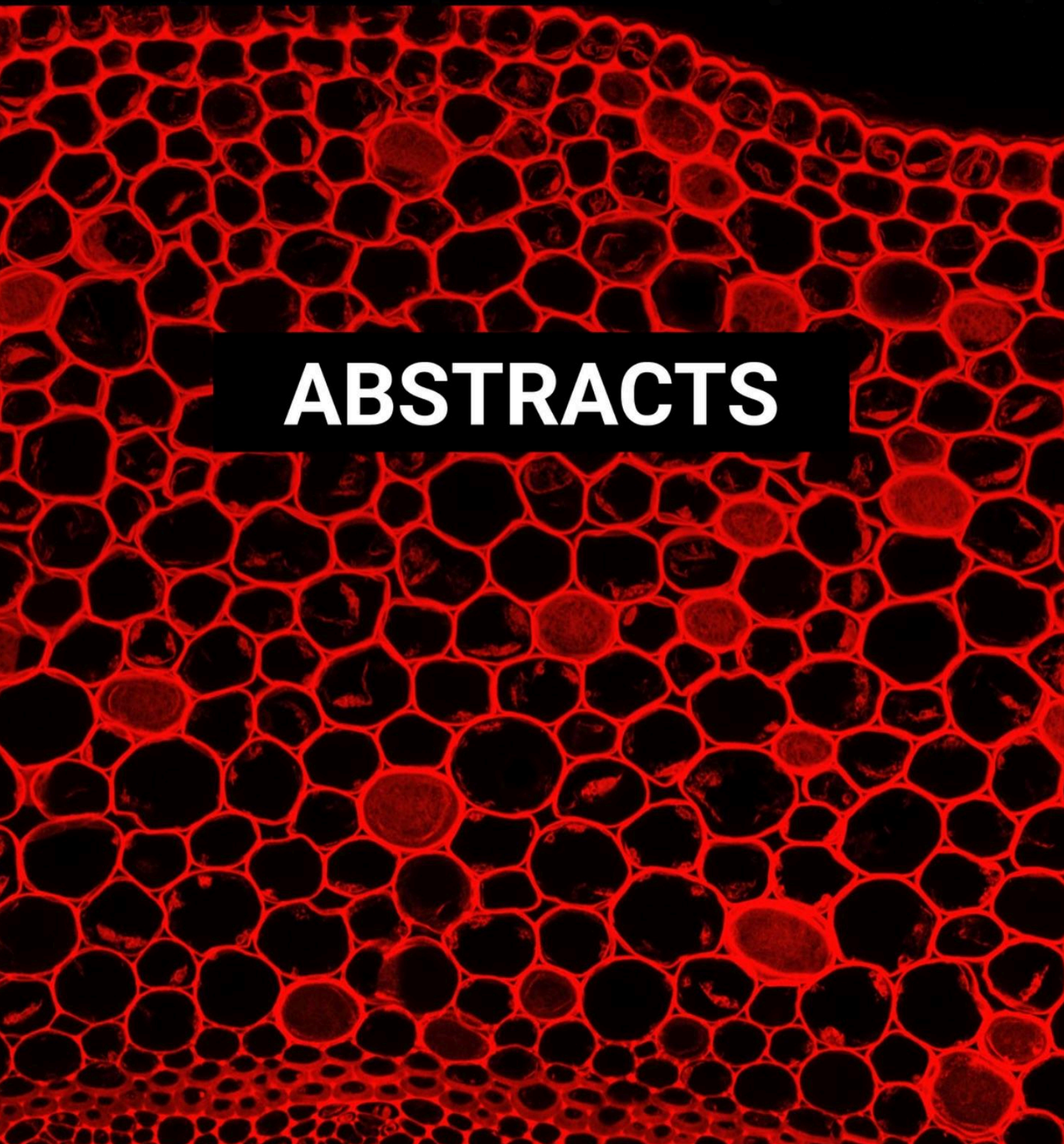
Norwich Single-Cell and Spatial Symposium 2026

Earlham Institute



ABSTRACTS

Keynote speaker

Early metazoan cell type diversity, evolution and regulation

Arnau Sebé-Pedrós[1]

[1]Centre for Genomic Regulation, Spain

Invited Speaker

4D spatial transcriptomics reveals nodule identity emerges through stacked parallel developmental programs

Min-Yao Jhu[1,2,10*], Jo Heffer[3], Chongjing Xia[1], Thiago Alexandre Moraes[1,7], Claire M. Mulvey[3,4], Dario Bressan[3,4,9], Chen Liu[1], Jin-Peng Gao[1,8], Philip Poole[5,9], Katharina Schiessl[6,9], Giles E. D. Oldroyd[1,2,9**]

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Legume root nodules enable symbiotic nitrogen fixation through the development of specialized cells that accommodate nitrogen-fixing bacteria intracellularly and support bacterial nitrogenase activity. However, how nodule identity is established and maintained remains unclear. Here, we present a 4D (3D space × time) spatiotemporally resolved transcriptomic atlas of Medicago truncatula nodulation using 405-gene Xenium in situ profiling, comprising >136,000 spatially mapped cells across nine nodule stages (1–49 days post inoculation) and five lateral-root stages (1-6 days post induction). The atlas maps specialized symbiotic cell types that develop alongside a conserved lateral-root-derived program that underpins vascularization. Dual-species spatial profiling of both plant and bacterial transcripts resolves distinct transcriptional states and previously unrecognized cell states. Integrating spatial organization with developmental time reveals that nodule cell diversification begins at the early primordium stages, where distinct precursor populations emerge around a shared meristem/primordium core. From this common origin, development proceeds through coordinated symbiotic, non-symbiotic, and vascular cell lineages defined by spatially organized transcriptional programs. Time-resolved spatial analysis of developmental regulator mutants uncovers a cascading series of cell-type-specific programs during nodule maturation. LSH1/LSH2 are central regulators of these programs, and lsh1/lsh2 mutants exhibit collapse of hormonal gradients and nodule identity. Strikingly, loss of nodule identity collapses to a primary-root identity rather than a lateral-root fate. This work reveals how tissue complexity emerges through stacked developmental programs sustained in distinct cellular compartments, allowing the emergence of cell types specialized for harboring nitrogen-fixing bacteria.

Selected Speaker

Deciphering novel gene regulatory networks governing avian embryonic hematopoiesis through single-cell multi-omics

Lydia Pouncey[1], Emily Smith[1], Brendan Ali[1], Andreas Nikolopoulos[1], Yuxuan Lan[2], Wilfried Haerty[2], Andrea Münsterberg[1], Iain Macaulay[2], Gi Fay Mok[1]

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During embryonic development, the hematopoietic and vascular systems form through highly orchestrated processes during gastrulation. Mesodermal cells, classified as hemato-endothelial progenitors (HEPs), give rise to both blood and vascular lineages. The first wave of hematopoiesis occurs in the extra-embryonic blood islands and definitive hematopoiesis occurs later within the embryo in the dorsal aorta. Although developmental hematopoiesis has been extensively studied, and several master regulators driving blood and endothelial fate have been uncovered, the gene regulatory networks (GRNs) involved in the early specification of HEPs from the mesoderm remain incompletely understood. Using the chicken embryo as a model, we generated single-nuclei RNA and ATAC datasets across a crucial window when mesodermal cells begin acquiring their hemato-endothelial identity. Integration of these datasets enabled the identification of candidate *cis*-regulatory elements associated with key hemato-endothelial transcription factors, including *GATA2* and *LMO2*, which were functionally validated using fluorescent reporter assays *in vivo*. Motif enrichment analysis of HEP-specific chromatin, combined with higher-resolution Smartseq-2 transcriptomic data, revealed transcription factors not previously implicated in hematopoiesis as putative early regulators of hemato-endothelial competence. We further validated the functional relevance of these factors using both global and hemato-endothelial-specific knockout approaches, providing insights into the earliest GRNs governing blood cell fate.

Selected Speaker

Resolving the cell state-specific regulatory logic of plant immunity with single-nucleus multiome profiling

Benjamin Tremblay[1], Hsuan Pai[1], Tatsuya Nobori[1]

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Plant immune responses are highly heterogeneous at the cellular level. Infection is spatially localized, and neighbouring cells can mount distinct transcriptional programs depending on their identity and proximity to the pathogen. Understanding the *cis*-regulatory code underlying these responses, including which enhancers are activated, which transcription factors act on them, and how this varies between cell states, is a prerequisite for engineering regulatory sequences that drive targeted defence gene expression while avoiding the growth penalties of constitutive immune activation.

To address this, we have generated a single-nucleus multiome dataset of the Arabidopsis response to the bacterial elicitor flg22, sampled at 30 minutes and 3 hours to capture the earliest regulatory events of pattern-triggered immunity. The dataset resolves the major cell types of the leaf and allows us to follow chromatin accessibility and transcription jointly as immune signalling unfolds in each cellular context. Integrating motif accessibility with matched transcription factor expression, we find that distinct cell types mobilise distinct transcription factor programmes in response to the same immune cue, and that the regulators inferred to be active in each state correlate with their expression at the single-nucleus level, supporting the interpretation that these factors are genuinely engaged at their binding sites in a cell type-dependent manner. Linking accessible regions to nearby genes yields candidate enhancer-gene pairs, forming the basis for building cell state-resolved enhancer-promoter regulatory networks for plant immunity, and a foundation for rational design of synthetic, cell state-specific immune-responsive regulatory elements.

Sponsor

The future of single cell RNA sequence - seamless scaleability with evercode V4

Mike Day[1]

[1]Parse Biosciences

Sponsor

TotalSeq for Surface, Intracellular and Nuclear Protein Detection

Amber Vaitkute[1]

[1]Biolegend

Sponsor

Looking to improve cell viability in single-cell analysis

Anish Senan[1]

[1]Cytiva

Sponsor

10x Genomics - From single cell to ~~I~~MPOSSIBLE

Marcus Levitt[1]

[1]10x Genomics

The Earlham Institute are up and running with 10x Genomics' Chromium scRNA-seq and Visium spatial transcriptomic platforms allowing you to obtain more from your precious sample. During our 5-minute slot we will tell you more about the future with Atera. Plenty of merch up for grabs so do come over to the booth and say hi!

Sponsor

QIAGEN solutions for Single-Cell Discovery

Patrick Hickland[1]

[1]Qiagen

An overview of QIAGEN's Sample to Insight approach to molecular biology workflows highlighting tools that support and empower single cell discovery pipelines. We will cover the REPLI-g whole genome amplification platform and how it enables highly uniform amplification of DNA from single cells. We will then explore how this technology integrates with QIAseq FX and QIAseq UPX library preparation solutions to provide a high throughput workflow for the sequencing of ultra-low input samples.

Sponsor

One Cell, Multiple Dimensions: Linking Phenotype, Function and Clonality with BD Rhapsody™

Hasi Patel[1]

[1]Waters Biosciences

One Cell, Multiple Dimensions: Linking Phenotype, Function and Clonality Across Model and Non-Model Systems

Single-cell technologies are transforming our understanding of biological complexity across human, animal, plant and environmental systems. As studies scale in size and scope, researchers require workflows that enable robust discovery while delivering reproducible results.

In this flash presentation, we will explore how the **BD Rhapsody™ Single-Cell Analysis Ecosystem**, coupled with automated sample processing, supports a streamlined discovery-to-insight workflow. Starting with unbiased Whole Transcriptome Analysis (WTA), researchers can identify novel cell populations, rare cellular states and biological pathways without prior assumptions. Automated workflows help reduce manual variability, improve consistency and support larger-scale studies across diverse sample types.

Through examples spanning model and non-model systems, we will demonstrate how scalable transcriptomic discovery can be complemented by targeted and multiomic approaches, enabling researchers to connect phenotype, function and lineage and move beyond cellular catalogues towards biological understanding.

Sponsor

CellCage™ Technology: a dynamic approach to single-cell functional genomics

Carole Chedid[1]

[1]Cellanome

The relationship between gene expression and cellular function is complex: transcriptomic measurements provide static snapshots, while cellular phenotypes unfold over time. To bridge this gap, we developed CellCage™ Technology, which leverages light-guided hydrogel polymerization to enable longitudinal imaging of individual cells coupled with endpoint transcriptomics. Within this system, imaging provides unambiguous readouts of complex cellular functions linked to underlying transcriptional programs.

To characterize information-rich imaging phenotypes, we leveraged DINOv2, a self-supervised vision transformer, to extract high-dimensional morphological features with dimensionality comparable to gene expression. This combination of imaging and transcriptomics represents a novel paired datatype that reveals biological insights inaccessible to transcriptomics alone.

In drug-treated lung cancer cells, longitudinal monitoring identified a stochastic, non-mutational resistant state associated with potassium channel overexpression and p53-mediated quiescence. In preadipocytes and microglia, paired data uncovered functional driver genes that transcriptomic clustering alone failed to identify.

Sponsor

Beyond the genome with multiomics - Unlocking deeper biology

Sam Hamlett[1]

[1]Illumina

Sponsor

All in one cell - Expanding single-cell multiomics from RNA to Spatial and Epigenetic Layers

Mark Lynch[1]

[1]Completomics on behalf of SeekGene

Founded in 2018, SeekGene is a technology-driven platform company dedicated to advancing single-cell sequencing technologies. Guided by the vision of technology-powered innovation, SeekGene focuses on decoding multidimensional biological information from individual cells — "All in One Cell".

Built around the SeekOne™ DD microfluidic system, SeekGene has established a platform that supports multiple single-cell assay workflows across transcriptomics, epigenomics, and spatial omics.

We will introduce how the SeekOne DD microfluidic system automates single-cell partitioning, capture and labelling to process up to 96,000 cells per run with an average capture rate of 65%.

We will demonstrate how our innovation has enabled robust multiomics applications such as methylation and RNA from the same cell as our next generation solution for epigenetics discovery featuring the SeekOne DD Single-Cell Multiome Methylation + RNA Kit) and SeekSpace™ Single Cell Spatial Transcriptome Kit.

More information can be found at https://www.seekgene.com/ and from our exclusive UK distributor Morpho Biotech info@morphobiotech.com.

Sponsor

Decoding Immune and Tumor Niches Through High-Plex Spatial Multi-Omics in Human Cancer Tissues

Mathias Van Bulck[1], Bin Wang, Kevin Hwang, Bing Yang, Yijia Sun, Yuan Cai, Cassandra Kysilovsky, Renchao Chen, Angela Vasaturo, Jiang He

[1]Vizgen

The tumor microenvironment (TME) is defined by extensive spatial and molecular heterogeneity, and single-biomarker assays often fail to capture the full complexity of cellular interactions that drive tumor progression and therapeutic response. To overcome these limitations, we introduce an expanded multi-omics workflow that increases protein detection capacity up to 30 targets while maintaining simultaneous detection of up to 1,000 RNA transcripts on the MERSCOPE ULTRA platform.
The workflow is initiated by staining with conjugated antibodies linked to optimized oligonucleotide tags, which are engineered to ensure high sensitivity and minimal background noise. This is immediately followed by MERFISH 2.0 chemistry based in situ RNA imaging.

The robustness and utility of these integrated methodologies were extensively validated across a broad range of tissue types and antibody panels, while RNA detection sensitivity remained unaffected by the additional protein measurements. We applied this multi-omics assay to archival FFPE human cancer specimens, achieving simultaneous imaging of a high-plex protein panel and a comprehensive, pre designed 815-gene immune-oncology gene panel.

A key advantage of the presented assay is the full customization of both protein biomarker and RNA panels by users in a single tissue assay. Leveraging the subcellular resolution of the MERSCOPE Ultra Platform, we performed granular single cell spatial profiling, successfully annotated different cell types within the tumor microenvironment.
By simultaneously capturing both protein and RNA expression at single-cell resolution, it provides an unparalleled framework for dissecting cellular interactions, identifying spatially organized biomarkers, and accelerating translational studies aimed at predicting therapeutic response.

Invited Speaker

The somatic CNV landscape of the Parkinson's disease brain at single cell resolution

Christos Poukakis[1]

[1]UCL & Royal Free NHS Trust

Parkinson's disease (PD), the second commonest neurodegenerative disorder, is mostly sporadic. Brain mosaicism due to a wide range of somatic mutations is increasingly recognised. We previously detected somatic CNVs of the key alpha-synuclein gene in PD brains using a targeted approach. We now aim to decipher the landscape of somatic CNVs (megabase-scale) at single cell resolution.

We have performed whole genome amplification (PicoPLEX) and low coverage WGS (0.1-0.5x) in single nuclei from 11 PD and 9 control post-mortem brains, together with three healthy individuals who had Lewy bodies, a PD hallmark, detected at autopsy. We analysed the cingulate cortex from all, and substantia nigra (SN), a key affected region in PD, from 9 PD and 7 controls. We used fluorescent-activated nuclear sorting in the cortex to separate neurons from other cells. In the SN, we isolated oligodendrocytes, a neuronal fraction, and all other cells.

After QC, 3,388 nuclei were available for analysis. We are currently refining CNV calls using ASCAT.sc, an adapted version of a cancer computational pipeline. This aims to eliminate calls due to uneven amplification by incorporating B allele frequencies of candidate CNVs. Provisional results suggest divergent patterns between cell types and between disease and controls. We detected a total of 4,762 CNVs, across the entire dataset, 65% of which were losses, including occasional aneuploidies. PD cells appeared to have fewer CNV than controls (0.93 vs 1.65 CNVs per cell).

We aim to provide the first large scale genome-wide analysis of somatic CNVs in a neurodegenerative disorder, with cell-type specific patterns which may indicate contribution to, or results of, the pathogenic process.

Selected Speaker

Single-nucleus profiling reveals replication-coupled epigenome remodelling across ploidy states

James Walker[1,2], Yufei Zhang[1], Kaixuan Qu[1], Zhaogu Sun[1], Anna Bartlett[3], Rosa Castanon[3], Joseph Nery[3], Renee Garza[1], Emma Sun[1], Muhan Li[1], Adrian Lee[1], Keya Gopi Krishna[1], Ge Yao[1], Kylee Mone[1], Liam Ostadan[1], Joseph R. Ecker[1,3,4]

[1] *Department of Plant Biology, The Salk Institute for Biological Studies, La Jolla, CA, USA*
[2] *Plant Molecular Genetics Department, Centre of National Biotechnology, Madrid, Spain*
[3] *Genomic Analysis Laboratory, The Salk Institute for Biological Studies, La Jolla, CA, USA*
[4] *Howard Hughes Medical Institute, The Salk Institute for Biological Studies, La Jolla, CA, USA*

Single-cell profiling provides a powerful framework to resolve how chromatin state is maintained during DNA replication across heterogeneous cell populations. However, how replication-associated processes shape epigenomic landscapes across cell types *in vivo* remains poorly understood.

Here, we use single-nucleus methylome–transcriptome profiling across ploidy states (2C to 6C) to dissect the impact of repeated DNA replication on chromatin state during development. We find that increasing ploidy drives a progressive reduction in DNA methylation, consistent with delayed and incomplete maintenance following DNA replication. Notably, we observe a transient reduction in methylation in S-phase cells, indicating that maintenance lags behind DNA replication *in vivo* rather than occurring synchronously at the replication fork.

Superimposed on this global effect, we identify coordinated, gene-level methylation changes that track with transcriptional specialization, revealing a second, actively regulated layer of chromatin remodeling linked to cell function.

Strikingly, specific lineages violate these dynamics. Phloem companion cells exhibit a near-complete failure to remethylate following replication, resulting in persistent global hemimethylation and revealing intrinsic constraints on maintenance in defined cellular contexts.

Together, our results establish how single-cell resolution enables dissection of replication-associated epigenome remodeling across diverse cell types, providing a framework for understanding chromatin state dynamics during development.

Selected Speaker

Role of the microbiome in shaping chemosensory organ development and homeostasis in mice

Ritika Siddiqui[1], Neal Anthwal[1], Oscar Harris[1] and Abigail Tucker[1]

[1]King's College London

Fitness and survival of an animal heavily rely on sensing the chemical landscape of its surroundings. Most mammals process chemosensory information using sensory neurons present in main olfactory epithelium (MOE), dedicated to sensing air-borne odours, and vomeronasal organ (VNO), specialised for sensing soluble pheromones. Both the MOE and VNO are exposed to the environment to allow the detection of chemical cues and consequently come in direct contact with the microbial communities that colonise the nasal passage. Clinical studies have shown that olfactory defects are associated with altered microbial diversity and relative proportions of specific bacteria in the nasal cavity. Similarly, germ free (GF) mice show altered olfactory responses compared to specific pathogen free (SPF) mice. **However, the molecular basis of how the microbiome affects olfactory capacity is unclear.**

We performed spatial transcriptomics of the MOE and VNO from adult GF and SPF mice, to investigate how presence of a microbiome affects the transcriptional landscape of the specialised cell types of the host's chemosensory organs. Interestingly, specific populations were impacted in the MOE, highlighting the essential role of the microbiome in the fate of olfactory cells. This study will enhance our understanding of the interactions between the microbiome and host cells, and address whether the microbiome influences the development of chemosensory organs or is restricted to a maintenance role.

Invited Speaker

When tendon grows up: cellular divergence from development to adult life

Alina Kurjan[1,2]

[1]University of Oxford & [2]Entelo Bio

Keynote speaker

Dissecting plant-microbe interactions with single-cell and spatial omics technologies

Tatsuya Nobori[1]

[1]The Sainsbury Laboratory

Plant-microbe interactions shape agricultural productivity and ecosystem dynamics. Decades of work have illuminated the molecular logic of plant immunity and microbial colonization, yet a fundamental question has remained elusive: how do individual plant cells, embedded in heterogeneous tissue environments, sense and respond to microbial colonisation? Bulk approaches treat infected tissues as uniform, obscuring the cellular architecture through which immune responses unfold in space and time.
To address this, we have applied single-nucleus multiomics and spatial transcriptomics to Arabidopsis thaliana leaves infected with bacterial pathogens [1]. Our analyses reveal a rich diversity of immune cell states, each defined by distinct transcriptomic and gene regulatory signatures and spatially organised relative to sites of infection. Among these, we identified a rare "primary immune responder" (PRIMER) cell state that emerges at the nexus of immune-active regions. Together, these findings support a new conceptual framework: immune cell states are fundamental building blocks of the plant immune system, and their collective behaviour rather than the average response of a tissue determines infection outcomes [2].
In this talk, I will present our ongoing efforts to map the diversity, regulation, and function of immune cell states. I will also introduce emerging approaches for dissecting plant-microbe interactions at cellular resolution and omics scale.

1. Nobori, T., Monell, A., Lee, T.A., Sakata, Y., Shirahama, S., Zhou, J., Nery, J.R., Mine, A. and Ecker, J.R., 2025. A rare PRIMER cell state in plant immunity. *Nature*, 638(8049), pp.197-205.
2. Nobori, T., 2025. Immune cell states: Critical building blocks of the plant immune system. *Cell Host & Microbe*, 33(8), pp.1227-1232.

Keynote speaker

Mapping the microbe-host interface with genomic-scale microscopy

Jeffrey Moffitt[1]

[1]Harvard Medical School & Boston Children's Hospital

The behavior of tissues in health and disease arises from the complex interplay of the diversity of cell type and states found within those tissues. Dissociated single-cell methods have revolutionized our understanding of a wide range of tissues by providing catalogs of the cell types and states found within; however, by dissociating cells, and understanding of the spatial organization of these cells within the tissue is lost. Spatial transcriptomics—a revolutionary new tool set that allows the direct mapping of RNA expression at the genome-scale within intact tissues—offers an exciting solution to this challenge by providing physical maps of gene expression across large tissue areas. I will introduce multiplexed-error robust fluorescence in situ hybridization (MERFISH), a leading spatial transcriptomics method that leverages massively multiplexed single-RNA-molecule imaging to provide deep molecular profiles of individual cells in their native tissue context, revealing both the cell types and states within the tissue and their spatial organization. I will highlight several exciting applications of this technology in our study of the structure of the healthy and inflamed gastrointestinal tract, and I will discuss recent advances that now provide the ability to profile the behavior of gut bacteria in their native intestinal environment.

Associate Professor, Program in Cellular and Molecular Medicine, Boston Children's Hospital

Associate Professor, Department of Microbiology, Blavatnik Institute, Harvard Medical School Boston, MA USA 02115

Invited Speaker

Single-cell (sub)type and state quantification at high resolution with uncertainty quantification

Ava Khamseh[1]

[1]Institute of Cancer & Genetics, The University of Edinburgh

Single cells are typically typed by clustering into discrete locations in reduced-dimensional transcriptome space. Stator is a data-driven method that identifies cell (sub)types and states without relying on cells' local proximity in transcriptome space. Stator labels the same single cell multiply, not just by type and subtype, but also by state such as activation, maturity or cell cycle sub-phase, through deriving higher-order gene expression dependencies from a sparse gene-by-cell expression matrix. Stator's finer resolution is clear from analyses of mouse embryonic brain, and human healthy or diseased liver.

Selected Speaker

Single-nucleus profiling of cooperative social behaviour in a reef fish

Debora Desantis[1,2], Celia Schunter[1,2*]

[1]Swire Institute of Marine Science, School of Biological Sciences, The University of Hong Kong, Pok Fu Lam, Hong Kong SAR, China, [2]State Key Laboratory of Marine Pollution, City University of Hong Kong, Hong Kong SAR, PR China

Social behaviours vary within and among species, ranging from simple interactions between individuals to more complex cooperative strategies such as mutualism, and play a fundamental role in shaping individual fitness. In vertebrates, brain functions associated with complex behaviours, including learning, memory and social interactions, are regulated in brain regions homologous to the teleost telencephalon. Therefore, given the central role of the telencephalon in modulating complex behaviours, understanding the transcriptional signatures of neuronal cell types and the neural basis underlying advanced social skills is of critical importance. In this study, we investigate, at an unprecedented single-cell resolution, the complexity of brain functions associated with cooperative behaviour in relation to the neural architecture of the coral reef fish cleaner wrasse (*Laborides dimidiatus*). Using ~65,000 nuclei isolated from adult telencephalons, we characterise the cellular landscape of *L. dimidatus* during mutualistic interaction behaviour. We identified signatures corresponding to six distinct cell type groups, including a population of cholinergic-GABAergic neurons specifically involved in the modulation of social behaviour. By combining neuroanatomically restricted a priori genes and cross-species comparison, we delineated the pallial and subpallial regional identities of mature neural clusters, supporting strong conservation of fish telencephalic cell populations. Gene expression analysis further revealed genes associated with signal transmission and axonal tiling in socially interacting fish. Overall, our work provides novel insights into the cellular organisation and composition of the teleost telencephalon, thereby advancing our understanding of the neural basis underlying cooperative social behaviour in this remarkable vertebrate species.

Selected Speaker

A pathway-centric framework for understanding VSMC diversity in ageing and disease

Alice Bradford[1]

[1]University of East Anglia

Changes to our vasculature system as we age remains a significant risk factor to the development of cardiovascular diseases, aneurysms, and other morbidities. Vascular smooth muscle cells (VSMCs) play a key role in the maintenance of blood pressure and vascular remodeling. They display substantial heterogeneity within the aortic wall, yet consistent interpretation of this diversity remains challenging. Although single-cell transcriptomics has improved resolution, variability in annotation and limited concordance across datasets hinder the definition of VSMC phenoplasticity.

We applied a pathway-level approach, focusing on the relative activity of core biological programs rather than individual genes. Curated marker sets representing contractile, extracellular matrix, and immune-associated pathways are used to quantify program activity across single-cell and bulk transcriptomic datasets. Similarity-based analyses and dimensionality reduction reveal a low-dimensional structure underlying VSMC diversity.

This framework supports a model in which VSMCs occupy a continuum defined by the dynamic weighting of functional programs. Shifts in these programs across age and disease are examined, providing a basis for distinguishing physiological adaptation from pathological remodeling, with the aim of identifying potential points for therapeutic intervention.

Selected Speaker

Comprehensive analysis of transcriptional noise in the plant root using snRNA-seq reveals cell-type specific mechanisms of variability

Connor Reynolds[1]

[1]Earlham Institute

Transcriptional noise across individual plants is believed to confer an adaptive advantage by increasing phenotypic diversity within populations. In particular, variation in stress and environmentally related gene pathways has been proposed to contribute to “bet hedging” – the concept that diversity in the expression of some critical pathways increases the likelihood that plant populations will survive extreme and unpredictable conditions.

Although previous works have explored cross-individual transcriptional noise using bulked seedling RNA-seq, little is known about how this noise is exhibited across different cell-types specifically in the root. To address this, we generated high-depth (200,000 reads per nuclei) snRNA-seq data across hundreds of pooled plant roots, yielding over 25,000 high-quality nuclei.

Using the Bayesian models BASiCS and Baynorm, we identified highly-variable genes (HVGs) and lowly-variable-genes (LVGs) across 16 distinct cell-types of the root. These genes were used to infer biological pathways and gene characteristics associated with transcriptional noise and stability throughout the root. Furthermore, we implemented an AI-driven approach to highlight potential genomic sites associated with transcriptional noise in the root using genomics large language models.

Invited Speaker

Epigenetic Adaptation Shapes Dormancy and Reveals Vulnerabilities in ER+ Breast Cancer

Dalia Rosano[1], Cynthia Lau[1], Solene Pezot[1], Adrián Martínez Tebar[1], Ziqing Xue[1], Roberto Rota[2] , Alberto Parasporo[1], Anya Nicholas[1], Marta Milan[1], Archana Thankamony[2], Bobby Bojovic[3], Paolo Piazza[3], Marco Bezzi[2], Cathrin Brisken[1,4], Luca Magnani[1]

[1]Division of Breast Cancer Research, The Institute of Cancer Research, London, UK, [2]Division of Cancer Biology, The Institute of Cancer Research, London, UK, [3] Centre for Human Genetics, University of Oxford, UK, [4]Swiss Federal Institute of Technology Lausanne.

Oestrogen receptor–positive breast cancer (ER+ BC) is the most common BC subtype, yet late relapse after adjuvant endocrine therapy (ET) remains a major barrier to cure. Relapse is thought to arise from residual tumour cells that survive therapy in a dormant state before reawakening years later. Defining how dormant cells persist and acquire vulnerabilities is critical to preventing recurrence.

Using lineage tracing integrated with multi-omic profiling, we showed that ET drives transition into dormancy, accompanied by extensive transcriptional and epigenetic reprogramming. Individual lineages can later reawaken with divergent phenotypes through epigenetic remodelling rather than recurrent genetic alterations.

We next translated these findings in vivo using the MIND orthotopic ER+ BC mouse model in which barcoded tumour cells are injected into mammary ducts. We showed that ET restrained tumour proliferation and dissemination, recapitulating key features of dormancy. Dormant lesions showed reduced ER expression, while spatially resolved lineage tracing revealed that ET reshapes clonal architecture, with divergent clonal selection across mammary glands.

Establishment of a repressive epigenetic state was required for survival under ET in vitro and inhibition of G9a and EZH2, impaired dormant-cell survival. Short-term inhibition at dormancy entry was as effective as prolonged treatment, suggesting that transient epigenetic intervention may block acquisition of the dormant state. We are now testing whether temporally targeted epigenetic therapy can eliminate dormant cells in vivo.

Together, these data identify ET-induced dormancy as an adaptive cell state governed by epigenetic reprogramming and highlight chromatin regulators as actionable vulnerabilities to prevent late relapse.

Keynote speaker

Methods of Integrating GWAS and single cell data

Ang Li[1]

[1]University of Oxford (Honorary Fellow at Institute for Molecular Bioscience, the University of Queensland

Genome-wide association studies (GWAS) have discovered numerous trait-associated variants, but their biological context remains unclear. Integrating GWAS summary statistics with single-cell RNA-sequencing expression profiles can help identify the cell types in which these variants influence traits. I will firstly present methods integrating these two datasets to help identifying the cell types in which genetic risk is most likely to act. The results highlight practical lessons for the field: robust interpretation depends on GWAS power, atlas breadth, appropriate cell-type specificity metrics, and careful control of false positives. For the 2nd part, I will then show how these principles can be applied to psychiatric genetics, where single-cell expression and chromatin accessibility implicate neuronal populations and early developmental stages in psychiatric disease risk. Together, these studies show how integration of GWAS with single-cell data can move from statistical association toward testable biological and clinical insight.

Poster

Clonal tracking of haematopoietic stem cells reveals lineage contributions to innate immune populations across tissues

Caoimhe Dwan[1]

[1]Earlham Institute

Understanding how individual haematopoietic stem cells (HSCs) contribute to blood and tissue-resident populations remains a central challenge in stem cell biology. While single-cell transcriptional approaches describe cellular states, complementary strategies are required to define lineage relationships and clonal dynamics in vivo.

Here, we apply lentiviral cellular barcoding to uniquely label murine HSCs prior to transplantation, enabling high-resolution tracking of clonal output across time, anatomical sites, and environmental changes. By combining transplantation models with downstream recovery of barcodes from defined populations, we aim to quantify how individual stem cell clones contribute to diverse innate immune lineages in the circulation and within peripheral tissues.

This framework allows us to examine heterogeneity in stem cell behaviour, evaluate lineage bias, and determine how challenges reshape clonal architecture. More broadly, the approach provides a flexible platform to integrate lineage tracing with phenotypic and molecular single-cell readouts.

Together, these studies seek to bridge functional transplantation assays with emerging single-cell technologies to better understand how stem cell fate decisions are executed in vivo.

Poster

An interactive exploration of new features in morphological space: towards a morpho-transcriptomic characterisation of megekaryocytes

Sonia Fonseca[1], James Wilsenach[2], Sebastian Ahnert[2], Edyta Wojtowicz[1]

[1]Earlham Institute, Norwich, UK
[2]University of Cambridge, Cambridge, UK

Megakaryocytes are a rare and highly heterogeneous population of bone marrow cells involved in the platelet production and immune response. Their variability results from a highly complex ontogeny involving an increase in ploidy from 2N to as much as 128N, and associated changes in size and morphology.

Image Activated Cell Sorting (IACS) utilising Imaging Flow Cytometry (IFS) provides a high-throughput means of firstly recording cell morphology and consecutively isolating single cells. Therefore, it leverages transcriptomic analysis to understand the link between morphology and gene expression programs in single cells.

Here, we have developed Flow cytometry Feature Importance (FlowFI), an interactive imaging flow cytometry tool which allows users to design novel parameters based on raw images with tailored preprocessing options and customisable preferences for removing noise from high-throughput imaging flow cytometry platforms. We show that the novel parameters designed in FlowFI provide a significant improvement in sample purity (14-30% depending on the subpopulation) and provide a framework for how such parameters can be refined using in-built unsupervised manifold learning and feature analysis tools.

Finally, we explore preliminary results from a pilot transcriptomic analysis, showing potential links between image-derived morphological features and cell-specific markers. This morpho-transcriptomic strategy can help identify changes in the relative abundance of morphological cell subpopulations, as well as the emergence or loss of specific subsets in pathological states. Integrating morphological information with transcriptomic analysis may also facilitate the discovery of new biomarkers and enable more targeted, morphology-guided cell isolation, thereby substantially reducing the cost of genomic analyses.

Poster

Single-nucleus profiling reveals replication-coupled epigenome remodelling across ploidy states

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Single-cell profiling provides a powerful framework to resolve how chromatin state is maintained during DNA replication across heterogeneous cell populations. However, how replication-associated processes shape epigenomic landscapes across cell types *in vivo* remains poorly understood.

Here, we use single-nucleus methylome–transcriptome profiling across ploidy states (2C to 6C) to dissect the impact of repeated DNA replication on chromatin state during development. We find that increasing ploidy drives a progressive reduction in DNA methylation, consistent with delayed and incomplete maintenance following DNA replication. Notably, we observe a transient reduction in methylation in S-phase cells, indicating that maintenance lags behind DNA replication *in vivo* rather than occurring synchronously at the replication fork.

Superimposed on this global effect, we identify coordinated, gene-level methylation changes that track with transcriptional specialization, revealing a second, actively regulated layer of chromatin remodeling linked to cell function.

Strikingly, specific lineages violate these dynamics. Phloem companion cells exhibit a near-complete failure to remethylate following replication, resulting in persistent global hemimethylation and revealing intrinsic constraints on maintenance in defined cellular contexts.

Together, our results establish how single-cell resolution enables dissection of replication-associated epigenome remodeling across diverse cell types, providing a framework for understanding chromatin state dynamics during development.

Poster

Role of the microbiome in shaping chemosensory organ development and homeostasis in mice

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Fitness and survival of an animal heavily rely on sensing the chemical landscape of its surroundings. Most mammals process chemosensory information using sensory neurons present in main olfactory epithelium (MOE), dedicated to sensing air-borne odours, and vomeronasal organ (VNO), specialised for sensing soluble pheromones. Both the MOE and VNO are exposed to the environment to allow the detection of chemical cues and consequently come in direct contact with the microbial communities that colonise the nasal passage. Clinical studies have shown that olfactory defects are associated with altered microbial diversity and relative proportions of specific bacteria in the nasal cavity. Similarly, germ free (GF) mice show altered olfactory responses compared to specific pathogen free (SPF) mice. **However, the molecular basis of how the microbiome affects olfactory capacity is unclear.**

We performed spatial transcriptomics of the MOE and VNO from adult GF and SPF mice, to investigate how presence of a microbiome affects the transcriptional landscape of the specialised cell types of the host's chemosensory organs. Interestingly, specific populations were impacted in the MOE, highlighting the essential role of the microbiome in the fate of olfactory cells. This study will enhance our understanding of the interactions between the microbiome and host cells, and address whether the microbiome influences the development of chemosensory organs or is restricted to a maintenance role.

Poster

Ploidy analysis of Megakaryocyte using single cell RNA-Seq

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Megakaryocyte is a type of blood cell that undergoes endoreduplication or endomitosis that leads to increased ploidy up to 128n. It is suspected that different ploidy levels may be associated with different cell functions, however without solid proof. Megakaryocytes were sorted using the image-based sorter BD FACSDiscover S8, then were manually labelled with ploidy information using cell imaging and morphological features. The cells were processed according to the G&T-Seq protocol. RNA-Seq reads were aligned using Kallisto and QC using Seurat. From both single cell and pseudo-bulking differential gene analysis, we discovered a set of genes that could be associated with cell ploidy.

Poster

Full-spectrum pipelines for single-cell and spatial transcriptomics analysis

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This poster presents two full-spectrum pipelines we developed at the Earlham Institute: EISCA pipeline for scRNA-seq data analysis, and EISTA pipeline for spatial transcriptomics data analysis. Both pipelines cover all phases of analysis from primary and secondary to tertiary. They are built on the Nextflow nf-core framework aiming to provide generalized, flexible, and scalable workflows.

EISCA (github.com/ EarlhamInst/eisca) is designed for droplet-based (10x) and plate-based (Smart-seq2) data. Its analysis stages include quality control, alignment, quantification, count conversion, cell filtering, clustering, cell-type annotation, differential expression analysis (DEA), cellular interaction. EISTA (github.com/ EarlhamInst/eista) is designed for Vizgen MERFISH data and 10x Xenium data. It includes Vizgen post-processing, count conversion, cell filtering, clustering, spatial statistical analysis, and will also support cell-type annotation, DEA and cellular interaction in the tertiary analysis phase.

The pipelines offer several key benefits. 1) They are easy to use, allowing users to launch them directly without the need to pre-download tools, and they can be run on local machines, HPC clusters, or cloud platforms. 2) They are flexible, supporting both end-to-end execution and specific analysis phases. Users can also tweak analysis to gain better insights. 3) The pipelines follow standardized practices, relying on widely used Python packages to efficiently process large data in a consistent manner. 4) They are extensible, serving as a foundation for basic analysis while allowing users to integrate task-specific analyses. As the first full-spectrum pipelines for single-cell analysis, they enable quick preliminary analyses and an out-of-the-box report, ensuring smooth data assessment and transition to advanced analyses.

Poster

Comprehensive analysis of transcriptional noise in the plant root using snRNA-seq reveals cell-type specific mechanisms of variability

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Transcriptional noise across individual plants is believed to confer an adaptive advantage by increasing phenotypic diversity within populations. In particular, variation in stress and environmentally related gene pathways has been proposed to contribute to “bet hedging” – the concept that diversity in the expression of some critical pathways increases the likelihood that plant populations will survive extreme and unpredictable conditions.

Although previous works have explored cross-individual transcriptional noise using bulked seedling RNA-seq, little is known about how this noise is exhibited across different cell-types specifically in the root. To address this, we generated high-depth (200,000 reads per nuclei) snRNA-seq data across hundreds of pooled plant roots, yielding over 25,000 high-quality nuclei.

Using the Bayesian models BASiCS and Baynorm, we identified highly-variable genes (HVGs) and lowly-variable-genes (LVGs) across 16 distinct cell-types of the root. These genes were used to infer biological pathways and gene characteristics associated with transcriptional noise and stability throughout the root. Furthermore, we implemented an AI-driven approach to highlight potential genomic sites associated with transcriptional noise in the root using genomics large language models.

Poster

A pathway-centric framework for understanding VSMC diversity in ageing and disease

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Changes to our vasculature system as we age remains a significant risk factor to the development of cardiovascular diseases, aneurysms, and other morbidities. Vascular smooth muscle cells (VSMCs) play a key role in the maintenance of blood pressure and vascular remodeling. They display substantial heterogeneity within the aortic wall, yet consistent interpretation of this diversity remains challenging. Although single-cell transcriptomics has improved resolution, variability in annotation and limited concordance across datasets hinder the definition of VSMC phenoplasticity.

We applied a pathway-level approach, focusing on the relative activity of core biological programs rather than individual genes. Curated marker sets representing contractile, extracellular matrix, and immune-associated pathways are used to quantify program activity across single-cell and bulk transcriptomic datasets. Similarity-based analyses and dimensionality reduction reveal a low-dimensional structure underlying VSMC diversity.

This framework supports a model in which VSMCs occupy a continuum defined by the dynamic weighting of functional programs. Shifts in these programs across age and disease are examined, providing a basis for distinguishing physiological adaptation from pathological remodeling, with the aim of identifying potential points for therapeutic intervention.

Poster

CellCage™ Technology: a dynamic approach to single-cell functional genomics

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The relationship between gene expression and cellular function is complex: transcriptomic measurements provide static snapshots, while cellular phenotypes unfold over time. To bridge this gap, we developed CellCage™ Technology, which leverages light-guided hydrogel polymerization to enable longitudinal imaging of individual cells coupled with endpoint transcriptomics. Within this system, imaging provides unambiguous readouts of complex cellular functions linked to underlying transcriptional programs.

To characterize information-rich imaging phenotypes, we leveraged DINOv2, a self-supervised vision transformer, to extract high-dimensional morphological features with dimensionality comparable to gene expression. This combination of imaging and transcriptomics represents a novel paired datatype that reveals biological insights inaccessible to transcriptomics alone.

In drug-treated lung cancer cells, longitudinal monitoring identified a stochastic, non-mutational resistant state associated with potassium channel overexpression and p53-mediated quiescence. In preadipocytes and microglia, paired data uncovered functional driver genes that transcriptomic clustering alone failed to identify.

Poster

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Mathias Van Bulck[1]

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Poster

Comprehensive Single Cell Transcriptome Profiling of FFPE Samples via GEXSCOPE® FFPE Single Nucleus Sequencing

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Background

Formalin-fixed paraffin-embedded (FFPE) processing enables long-term archiving of oncology tissue samples, resulting in an estimated >400 million stored cancer specimens worldwide. Despite this extensive resource, single-nucleus RNA sequencing (snRNA-seq) for FFPE material remains difficult because RNA is often highly fragmented and chemically modified. Current commercial probe-hybridisation–based workflows rely on predefined gene panels, lacking flexibility for broader transcriptome discovery, including non-coding RNAs (ncRNA) and alternative splicing.

Methods

We present a single-nucleus analysis workflow for comprehensive RNA analysis. It utilises random primers for reverse transcription (RT) to capture both mRNA and ncRNA species. Following RT, unique tag sequences are added to the cDNA, which are then captured by barcoding beads. This approach enables 5’ to 3’ coverage of the gene body, allowing for the analysis of the whole transcriptome.

Results

The platform generated high-quality data across diverse human and murine tissues, including lung, liver, bladder, brain, and stomach. Results demonstrated high median gene detection per cell and consistent cell-type composition across biological replicates. The method achieved full gene body coverage and successfully identified various ncRNA species, including microRNAs and long non-coding RNAs. We also showed the ability to detect alternative splicing in specific transcripts, such as CD44. The workflow maintained robust gene detection in human FFPE samples with low DV200 scores and high RNA degradation.

Conclusions

The FFPE single nuclei analysis workflow provides a comprehensive solution for the detection of non-coding RNA and alternative splicing from archived clinical material. This approach supports deeper molecular characterisation in oncology research and facilitates the use of banked FFPE tissues for biomarker discovery or mechanistic analysis for precision medicine.

Poster

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