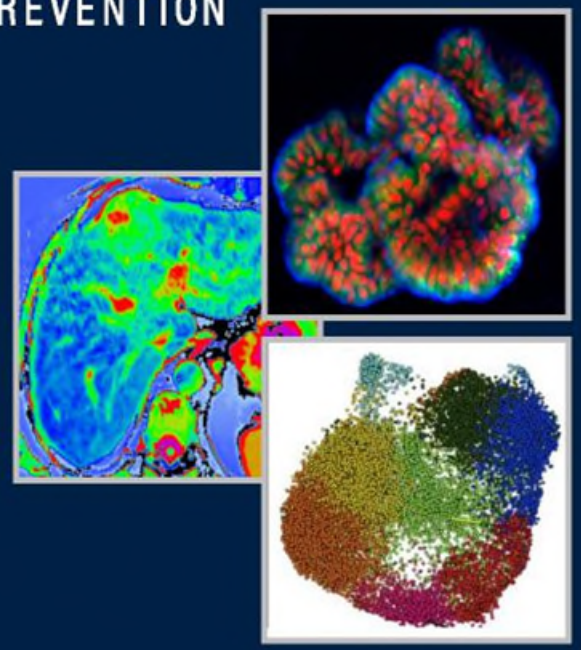
OXFORD CENTRE FOR CANCER EARLY DETECTION AND PREVENTION

UNIVERSITY OF OXFORD



Annual Symposium – Abstract Book 2025

Programme Monday 8th December 2025

09.00 *Arrival, registration and coffee*

09.30-09.40 **Welcome** **Xin Lu**, OxCODE Director

09.40-11.00 **Session 1: Early detection** ***Chair: Ruth Travis***

09.40 **Keynote talk: Ros Eeles- "**Genetic predisposition to prostate cancer and opportunities for targeted early detection and prevention"

10.20 **Parinaz Mehdipour**– **"**Circular RNA biomarkers for early detection of colorectal serrated lesions"

10.40 **Brian Nicholson and Tanvi Rai** – "Approaches to inclusion in the AcceleRated Multi-cAncer DIagnostic EvaLuatiOn (ARMADILO) platform"

11.00 *Coffee*

11.30-12.30 **Session 2: Panel Discussion & Lightning talks** ***Chair: Tim Elliot***

Panel Discussion: Are industry/academia partnerships essential for advancing early detection and prevention research for patient benefit?

- *Dave Chuter, PPI representative*
- *Chloe Moss, Associate Director Moderna*
- *Fergus Gleeson, Professor of radiology*
- *Paul Whyte, Oxford BRC Business Development Lead*

12.10 **Tereza Kacerova** – **"**Integrating NMR Metabolomics and Glycomics for Early Cancer Detection in the SCAN2 Cohort"

12.15 **Martijn Kolijn**– **"**Multi-Cohort High-Dimensional Proteomics Reveals Early Risk Markers for Lymphoid Cancer Subtypes"

12.20 **Ella Mi**– "A tri-level cytosine atlas of normal and tumour tissues for early detection of cancer from multimodal cfDNA epigenetic sequencing"

12.25 **Dimitris Vavoulis** – **"**Nanopore Whole-Genome Sequencing of cfDNA for Multi-Cancer Early Detection"

12.30 *Lunch & Posters (13.00-14.00)*

14.00-15.00 **Session 3: Cancer risk stratification** ***Chair: Mark Middleton***

14.00 **Pradeep Virdee** – "Test trends for cancer detection in patients presenting with non-specific symptoms in primary care: a diagnostic accuracy, longitudinal cohort study"

14.20 **Karl Smith Byrne** – "Proteomics and the potential to improve early detection and patient stratification"

14.40 **Anneke Lucassen** – "Genomic risk stratification for cancer prevention: bridging the gap between promise and implementation"

15.00 *Coffee*

15.30-16.50 **Session 4: Biology-informed prevention** ***Chair: Simon Leedham***

15.30 **Karin Hellner – "**The future of HPV Cancer Prevention: Advancing Therapeutic Vaccine Strategies"

15.50 **Zinaida Dedeic** and **Maria Aggelakopoulou** – **"**Preventing Lung Cancer with Precision Vaccination: The promise of Lungvax"

16.10 **Keynote talk: Phil H Jones – "Pro- and anti- oncogenic mutants in normal epithelia"**

16.50-17.00 **Closing remarks**

Simon Leedham, OxCODE Associate Director

17.00 *Drinks reception and canapés*

OXFORD CENTRE FOR CANCER EARLY DETECTION AND PREVENTION

Lightning talks

Tereza Kacerova

“Integrating NMR Metabolomics and Glycomics for Early Cancer Detection in the SCAN2 Cohort”

Poster #12

Tereza Kacerova[1,2,3], Abi G. Yates[4], Boris Shulgin[4], James R. Larkin[4], Philippa Gleave[4], Sebastian de Jel[5], Jack Cheeseman[6], Georgia Elgood-Hunt[6], The SCAN consortium, Eric Schiffer[5], Daniel I. R. Spencer[6], Suzie Anthony[7], Daniel C. Anthony[4]

[1]Chemistry Research Laboratory, Department of Chemistry, University of Oxford, Oxford OX1 3TA, UK; [2] Kavli Institute of Nanoscience Discovery, Dorothy Crowfoot Hodgkin Building, Oxford OX1 3QU, UK; [3] Physical and Theoretical Chemistry, University of Oxford, Oxford OX1 3QZ, UK; [4] Department of Pharmacology, University of Oxford, Oxford OX1 3QT, UK; [5] numares AG, Regensburg 93053, Germany; [6] Ludger Ltd, Culham Science Centre, Abingdon, UK; [7] Department of Radiology, University of Oxford, Oxford, UK

Early diagnosis of cancer in patients with nonspecific symptoms remains a major clinical challenge. Building on our previous work in the Oxfordshire Suspected CANcer (SCAN) pathway, this study evaluates whether integrating AXINON-derived NMR metabolomics with glycomics (high-performance liquid chromatography mass spectroscopy (HPLC-MS)) enhances cancer detection. In the original SCAN1 study, plasma NMR metabolomics identified cancers with high accuracy (AUC 0.83), revealing systemic inflammation and altered glycoprotein metabolism, particularly elevated GlycA, as key biomarkers.

The SCAN2 study analysed 369 patients (59 cancers, 310 non-cancer) recruited under stricter blood collection protocols. Cross validated NMR-based models reproduced SCAN1 performance (AUC 0.78), confirming robustness despite a more heterogeneous cohort. Integrating glycomics features improved discrimination, with a refined subset excluding major comorbidities achieving an AUC of 0.88.

Specific bi- and tri-antennary glycans (e.g., FA2G2S1, FA2BG1, M5A1G1S1) differentiated cancer cases, reflecting tumour-associated glycosylation and inflammatory processes. A separate model for metastatic disease achieved an AUC of 0.79.

Together, these findings validate the SCAN1 metabolomic signature and demonstrate that combining metabolomics and glycomics provides a scalable, clinically relevant multi-omics framework for earlier and more accurate cancer detection, with clear potential to support improved triage, diagnostic accuracy, and patient outcomes in real-world clinical settings.

Lightning talks

Martijn Kolijn

Utrecht University | Institute for Risk Assessment Sciences (IRAS)

OXFORD CENTRE FOR CANCER EARLY DETECTION AND PREVENTION

“Multi-Cohort High-Dimensional Proteomics Reveals Early Risk Markers for Lymphoid Cancer Subtypes”

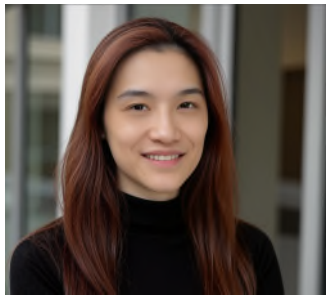
Poster #16

P. Martijn Kolijn1,2,3, Karl Smith-Byrne4, Vernon Burk5, Vivian Viallon6, Matthew A. Lee6,7, Keren Papier4, Ziqiao Wang8, Anton W. Langerak3, Florentin Späth9, Arjan Diepstra10, Christina M. Lill11,12, Raul Zamora-Ros13, Alessandra Macciotta14, Amaia Aizpurua15, 16, Rosario Tumino17, Nilanjan Chatterjee8, Ruth C. Travis4, Marc J. Gunter6,18, Elizabeth A. Platz5, Elio Riboli18, James McKay6, Roel C.H. Vermeulen1,2#
Corresponding author

1.Division of Environmental Epidemiology and Veterinary Public Health, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands.; 2.Julius Global Health, the Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, The Netherlands.;3.Department of Immunology, Erasmus MC, Rotterdam, the Netherlands.;4.Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK.;5.Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.;6.International Agency for Research on Cancer (IARC) - World Health Organization, Lyon, France.;7.Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK;8.Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America;9.Department of Diagnostics and Intervention, Umeå University, Umeå, Sweden;10.Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands.;11.Institute of Epidemiology and Social Medicine, University of Münster, Münster, Germany;12.Ageing Epidemiology Research Unit, School of Public Health, Imperial College, London, United Kingdom.;13.Unit of Nutrition and Cancer, Cancer Epidemiology Research Program, Catalan Institute of Oncology (ICO), Bellvitge Biomedical Research Institute (IDIBELL), 08908, Barcelona, Spain.;14.Centre for Biostatistics, Epidemiology and Public Health (C-BEPH), Department of Clinical and Biological Sciences, University of Turin, 10043 Orbassano, Italy.;15.Sub-Directorate for Public Health and Addictions of Gipuzkoa, 20010 Donostia, Spain.;16.Biodonostia Health Research Institute, Epidemiology of Chronic and Communicable Diseases Group, 20014 San Sebastián, Spain.;17.Hyblean Association for Epidemiology Research, AIRE-ONLUS, Ragusa, Italy;18.Cancer Epidemiology and Prevention Research Unit, School of Public Health, Imperial College London, London, UK

This study aims to investigate the early stages of lymphoid malignancy pathogenesis and identify pre-diagnostic proteomic markers for lymphoma. Using the SomaScan-7K platform, we analyze 6412 unique plasma proteins in a case-cohort study nested within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, comprising 4565 participants (484 incident lymphoid malignancy cases, median follow-up 9 years). We identify over 500 unique protein-lymphoid malignancy associations. Enriched pathways include viral protein interactions, cytokine signaling, B-cell receptor signaling, and NF-κB activation, reflecting key mechanisms in lymphoma pathogenesis. Cross-cohort validation of the top 20 FDR-significant proteins reveals concordant nominal significance for 70%-95% of the associations in the UK Biobank (Olink) and ARIC (SomaScan) studies. Time-stratified analyses reveals that a subset of these protein-lymphoma associations is evident over a decade before diagnosis. These findings highlight the potential of circulating proteomic markers in risk stratification, early diagnosis, and targeted prevention strategies for lymphoid malignancies.

Lightning talks



Ella Mi

“A tri-level cytosine atlas of normal and tumour tissues for early detection of cancer from multimodal cfDNA epigenetic sequencing”

Poster #13

Ella Mi[1], Jingfei Cheng[1], Jinfeng Chen[1], Masato Inoue[1], Felix Jackson[1], Chunxiao Song[1]

1 Ludwig Institute for Cancer Research, Nuffield Department of Medicine, University of Oxford, Oxford, UK

Background: 80% of PDAC are diagnosed late with <10% 5-year survival. cfDNA epigenetic biomarkers e.g. 5-hydroxylmethylcytosine (5hmC) are promising for early detection. We developed TAPS and CAPS+, bisulfite-free DNA methylation sequencing technologies detecting modified cytosines non-destructively, preserving cfDNA for combined genomic/epigenomic analysis, with improved sequencing quality.

Aims and Methods: This is the first application of CAPS+ to cfDNA 5hmC sequencing, first integrated 5hmC and 5mC analysis of cfDNA using cfTAPS and cfCAPS+ and first application of our comprehensive TAPS and CAPS+ atlas of normal and tumour tissues in cfDNA tissue deconvolution to identify cancer. We investigate their capability for early detection of PDAC from hepatocellular carcinoma and control.

Results: cfCAPS+ sequencing had high mapping rate 94.5%, conversion rate 93.7% and low false-positive rate 0.13%. Multimodal AI models integrating genebody 5hmC and 5mC plus fragmentomics distinguished PDAC from control with AUC 0.85 (improved to 0.89 with known pancreas-specific genes, feature-importance revealed genes associated with tumour development), and PDAC/HCC/control with >70% accuracy for each cohort. Deconvolution with our atlases revealed distinct cfDNA tissue signatures in PDAC, HCC and control.

Conclusions: cfCAPS+ provides high-quality, sensitive, specific sequencing. A multimodal approach (5hmC, 5mC, fragmentomics, tissue deconvolution) accurately identifies early cancers, including in shallow sequencing.

Lightning talks

Dimitris Vavoulis

“Nanopore Whole-Genome Sequencing of cfDNA for Multi-Cancer Early Detection”

Poster #9

D. Vavoulis[1,2], A. Burns[1], D. Maxen[1], A. Cutts[1], H. Dreau[1], J.C. Taylor[2], B.D. Nicholson[3], A. Schuh[1]

[1]Oxford Molecular Diagnostics Centre, Department of Oncology, University of Oxford, Oxford, UK; [2]Centre for Human Genetics, Nuffield Department of Medicine, University of Oxford, Oxford, UK; [3]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

Background: Multi-cancer early detection using liquid biopsies offers a transformative route to earlier diagnosis, but current methods are often cost-prohibitive. We previously developed TriOx, a TAPS-based multi-modal assay with high sensitivity. Here, we adapt TriOx to shallow Oxford Nanopore Technologies (ONT) whole-genome sequencing (WGS) to create an affordable triage tool.

Methods: We analysed cfDNA from 100 plasma samples, including 54 non-cancer controls and 46 cancers spanning colorectal, pancreatic, renal, ovarian, thoracic, breast, head&neck, and paediatric lymphomas. Shallow ONT WGS (0.25x–10x) enabled simultaneous assessment of five data modalities: copy number aberrations, fragmentomics, methylation, structural variation, and viral cfDNA.

Results: At 1x coverage, the assay achieved 89.3% sensitivity (95% CI: 76.4–95.4%) and 99.1% specificity (95% CI: 90.9–99.9%). Fragmentomics and methylation were the most sensitive modalities. Even at 0.25x, sensitivity remained 76.7% with 99.2% specificity. Furthermore, methylation patterns permitted inference of the tissue-of-origin of individual cfDNA fragments.

Conclusions: Shallow ONT sequencing of cfDNA enables accurate, low-cost cancer detection across multiple tumour types, retaining performance at very low sequencing depths. This scalable approach is well-suited to early triage in diverse clinical settings, including low-resource environments. Larger, independent cohorts are essential to validate these findings, further develop TriOx, and refine performance estimates.

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Poster Abstracts

Poster #1 –Nicholas Philips

Prediction models for primary cutaneous melanoma incidence in adults: a systematic review

Nicholas Phillips1,2,3, Francess Adlard1, Ruth Omenyo3, Sunil Patel4, Sahani De Silva1, Kiara Wild1, Jessica Wild1, Anjali Trivedi5, Amar Dababneh6, Christiana Kartsonaki7
1. University of Oxford
2. Oxford University Hospitals NHS Foundation Trust
3. Cardiff University
4. University Hospitals Birmingham Foundation Trust
5. East Suffolk and North Essex NHS Foundation Trust
6. Swansea Bay University Health Board
7. Oxford Population Health (Nuffield Department of Population Health)

Introduction: Melanoma is one of the fastest-rising cancers in the UK, accounting for ~4% of new cases but over 80% of skin cancer deaths. (1,2) Early-stage melanoma is highly curable, while advanced disease carries poor survival, driving interest in risk prediction models for targeted screening. (3) This project systematically identifies, appraises, and synthesises all published models predicting primary cutaneous melanoma in adults, including genetic and traditional factors, to assess their quality, performance, and generalisability.

Methods: Searches were conducted in MEDLINE (Ovid), Embase (Ovid), and Scopus to 3 March 2025 (PROSPERO CRD420250644966). Search design was supported by a medical librarian, and results were managed in Covidence.
Two reviewers independently performed data extraction, risk of bias, and reporting assessments using CHARMS, PROBAST-AI, and TRIPOD adherence tools. Disagreements were resolved by CK acting as third reviewer as the conflict resolution protocol.

Results: Seventy papers were identified, including model development, external validation, incremental validation, and systematic reviews. Existing reviews were screened to capture missed studies. Data analysis is in progress and will be completed before presentation.

Poster #2 –Qian Yang

Multi-omics Integration Reveals Clonal Diversity and Antigen Processing Machinery Alterations in Microsatellite-Stable Colorectal Cancer

Qian Yang1, Aleksandra Dzhoneva1, Philip Carter2, Dan Woodcock2, COMBATCancer consortium, Timothy Elliott1, Nicola Ternette3, Eleni Adamopoulou1.
1. Centre for Immuno-Oncology, Nuffield Department of Medicine, University of Oxford, UK
2. Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK
3. School of Life Sciences, 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. In this study, we investigate the identification of true tumor cells by integrating multi-omics modalities.

Methods: Multi-region samples from primary tumours and paired adjacent non-malignant tissues were collected from six treatment-naive MSS CRC patients. Whole genome sequencing (WGS), single-cell RNA sequencing (scRNAseq) and mass spectrometry-based HLA-I immunopeptidomics (ImP) was performed to detect somatic mutation, profile single cell populations and identify HLA-I bound peptides, respectively.

Results: We demonstrate single-cell transcriptome-based robust identification and delineation of phylogeny tree of true tumour cells. Our analysis reveals that tumour cells exhibit divergent alterations in antigen processing machinery (APM) genes across different inter- and intra-tumour subclones, which can influence their APM sensitivities. In silico neoantigen predictions was performed and validated with ImP.
Conclusions: We integrate WGS, scRNAseq and ImP to delineate the clonality of true tumour cells from six MSS CRCs. The identification of WGS-supported neoantigen through ImP underscores their potential as targets for cancer vaccination strategies.

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Poster Abstracts

Poster #3 –Bruno Beernaert

In situ detection of chromosomal instability in cancer

Bruno Beernaert, Erkin Erdal, Juliet E Martin, Amy Burley, Leticia Campo, Molly Browne, Alistair Easton, Eileen E Parkes

Department of Oncology, University of Oxford

Chromosomal instability (CIN) – a form of genomic instability characterized by elevated chromosome mis-segregations during cell division – is a defining feature of many cancers that drives tumor heterogeneity, genome plasticity, and aberrant immune activation. Collectively, these effects underpin the strong associations of CIN with disease progression, metastasis, poor prognosis, and therapeutic resistance across cancers.

Quantitative evaluation of CIN therefore holds significant promise as a prognostic and predictive biomarker. However, current methods remain costly, laborious, and largely indirect, relying on static genomic proxies that fail to capture ongoing mis-segregation rates.

Here, we present a new image-based approach to quantify CIN in clinical tissue by detecting micronuclei (MN) – direct by-products of chromosome mis-segregation – as a quantitative readout of ongoing CIN. Our method shows a selective increase of MN in pre-cancerous and malignant cells, consistent with CIN as a hallmark of cancer cells. Whole-genome sequencing confirms strong associations between MN frequency and CIN-associated genomic abnormalities. In prospectively collected clinical samples, CIN detection predicts resistance to STING agonist treatment.

By expanding candidate CIN markers, optimizing multimodal tissue staining, and developing automated analysis pipelines, we aim to establish in situ CIN feature detection as a robust and more biologically grounded alternative to sequencing-based CIN evaluation methods.

Poster #4 –Alison Dillman

Pre-Diagnostic Circulating Proteins and Risk of Bladder Cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC)

Alison Dillman, Zhe Huang, Vivian Viallon, Keren Papier, Pietro Ferrari, Marc Gunter, Elio Riboli, Tim J Key, Karl Smith-Byrne, Ruth C Travis

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

Background. Bladder cancer is the tenth most common cancer globally. Circulating proteins are key regulators of cellular functions, and proteomic analyses allow for a comprehensive investigation of proteins that may have causal roles in cancer development.

Methods. We investigated the association between plasma proteins and bladder cancer risk in a case-cohort study within EPIC, comprising 4,349 sub-cohort members and 258 bladder cancer cases. Prentice-weighted Cox regression models, adjusted for smoking and other risk factors, were conducted with false discovery rate correction. Replication analyses were performed in the Atherosclerosis Risk in Communities (ARIC) study for external validation of significant associations.

Results. Of 7,363 aptamers, we identified 33 associated with bladder cancer risk. Subgroup analyses identified 45 proteins associated with urothelial cell carcinoma (UCC) and 32 proteins associated with aggressive tumours. Thirteen proteins were significant ≥10 years from blood collection. Consistent results were observed for I3L1E1 (HR:1.22, 95%CI:1.11-1.35) among never-smokers and ≥10 years from blood collection. We observed two significant associations (TREML1, CARD19) in the replication study that were directionally concordant with results from the prospective analyses.

Conclusions. Evidence for several protein-cancer associations suggests potential as novel biomarkers and provides insight into bladder cancer aetiology

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Poster Abstracts

Poster #5 –David Maxen

Using deep learning anomaly detection approaches to identify circulating tumour DNA in liquid biopsies for early cancer detection

David Maxen, Adam Burns, Anthony Cutts, Helene Dreau, Anna Schuh, Dimitris Vavoulis

Department of Oncology, University of Oxford

Detection of circulating tumour DNA (ctDNA) from plasma samples represents a unique opportunity to screen for multiple cancer types at early stages. However, many early stage cancers have incredibly low fractions of tumour-originating fragments, and only a small proportion of ctDNA fragments can inform ctDNA detection. Hence, to improve the cancer signal to noise ratio, an anomaly detection method can be to identify fragments with abnormal DNA methylation for use in further analysis. However, only one method has been developed for this task1, making it a promising but underexplored avenue to more sensitive and specific early detection tests.

We have developed a novel transformer-based deep learning approach to detect DNA fragments with anomalous methylation. Using shallow whole-genome Oxford Nanopore sequencing, we were able to train a model which, given the DNA sequence of a fragment, can predict the likelihood of each CpG site being unmodified, methylated or hydroxymethylated, and is able to account for variability between genomic locations and within CpG sites on the same fragment. Fragments with discordant predicted and observed CpG modifications are identified as anomalous, and we observe that the cancer cases in our cohort have more anomalous DNA methylation on average.

Poster #6 –Ruth Harman

Enhancing Sample Management in Clinical Trials: The Role of the Translational Support Unit

Kendra Perez-Smith, Sruthi Shakthivel, Ruth Harman

Department of Oncology, University of Oxford

Abstract: Effective sample management in clinical trials has traditionally been underestimated, with planning often limited to sample types and collection timepoints. Critical aspects such as intended use, feasibility and resource allocation, have frequently been overlooked or the expertise was unavailable to appropriately support them.

Recognising this gap, OCTO established the Translational Support Unit (TSU) to support its precision prevention and early detection studies. From trial proposal to close-out, the TSU provides end-to-end oversight, addressing critical operational challenges and enhancing efficiency.

The TSU operates through ten core themes:
1. Trial design – Supports sample logistics, cost estimations, and identification of specialist laboratories.
2. Documentation – Contributes to trial protocols, sample handling manuals, and risk assessments.
3. Training – Delivers specialist training for sample processing consistency and compliance.
4. Sample Management – Ensures proper receipt, storage, processing, and onward shipping.
5. Tracking – Utilises a laboratory information management system (LIMS) for real-time sample traceability.
6. Standard Procedures – Maintains standardised processes for consistency across trials.
7. Quality Assurance – Ensures compliance with GCLP and GCP guidelines.
8. Data Linkage – Facilitates improved integration of trial data.
9. Sustainability – Promotes waste reduction, e.g. through trial kit recycling.
10. PPIE – Supports public and patient engagement with trials, including development of appropriate learning resources.

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Poster Abstracts

Poster #7 –Adam Norton-Steele

Identifying phenotype-genotype-function coupling in 3D organoid imaging using SPOT

Ludwig Institute, University of Oxford

Live cells in tissue are plastic, phenotypically dynamic, and modify their function in response to genetic and environmental perturbations. To unleash the power of live-cell imaging to identify phenotype-genotype-function coupling over time, we report the development of a standardized Shape-Appearance-Motion (SAM) “phenome” and SAM-Phenotype-Observation-Tool (SPOT) to provide unbiased and comprehensive description of morpho-dynamic phenotypes without prior knowledge.

We developed and applied SAM-SPOT to our simulated organoids database with known ground-truth and >1.6 million mouse and human organoid instances with defined genetic and chemical perturbations. SAM-SPOT can effectively and robustly characterize 3D morpho-dynamics from 2D projection videos, advancing biomedical discovery by enabling phenotype-genotype-function relationships to be identified through large-scale and cost-effective label-free live-cell imaging.

Poster #8 –Brad Segal

Dysregulated Immune Proteins in Plasma in the UK Biobank Predict Multiple Myeloma up to 12 years Before Clinical Diagnosis

Joshua Fieggen, Bradley Segal, Anshul Thakur, Christopher C Butler, Karthik Ramasamy, Anjan Thakurta, David A Clifton, Lei Clifton

Oxford Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford

Background: Multiple myeloma (MM) is frequently diagnosed at advanced stages following clinical complications. We investigated whether plasma proteomics could identify novel predictors of MM using machine learning and statistical approaches.

Methods: We analysed proteomic profiles from over 50,000 UK Biobank participants, applying XGBoost with SHAP feature-importance measures to identify key biomarkers. The top 10 proteins and established clinical predictors were evaluated using Cox proportional hazards models.

Results: Seven of the top 10 identified proteins have known roles in immune function and lymphoid cell activation, with two being validated MM therapeutic targets. The proteomic biomarkers significantly outperformed clinical predictors (age, sex, haematological parameters, symptoms), achieving a C-index of 0.90 versus 0.67 and time-dependent AUC of 0.85 versus 0.69 in held-out test data. Superior performance was maintained over 12 years of follow-up. Sensitivity analyses excluding early diagnoses (<5 years) and MGUS cases confirmed robustness of proteomic associations.

Conclusions: Dysregulated plasma immune proteins in otherwise healthy individuals may serve as early indicators of MM risk. This hypothesis-free approach identifies potential avenues for understanding MM biology and developing proteomics-based screening tools—particularly relevant given increasing discussion around population-level MGUS screening.

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Poster Abstracts

Poster #10 –Shizhe Xu (Presented by Christiana Kartsonaki)

Unraveling Breast Cancer Genetic Risk in Chinese Women: Integrating GWAS and Fine-Mapping in the China Kadoorie Biobank

Nuffield Department of Population Health, University of Oxford

Genome-wide association studies (GWAS) identify genetic variants, typically single nucleotide polymorphisms (SNPs), associated with traits or diseases by scanning the genomes of large cohorts. This approach reveals loci contributing to disease susceptibility.

Recent GWAS have identified approximately 200 genomic regions containing common genetic variants associated with breast cancer risk. However, pinpointing the causal variants remains challenging due to linkage disequilibrium (LD), the non-random association of alleles at nearby loci, and most associated variants are located in non-coding regions.

Fine-mapping tools are introduced to distinguish the causal ones by estimating posterior inclusion probabilities. Most previous GWAS and fine-mapping studies focused on individuals of European ancestry due to limited sample sizes in other populations such as Asian and African cohorts. In this study, we aim to use these approaches on 57,660 Chinese women from the China Kadoorie Biobank (CKB), with the objective of identifying potential risk regions and susceptibility genes for breast cancer.

In addition, we aim to integrate its summary statistics with publicly available data from the Breast Cancer Association Consortium (BCAC) and the Asia Breast Cancer Consortium (ABCC) to perform multi-ancestry fine-mapping analyses, with the goal of refining the credible sets.

Poster #11 –Christiana Kartsonaki

Infection with Toxoplasma gondii and risk of prostate cancer

Christiana Kartsonaki, Hannah Fry, Jonathan Clarke, Zhengming Chen, Iona Millwood, Ling Yang

Nuffield Department of Population Health, University of Oxford

Background: Not many modifiable risk factors for prostate cancer exist therefore opportunities to develop prevention strategies are limited. An animal study has shown that Toxoplasma gondii (T. gondii) can disseminate to the prostate and lead to prostate inflammation. No studies have evaluated the associations between infections and risk of prostate cancer in humans.

Methods: We conducted a case-cohort study including 588 cases of prostate cancer and a subcohort of 3321 men within the China Kadoorie Biobank, a prospective cohort of 0.5M adults. IgG antibody titres against antigens for various pathogens were measured in stored plasma samples collected at study entry. Their associations with risk of prostate cancer were assessed using Cox regression.

Results: In the subcohort, the seroprevalence of antibodies against T. gondii P22 and SAG1 was 10.1% and 17.3%, respectively. P22 seropositivity was associated with a higher risk of prostate cancer, with an adjusted hazard ratio of 1.57 (95% confidence interval [CI] 1.06-2.27). There was no association of SAG1 with risk of prostate cancer (HR 1.03, 95% CI 0.74-1.44).

Conclusions: Infection with T. gondii may be associated with risk of a future prostate cancer diagnosis. Further work is warranted to understand its role and potential utility for preventive strategies.

Poster Abstracts

Poster #14- Simon Wikeley

Microfluidic On-chip Exosome Isolation and Analysis for Early Disease Diagnosis

Simon Wikeley, Jason J. Davis

Department of Chemistry, University of Oxford

Exosomes offer much as non-invasive biomarkers for cancer owing to the tumour-specific protein and nucleic acid payloads. The highly efficient selective isolation and subsequent quantitative analysis these (and their payloads), however, remains a major challenge. Conventional ultracentrifugation, size – exclusion or precipitation methods of isolation are time consuming, difficult to manipulate at low blood volumes (<50uL) and yield mixtures containing non-specific vesicles and other contaminants. We have shown that a combination of carefully engineered antifouling nanoparticles and 3D printed magnetic microfluidics enables high-fidelity, efficient capture and isolation of EVs with negligible background.

Exemplified here in establishing a pre-symptomatic Parkinson's assay, we have established a capability to cleanly isolate neuronal exosomes from one droplet of systemic blood within minutes. The so-captured vesicles are then controllably lysed and their protein content assayed. We have specifically developed an amplified femto-molar on chip assay that quantifies alpha synuclein payload in a manner that shows correlation between disease status.

The platform is generic and can be applied to the isolation and assaying of exosomes generally with very low internal marker detection limits. The work has applications, then, to the diagnostically-relevant analysis of exosomal fibronectin, various miRNAs and phosphatidylserine, for example.

Poster #11 –Konstantin Koshechkin

Perspectives on Artificial Intelligence in Cell-Free DNA Analysis for Early Cancer Detection

Konstantin Koshechkin,

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

Artificial intelligence (AI) and deep learning are increasingly applied to circulating cell-free DNA (cfDNA) to enable early cancer detection with enhanced resolution and scale. A large multi-cancer early detection (MCED) study using whole-genome sequencing of cfDNA achieved 87.4% sensitivity, 97.8% specificity, and 82.4% tissue-of-origin accuracy in an independent cohort (3,021 cancers, 3,370 controls). [Nature]

Multimodal fragmentomic integration via a two-stage neural network (ELSM) on 1,994 samples across ten cancer types achieved AUC 0.972 and tissue-origin accuracy 0.683. [OUP Academic]

Deep-learning applied to methylation-based epigenomics shows significant potential: reviews highlight graph-based and convolutional networks transforming classification of cfDNA methylomes. [BioMed Central]

Key challenges remain: standardised data pipelines, algorithmic interpretability, low tumour-fraction sensitivity (<0.1% tumour-derived DNA), and generalisation across library chemistries and populations. Infrastructure established for cloud and federated learning supports scalable deployment in NGS pipelines.

The perspective presented here emphasises technical integration of AI models with fragmentomic, epigenomic, and mutational features, rather than specific assays. These approaches shift the paradigm of cfDNA analytics towards high-throughput, data-driven inference, enabling clinically relevant early detection of multiple cancer types.

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