identify a central role of TMEM33 in shaping the tumour immune microenvironment and T cell functionality.

## Methods

Following subcutaneous growth in WT and *Tmem33*$^{-/-}$ mice, B16F10-OVA tumours and draining lymph nodes (DLNs) were harvested and immune-phenotyped using high dimensional spectral flow cytometry. Naïve splenic CD8$^{+}$ T cells were also stimulated *ex vivo* to assess their activation potential. Antigen cross-presentation was additionally examined in co-culture studies using OVA-pulsed bone marrow-derived dendritic cells (BMDCs) from WT and *Tmem33*$^{-/-}$ mice.

## Results

*Tmem33*$^{-/-}$ mice exhibited significantly attenuated B16F10-OVA tumour growth and enhanced CD8$^{+}$ T cell tumour infiltration compared to wild-type (WT) controls, while CD206$^{+}$ M2-like macrophages were diminished. CD8$^{+}$ T cell enrichment also occurred in MC38 tumour-bearing *Tmem33*$^{-/-}$ hosts. Unchallenged mice displayed no overt phenotypic or immunological differences compared to WT, however. Tumour growth restrictions persisted in *Tmem33*$^{-/-}$*Sting*$^{-/-}$ mice, suggesting that the observed tumour protection occurs independently of host STING. Using the B16F10-OVA model, progenitor exhausted (Tpex) TCF-1$^{+}$PD-1$^{+}$ tumour infiltrating lymphocytes (TILs) were significantly enriched in *Tmem33*$^{-/-}$ hosts, notable given that Tpex are responsive to checkpoint blockade therapy and associate with improved patient prognosis. Compared to WT counterparts, OVA-specific *Tmem33*$^{-/-}$ TILs exhibited increased cytotoxicity and effector function, expressing elevated granzyme-B, perforin-1, and TNF-α. Moreover, EOMES$^{lo}$T-bet$^{hi}$ TILs were more frequent among TCF-1$^{+}$PD-1$^{+}$ and TCF-1$^{+}$ populations in *Tmem33*$^{-/-}$ hosts further suggestive of a more persistent CD8$^{+}$ precursor pool, while inhibitory receptor expression was blunted, indicating reduced exhaustion. In DLNs of *Tmem33*$^{-/-}$ mice, antigen-specific CD8$^{+}$ populations demonstrated enhanced effector memory (CD44$^{+}$CD62L$^{-}$) phenotypes alongside elevated CXCR3 expression, suggesting increased tumour-migratory potential. Naïve *Tmem33*$^{-/-}$ CD8$^{+}$ T cells isolated from spleens exhibited enhanced activation upon *ex vivo* anti-CD3/anti-CD28 stimulation, suggestive of a T cell-intrinsic role for TMEM33. Consistently, TMEM33 deficiency did not impact BMDC antigen-cross presentation in co-culture assays, or alter dendritic cell abundance in tumour studies. Finally, analysis of OxCITE cohort data revealed that lower CD8$^{+}$ T cell-specific TMEM33 expression significantly correlates with improved progression-free and overall survival in patients.

## Conclusions

In summary, we have identified TMEM33 as a novel immunoregulatory factor, the loss of which in hosts majorly reshapes the tumour-immune landscape and ameliorates CD8$^{+}$ T cell fitness. The current evidence suggests that TMEM33 functions intrinsically within T cells to fine-tune their activity.

**Contact email** matthew.jackson@stcatz.ox.ac.uk

19

# Cytomegalovirus seropositivity alters toxicity risk in melanoma following Immune Checkpoint Blockade

**Theme:** Immuno-Oncology
**Author:** Gusztav Milotay
**Department:** Department of Oncology

## Background

Immune Checkpoint Blockade (ICB) forms a core systemic treatment for melanoma. However, treatment-related side effects – so called immune-related adverse events (irAEs) are common, affecting over 60% of combination anti-PD-1/anti-CTLA-4 recipients. Consequently, there is an unmet need to identify predictive biomarkers of irAEs for improved treatment stratification and personalised care. Our work sought to explore possible environmental determinants of irAE risk following ICB, with a focus on Cytomegalovirus (CMV), a chronic viral infection demonstrating profound immune-modulatory effects.

## Method

Pre-treatment peripheral blood samples were collected from a longitudinal cohort of 341 melanoma patients (OxCITE) receiving anti-PD-1 alone or in combination with anti-CTLA-4. Peripheral blood mononuclear cells and plasma were separated using Ficoll-Paque. $CD8^+$ T cells were isolated following magnetic selection (Miltenyi) for T-cell receptor (TCR) mapping using MiXCR. CMV IgG titres were measured from plasma (Abbott). Patient demographic and clinical data were extracted from electronic records and irAEs were assessed according to the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 5.0.

## Results

We find CMV seropositivity to be protective against Grade 3+ but not Grade 1-2 irAEs, representing the most clinically relevant toxicities, along with reduced steroid and second-line immunosuppressant requirements. Furthermore, the reduced incidence of severe irAEs is anti-CMV IgG titre-dependent, with patients who have a higher titre displaying lower risk. CMV seropositivity also has pervasive organ-specific effects with decreased incidence of pneumonitis, myalgia, and colitis, an association which replicates in a pan-cancer cohort. Finally, we note that seropositive individuals have increased incidence of dermatitis, an irAE associated with improved ICB outcomes in melanoma. Leveraging TCR sequencing, we find that this observation is driven by a depletion of mucosal-associated invariant T cells in seropositive individuals, a population with reported regulatory function in the skin.

## Conclusion

Our study highlights the potential for CMV antibody testing as a peripheral treatment stratification biomarker and opens avenues for exploration of divergent organ-specific trafficking of T cells following ICB in the context of chronic viral infection.

**Contact:** gusztav.milotay@oncology.ox.ac.uk

20

# Advancing Esophageal Cancer Management with Machine Learning: Multicentre Survival Prediction Models and Novel Insights

**Theme:** Digitally-Enabled Research
**Author(s):** Yuhan Zheng, Jessie Elliott, Sheraz Markar, Bartłomiej Papież, ENSURE Study Group
**Department(s):** Nuffield Department of Population Health

**Background**
Esophageal cancer remains a leading cause of cancer-related mortality, characterised by poor survival outcomes and high risk of recurrence following surgery. This study focuses on the development of accurate, robust and explainable time-to-event prediction models that are crucial for improving patient stratification and optimising post-operation surveillance strategies, which in turn hold the potential to facilitate early recurrence detection and enable timely intervention.

**Method**
This study leverages the European iNvestigation of SUrveillance after Resection for Esophageal cancer (ENSURE) study, one of the largest multicentre datasets on esophageal cancer to date, to conduct survival analysis. A total of 4972 patients who underwent curative intent treatment June 2009 to June 2015 from 20 European centres across 11 countries were included. We developed and validated four representative predictive models - Cox Proportional Hazards (CoxPH), machine-learning-based (XGBoost) and deep-learning-based (DeepSurv and DeepHit) models - to estimate Disease-Free Survival (DFS), Overall Survival (OS) and Disease-Specific Survival (DSS). Model robustness was subsequently assessed across all centres. To enhance transparency and clinical applicability, Shapley Additive exPlanations (SHAP) was employed to identify key prognostic factors. Finally, to facilitate external validation and user access, we have developed a user-friendly, web-based interactive medical calculator, enabling local input of patient data and prediction access.

**Results**
All four models demonstrated promising predictive capabilities, each with distinct strengths and characteristics. XGBoost achieved the highest concordance indices for DFS (0.739), OS (0.763), and DSS (0.776). However, CoxPH and DeepSurv demonstrated superior overall performance, excelling in both discrimination and calibration performances. Robustness was confirmed across all centres, underscoring the advantages of training on a multicentre heterogenous dataset. Consistent with the clinical literature, pathological staging characteristics, including pathological T and N stage, emerged to be significant predictors across all tasks. Notably, novel findings were uncovered: reduced risks were associated with higher GDP levels of the country where the centre is located, a higher number of tumour resections conducted annually, and greater number of analysed lymph nodes. Furthermore, a concerning increase in disease-specific mortality risk among patients under age of 55 was revealed.

**Conclusions**
This study provides a comprehensive analysis of survival predictions, establishing a robust data-driven framework for survival modelling and patient stratification. The findings offer actionable insights for refining surveillance protocols, optimising treatment strategies, and improving healthcare resource allocations, which could potentially lead to improved outcomes.

**Contact:** yuhan.zheng@univ.ox.ac.uk

21

# Unbiased Spatial Analysis Reveals Distinct B Cell-Enriched Immune Landscapes Associated with Survival in Pancreatic Ductal Adenocarcinoma

**Theme:** Immuno-Oncology

**Author(s):** Sakina Amin[1*], Shihong Wu[1,2*], Nabeel Merali[3*], Nicola Annels[3], Kim Midwood[4], Alex Goron-Weeks[2], Adam Frampton[3], Michael Dustin[4], Rachael Bashford-Rogers[1,2]

**Department(s):** 1 Department of Biochemistry, University of Oxford, 2 Oxford Cancer Centre, University of Oxford, 3 University of Surrey, United Kingdom, 4 Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom

**Background**: The spatial organization of immune cells within the tumour microenvironment is crucial for cancer progression and patient outcomes in pancreatic ductal adenocarcinoma (PDAC). Current spatial analysis methods are often labour-intensive and subjective.

**Methods**: We developed advanced computational pipelines for unbiased analysis of imaging data, automating quality control, phenotyping, encoding, and dimensionality reduction of thousands of metrics describing tissue architecture. This allowed for detailed characterization of immune and tumour microenvironment. We applied this approach to treatment-naïve PDAC patient samples, comparing the immune landscapes of long-term survivors (LTS) and short-term non-survivors (STS).

**Results**: LTS exhibited a higher density of tertiary lymphoid structures (TLS), particularly within the tumour region. Within the invasive region, LTS were characterized with significantly increased CD19+ CD20 low B cells, dendritic cells, and macrophages, alongside a decreased proportion of CD4 Tregs. Notably, a significant proportion of CD19+ CD20 low B cells was also observed at the tumour boundaries in LTS.

**Conclusions**: LTS in PDAC are associated with a distinct B cell-enriched immune phenotype and a more mature TLS structure, linked to favourable outcomes. Comparing STS and rare LTS provides a unique opportunity to identify prognostic patterns, contributing to a deeper understanding of PDAC biology. This knowledge has the potential to improve risk stratification and ultimately enhance patient outcomes.

**Contact:** sakina.amin@sjc.ox.ac.uk

22

# Mapping the human bone marrow using spatial transcriptomics

**Theme:** Digitally-Enabled Research and Immuno-Oncology.
**Author(s):** Rosalin A Cooper*[1,2] Emily Thomas[1,3], Dawood Muhammad[1,3], Hosuk Ryou[3], Carlo Pescia[4], Anna Sozanska[1], Oliver McCallion[5], Renuka Teague[5], Alan Liu[2], Joanna Hester[5,] Fadi Issa[5], Bethan Psaila[2,6], Adam Mead[2,6], Dan Woodcock[4], Jens Rittscher[6,7], Daniel J Royston[1,2].
**Department(s)**: 1. Nuffield Division of Clinical Laboratory Sciences, University of Oxford, UK; 2. Oxford University Hospitals, Oxford, UK; 3. Department of Biomedical Engineering, University of Oxford, UK; 4. University of Milan, Milan, Italy; 5. Nuffield Department of Surgical Sciences, University of Oxford, UK; 6. MRC Weatherall Institute of Molecular Medicine, University of Oxford, UK.

## Background

Myeloproliferative neoplasia (MPN) is a blood cancer characterised by a well-defined molecular landscape and variable clinical phenotype. A minority of patients will develop bone marrow (BM) fibrosis (‘myelofibrosis’), which is associated with a poor clinical prognosis. The BM microenvironment underpins fibrotic progression, however mechanisms that drive this are not fully defined. There is also a pressing need for improved clinical risk stratification in patients with MPN. Emerging spatial transcriptomic (ST) platforms now offer up to subcellular resolution for comprehensive spatial profiling. We systematically and quantitively map the human BM, identifying microenvironmental features that characterise the BM in both health and in MPN.

## Method

We used the *10x Xenium* platform to perform ST analysis on human archival formalin-fixed paraffin embedded (FFPE) bone marrow trephines (BMTs), including those showing normal/reactive features (n = 5) and BMTs from patients with MPN (n = 25). We develop a bone marrow spatial transcriptomic analysis pipeline informed by the application of computational artificial-intelligence tools.

## Results

We provide a comprehensive spatial map of the human BM across a total of 6,304,447 cells. We identify a peri-adipocytic haematopoietic stem cell (HSC) niche and spatial trajectory of myelopoiesis. We identify expression-based correlates of cellular cytomorphology that define haematopoiesis. We find widespread topological perturbation of nearly all lineages in myelofibrosis and identify an immune signature of BM fibrosis. We also identify novel microenvironmental signatures that define the BM in both health and in MPN.

## Conclusion

We provide a quantitative map of the human BM, identifying microenvironmental features that underpin BM fibrosis, and spatial feature sets that have potential clinical utility in patients with MPN.

**Contact:** rosalin.cooper@ndcls.ox.ac.uk

23

# Mapping Tumour Cell Phenotypes with Multiplexed Spatial Proteomics Imaging

**Theme:** New to Oxford
**Author:** Johannes Lehmann, Manager of the Digital Pathology Omics Core
**Department:** Kennedy Institute of Rheumatology, NDO

Just as genetic intra-tumour heterogeneity has reshaped our understanding of tumours, phenotypic heterogeneity is now recognized as a key factor in clinical outcomes including treatment response, dormancy, and metastasis formation. Highly multiplexed spatial proteomics enables the mapping of tumour cell phenotypes and their microenvironment by capturing highly resolved signals from dozens of protein biomarkers across tissue samples. The resulting cellular landscapes can identify local interactions between tumour cells and their surrounding as well as highlight rare cell subtypes for patient stratification.

The Digital Pathology Omics Core (DPOC) bridges the gap between state-of-the-art multiplexed imaging system and individual researchers by providing comprehensive access to spatial proteomics capabilities. Through expert support and optimized workflows, we transform complex tissue imaging data containing millions of cells into actionable biological insights. Our extensive platform validation, robust antibody panel library, and tissue-specific processing protocols ensure consistent, high-quality data acquisition and analysis. Thanks to a diverse technology portfolio, we can address a wide range of experimental needs - from high-throughput multiplexing to whole-mount 3D visualization. We offer cutting-edge platforms including **CellDIVE** and **PhenoCycler** for whole slide multiplex scanning, **MIBIscope** for subcellar imaging, **open-top light-sheet** for 3D imaging, and innovative **in-house developed methods**. This technical breadth allows us to tailor experimental designs to specific research question while maintaining data quality and reproducibility.

In this poster, we will showcase the capabilities of the Digital Pathology Omics Core and highlight how accessible multiplexed spatial proteomics can unlock new insights into tumour biology and patient stratification.

# 24

# The role of bile reflux in stomach cardia adenocarcinoma subtype

**Theme:** Early detection
**Author:** Dr Antonella D'Amore
**Department:** Ludwig Cancer Research Institute NDM

Epidemiological evidence suggests that *Helicobacter pylori* infection, reflux, high-salt diet, smoking and alcohol consumption correlate with an increased incidence of gastric cancer development. Among all the risk factors, *Helicobacter pylori* infection represent a major cancer risk factor, and the mutagenic process has been linked to the ability of this bacterium to induce DNA double-stranded breaks (DSBs) in infected cells, thereby increasing the risk of cellular transformation. However not all gastric cancers can be attributed to *H.pylori* and the direct contribution of the other risk factors remain unclear. Interestingly, new evidence suggests that bile reflux from the duodenum is associated with the development of intestinal metaplasia in the stomach cardia. Metaplasia is a pre-cancerous lesion, and this finding suggests that bile can also play a role in early carcinogenesis. **I hypothesise that bile contributes directly to carcinogenesis by damaging the stomach epithelium while inducing DNA damage.** I will use the organoid and mucosoid cultures, the latter is a 3D culture of healthy patient-derived stomach epithelial cells that can replicate stomach barrier and produce mucus, developed in Boccellato's lab. Using human bile samples derived from no-cancer patients, I aim to understand how bile reflux causes genomic instability, accumulation of somatic mutations, death, and regeneration of the stomach epithelium.  My results will contribute to clarify the role of bile in the aetiology of gastritis and gastric cancer. This will be an important step to identifying those patients most risk, and to direct research into future preventive and therapeutic treatment.

**Contact:** antonella.damore@ludwig.ox.ac.uk

25

# Exploring the Role of USP18 and ISG15 in Cancer Antigen Processing and Presentation

**Author(s):** Hedib Alrawili[1], Alice Beard[1], Beatrice Salerno[1], Haofeng Chen[1], Simeon Draganov[1], Simon Davis[3], Zhu Liang[3], Tim Elliott[2], Eleni Adamopoulou[2], Tao Dong[1], and Adán Pinto-Fernández[1]

**Department(s):** [1]Chinese Academy of Medical Sciences Oxford Institute, Nuffield Department of Medicine, University of Oxford, Oxford, UK, [2]Oxford Cancer Centre for Immuno-Oncology and CAMS-Oxford Institute, Nuffield Department of Medicine, University of Oxford, Oxford, UK, [3]TDI Mass Spectrometry Laboratory, Target Discovery Institute, Nuffield Department of Medicine, University of Oxford, Oxford, Roosevelt Drive, Oxford, OX3 7FZ, UK.

**Background**

Cancer immunotherapy has shown success in some cancers, but resistance remains a major challenge. Resistance mechanisms include defects in interferon signalling and antigen presentation pathways. USP18 is a deISGylating enzyme, reversing modification of proteins by ISG15, and is a master regulator of type I interferon responses. Interestingly, USP18 and ISGylation have been previously suggested to affect MHC-I antigen presentation. This study aims to investigate how USP18 and ISGylation influence antigen processing and presentation, with the goal of identifying novel therapeutic strategies to enhance anti-tumour immunity.

**Methods**

To explore the roles of USP18 and ISG15 in antigen presentation, we utilized HAP1 cell lines, including wild-type, USP18 knockout (KO), ISG15 KO, UBA7 KO, USP18-UBA7 double knockout (dKO), and USP18-ISG15 dKO cells. Some of these cell lines were generated in our lab using CRISPR/Cas9-mediated gene editing. Cells were treated with IFN-α2 (500 U/mL) to activate immune responses. Western blotting was used to analyze the expression of antigen presentation machinery (APM) components, while immunopeptidomics identified MHC-I-restricted peptides. Additionally, GlyGly-peptidomics mapped ISG15 modifications to uncover their impact on antigen presentation.

**Results**

USP18 KO cells exhibited increased ISGylation and upregulated APM components, suggesting that USP18 normally suppresses immune activation. Catalytically inactive USP18 similarly enhanced APM expression, highlighting its therapeutic potential. While USP18-ISG15 dKO cells mirrored the effects of USP18 KO, ISG15 and ISGylation may still play a role in MHC-I peptide presentation. Our data show a correlation between ISGylated proteins and MHC-I peptides, though the exact relationship remains to be fully elucidated.

**Conclusions**

These findings establish USP18 as a critical regulator of antigen presentation. Inhibiting USP18 enhances MHC-I-mediated antigen presentation, potentially improving the immune recognition of cancer cells. Targeting the USP18-ISG15 axis emerges as a promising strategy to combat immune evasion and to improve immunotherapy efficacy, offering new hope for more effective cancer treatments.

**Contact:** Hedib.Alrawili@Wolfson.ox.ac.uk

# 26

# Integrating digital histopathology slides of colorectal cancer biopsies into UK Biobank: a pilot study

**Theme:** Digitally-Enabled Research
**Authors:** Kezia Gaitskell,[1-3] Andrew Blake,[4] Howard Callen,[1] Waseem Qureshi,[4] Enric Domingo,[4] Chen-Chun Pai,[4] Elizabeth H Mann,[4] David Maldonado-Perez,[5] Sorayya Moradi,[5] Maxime Lafarge,[6, 7] Viktor Koelzer,[4, 6, 7] Jens Rittscher,[8] Tim Maughan,[4] Naomi Allen[1]
**Department(s):** [1] Nuffield Department of Population Health, University of Oxford, [2] Nuffield Division of Clinical Laboratory Sciences, Radcliffe Department of Medicine, University of Oxford, [3] Department of Cellular Pathology, John Radcliffe Hospital, Oxford University Hospitals, [4] Department of Oncology, University of Oxford, [5] Oxford Centre for Histopathology Research, University of Oxford, [6] Institute of Medical Genetics and Pathology, University Hospital of Basel, [7] Computational and Translational Pathology Group, Department of Biomedical Engineering, University of Basel, [8] Nuffield Department of Medicine and Department of Engineering Science, University of Oxford.

## Background

UK Biobank is a prospective study of 0.5 million UK adults, aged 40-69 at recruitment between 2006 and 2010, with detailed prospective phenotyping data and follow-up via linkage to routine national health records. After 10 years of follow-up, over 49,000 incident cancers have accrued, including over 5,500 incident colorectal cancers. To enhance the utility of UK Biobank as a resource for cancer research, we conducted a pilot project to retrieve and integrate more detailed histopathology information and digital slides for colorectal cancers.

## Methods

UK Biobank participants diagnosed or treated for colorectal cancer in a single hospital centre (Oxford) were identified. Original histopathology reports were reviewed to extract tumour characteristics from the original biopsy and/or excision (resection) specimen, including tumour histological type, grade, stage, and molecular testing. Where available, the original glass slides from the diagnostic biopsy were scanned to create digital whole-slide images.

## Results

From an initial list of 199 UK Biobank participants with a pathology record of possible colorectal cancer in Oxford, 157 cases were identified with a relevant biopsy showing primary colorectal adenocarcinoma. Among them, 150 (96%) had slides that could be retrieved and scanned to make digital whole-slide images. The digital slides were analysed with a previously-developed algorithm [1] to classify the tumours into consensus molecular subtypes, and these showed separation in survival analyses, providing indirect validation.

## Conclusions

This pilot study demonstrates the feasibility of retrieving and integrating information on tumour characteristics and digital histopathology slides for UK Biobank participants diagnosed with cancer. We aim to expand this work to include other cancer types and hospital sites. This will form an invaluable resource for researchers aiming to investigate factors associated with incidence and survival of specific morpho-molecular cancer histological types and develop clinically-applicable AI algorithms to facilitate diagnosis and stratification for treatment.

**References**

[1] Sirinukunwattana K, Domingo E, Richman SD et al. Image-based consensus molecular subtype (imCMS) classification of colorectal cancer using deep learning. *Gut*. 2021 Mar;70(3):544-554. doi: 10.1136/gutjnl-2019-319866.
Note: Some of this work was previously presented at the Sheffield Pathology conference in 2024 (J.Pathol.2024;264(S2). https://doi.org/10.1002/path.6365)

27

# The role of LARP1 in regulating macrophage metabolism and polarisation in the tumour immune microenvironment

**Themed**: Immuno-Oncology
**Authors**: Chenwan Jin[1], James Chettle[1], Fenella Gross[1], Jelena Bezbradica-Mirkovic[2], Sarah Blagden[1]
**Department(s):** Department of Oncology, University of Oxford, Kennedy Institute of Rheumatology, University of Oxford

## Background

Macrophage polarisation and metabolism are closely interconnected, and thus altered metabolic activity is frequently observed in tumour-associated macrophages (TAMs). These metabolic changes can promote polarisation towards a more immunosuppressive phenotype, thereby driving the establishment of a pro-tumoural immune microenvironment. Our lab has previously demonstrated that the pro-oncogenic RNA-binding protein LARP1 is highly expressed in tumour cells and promotes multiple aspects of metabolism including mitochondrial oxidative phosphorylation. Furthermore, we previously discovered that LARP1 is also expressed in immunosuppressive M2-like macrophages, indicating that it could influence the tumour immune microenvironment by driving immune evasion. We aimed to explore the impact of LARP1 on macrophage polarisation and the underlying mechanisms.

## Method

THP-1-derived and healthy donor-derived monocytes were used to study macrophage polarisation with a focus on the role of LARP1. Polarisation and metabolic processes were evaluated using qPCR, western blotting, immunostaining and Seahorse assay. Comparative analyses were performed using bulk RNA-seq analysis.

## Results

We demonstrate that LARP1 facilitates the polarisation of macrophages towards a more immunosuppressive M2-like phenotype by post-transcriptionally regulating the expression of proteins involved in various metabolic processes including the mitochondrial electron transport chain/oxidative phosphorylation and fatty acid metabolism. Depletion of LARP1 in macrophages results not only in reduced aerobic respiration and altered fatty acid metabolism but also in reduced expression of several key M2-like macrophage markers, consistent with LARP1's role in promoting immune suppression. Specifically, we show that LARP1 modulates the expression of the metabolic regulators STAT6 and PPAR family members in a complex compensatory manner, leading to alterations in fatty acid metabolism and peroxisome activity.

## Conclusions

In summary, we demonstrate that the proto-oncogenic RNA-binding protein LARP1 can drive altered metabolism causing macrophage polarisation through regulation of STAT6 and PPAR family members, resulting in altered fatty acid metabolism and macrophage polarisation.

**Contact:** chenwan.jin@oncology.ox.ac.uk

28

# Mapping the specificity and cross-reactivity of wild-type and engineered T cell receptors

**Theme:** Immuno-Oncology
**Authors:** Kristen Koopmans, Adam Bates, Dan Hudson, Yanchun Peng, Elie Antoun, Tao Dong, Ricardo Fernandes
**Department:** Nuffeild Department of Medicine

## Background

T cells use the T cell receptor (TCR) to detect and eliminate cancer and infected cells through the recognition of antigens presented by the major histocompatibility complex (pMHC). Deciphering the principles of TCR-pMHC interactions and origins of cross-reactivity remains a significant challenge for developing efficient TCR-based immunotherapies. Here we develop a pipeline to characterise the binding landscape and cross-reactivity of tumour-reactive TCRs.

## Method

We engineered a HLA-A*02:01 pMHC yeast library which has up to $10^9$ peptide diversity. Next we screened the engineered TCRs, DMF5 and Tebentafusp, and TCR-011, a wild-type, ‘orphan’ TCR isolated from a non-small cell lung cancer biopsy. By combining affinity-based selections, deep sequencing, computational analysis, and functional assays, our workflow offers a systematic method for mapping TCR reactivity.

## Results

For the engineered TCRs, peptide enrichment analysis revealed conserved motifs strikingly similar to their known target peptides. However, high-affinity TCRs continue to display reactivity against off-target peptides, suggesting additional strategies are necessary to enhance specificity. The wild-type TCR, TCR-011, recognised two distinct peptide motifs, highlighting the role of cross-reactivity in tumour antigen recognition. Using newly developed *in silico* workflows, we predicted and confirmed binding to wild-type candidate peptides which present these two distinct motifs.

## Conclusion

By deconvoluting the complexities of TCR-pMHC interactions, we expect to be able to de-risk and de-orphanise TCRs to guide the development of safer and more effective therapies.

**Contact:** kristen.koopmans@new.ox.ac.uk

Oxford Cancer | CRUK Oxford Centre
University of Oxford
Churchill Hospital
Oxford
OX3 7LE
Email: **cancer@medsci.ox.ac.uk**