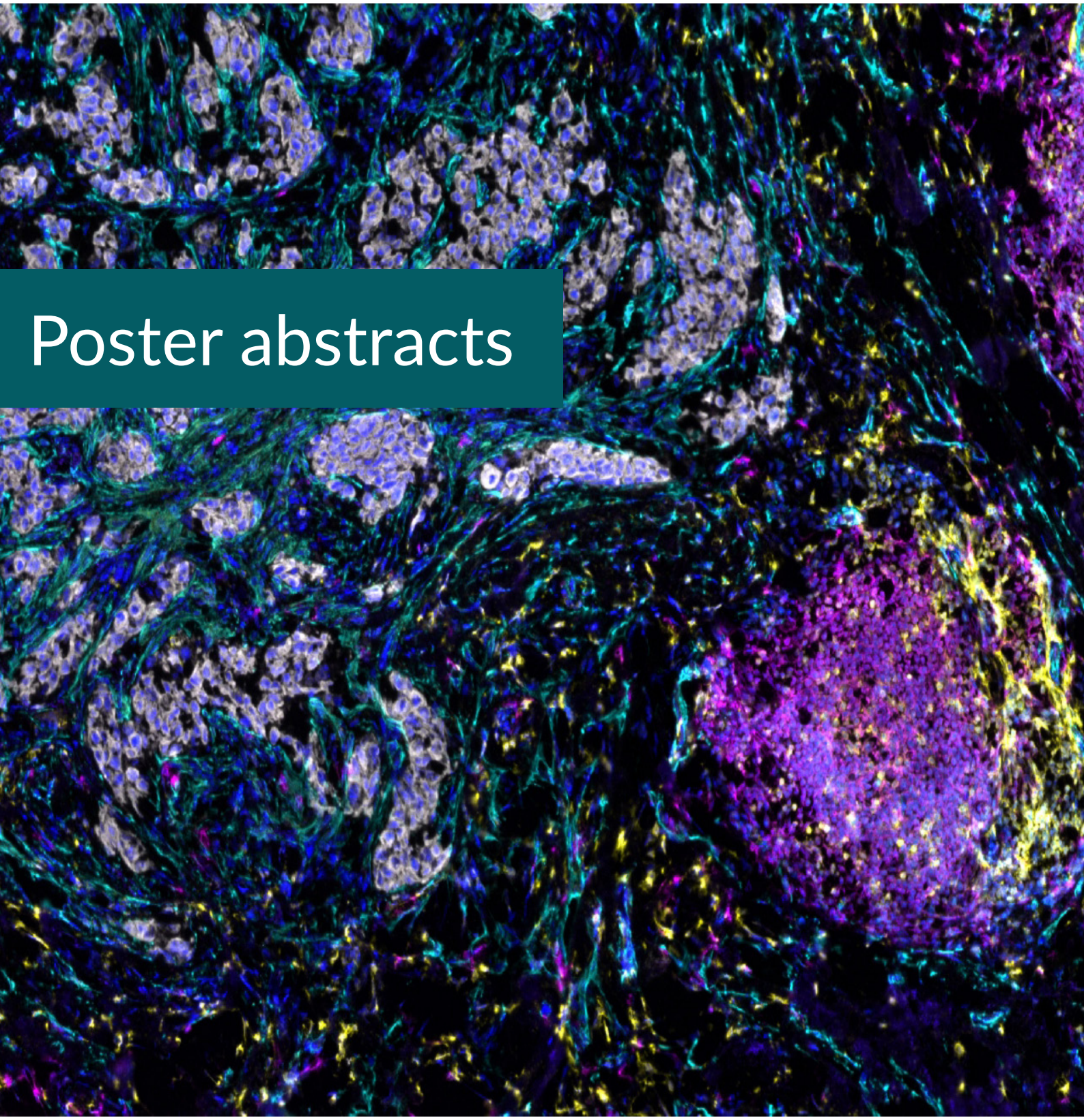
Cancer Research: Translating Life Science Discoveries to Clinical Breakthroughs

SciLifeLab Science Summit 2026



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SciLifeLab

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1. The Emerging Role of Steroidogenic Mast Cells in Lung Metastasis and T Cell Immunity

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Mast cells are important regulators of the tumor microenvironment, yet the mechanisms by which they influence anti-tumor immunity remain poorly understood. Cytochrome P450 family 11 subfamily A member 1 (Cyp11a1), a key enzyme in steroidogenesis, is highly expressed in mast cells and may contribute to immune suppression during tumor progression. To investigate its role, we generated mast cell-specific Cyp11a1-deficient mice and evaluated tumor growth and metastatic dissemination in experimental cancer models. Loss of Cyp11a1 in mast cells significantly reduced pulmonary metastatic burden and was associated with enhanced anti-tumor immune responses. Tumors from deficient mice exhibited increased infiltration and activation of $CD8^+$ T cells together with elevated production of effector cytokines, including IFN-γ. These findings indicate that mast cell-derived Cyp11a1 suppresses protective T cell immunity and promotes metastatic progression. Targeting the Cyp11a1 pathway in mast cells may therefore represent a promising therapeutic strategy to enhance anti-tumor immunity and limit cancer metastasis.

Mast Cells, Cyp11a1, Tumour Metastasis, T Cell Immunity, Cancer Immunotherapy

2. State-dependent interactions between cancer-associated fibroblasts and the immune microenvironment in mucosal head and neck squamous cell carcinoma: a systematic review.

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Background: Cancer-associated fibroblasts (CAFs) shape the tumor immune microenvironment of mucosal head and neck squamous cell carcinoma (HNSCC). CAF-immune interactions may influence responses to immunotherapy in a state-dependent manner.

Methods: PubMed and Scopus were searched on 11 September 2026 for English language original studies published from 2021 onward. Eligible studies investigated invasive mucosal HNSCC, defined a defensible CAF population, and reported CAF-immune interactions.

Results: Fourteen studies were included. Immunosuppressive programs, as well as immunostimulatory-associated states were identified. Immunosuppressive states involved regulatory T-cell induction or recruitment, CD8+ T-cell dysfunction, and myeloid-cell reprogramming. Selected states were associated with dendritic cell recruitment, cytotoxic lymphocyte-rich niches, or tertiary lymphoid structures. Macrophage-to-myofibroblast

transition (MMT) further highlighted the diverse cellular origins and functional states of immunosuppressive CAF-like cells.

Conclusions: CAF-immune interactions are predominantly immunosuppressive but vary across fibroblast states and multicellular niches. State-specific CAF programs require further prospective validation before clinical translation.

Cancer-associated fibroblasts; head and neck squamous cell carcinoma; tumor immune microenvironment; immune evasion; systematic review

3. Constraint-based non-coding mutation profiling identifies targets in glioblastoma

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Glioblastoma (GB) is a lethal, heterogeneous brain tumour needing improved molecular stratification. We integrated Zoonomia evolutionary constraint scores with matched tumour–normal whole-genome sequencing from 136 GB patients. Non-coding constraint mutations (NCCMs) with regulatory potential clustered as hotspots in PTEN, LRFN5 and MIR99AHG, and were enriched at transcription factor loci including FOXA1, HOXA and, most strongly, DLX5/6, which showed increased expression. The top 10% of candidate genes were significantly overrepresented for COSMIC Cancer Gene Census genes, yet had lower coding mutation rates, indicating our approach identifies candidates not captured by conventional analyses. NCCMs in SEM1 were associated with significantly poorer survival. Sequencing of 63 corresponding patient-derived cell lines showed high mutational concordance with the tumours, providing a robust experimentally tractable platform for functional validation. We conclude that since evolutionary constraint is agnostic to cell type and disease stage, it is a powerful predictor of function and a route to improved patient stratification.

glioblastoma, non coding constraint mutation (NCCM), genomics, cancer

4. Immunostimulatory gene therapy targeting CD40, 4-1BBL and PD-L1 reactivates T cell immunity

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Immunotherapy harnesses the immune system to recognize and eliminate cancer cells. However, immune activation can induce PD-L1 expression on tumor cells, promoting immune suppression and limiting antitumor responses. To overcome this, we developed Ad825, a novel adenoviral vector combining the immune-stimulatory transgenes TMZ-CD40L and 4-1BBL with a PD-L1-targeting Affibody molecule for localized delivery within the tumor microenvironment (TME). We evaluated transgene expression following Ad825 infection of cancer cells, assessed the functionality of the Affibody molecule using a luciferase assay, and investigated immune activation in a cancer/immune cell co-culture model. Ad825 mediated expression of all three transgenes, and the secreted Affibody effectively blocked PD-1/PD-L1 signaling. Furthermore, Ad825 enhanced dendritic cell maturation and promoted differentiation of T cells toward a central memory phenotype. Ad825-induced immune activation also significantly increased IFN-γ secretion, indicating sustained antitumor immune activity. These findings support the potential of Ad825 to elicit durable antitumor immune responses.

Immunotherapy, TME gene engineering, PD-L1 , Adenoviral therapy

5. SciLifeLab Clinical Genomics

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The Clinical Genomics platform supports development, validation and implementation of new high-throughput technologies for clinical and translational research projects, clinical trials and diagnostics within healthcare. Key technologies include next generation sequencing, single cell analysis and ultrasensitive variant detection. The aim of the Clinical Genomics platform is to facilitate the translation of new high-throughput technologies into clinical use. We provide technological, bioinformatic and medical expertise, along with access to clinical validation cohorts, to enable a unique end-to-end service.

6. The SciLifeLab CRISPR Functional Genomics unit

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Anneke Navis, Soniya Dhanjal, Olga Khorosjutina, Mubasher Mohammed, Hirofumi Noguchi, Miriam Selle, Bernhard Schmierer. CRISPR Functional Genomics - a SciLifeLab national infrastructure and Karolinska Institutet core facility, department of Medical Biochemistry and Biophysics, Karolinska Institutet.

CRISPR-Cas systems enable a wide range of molecular biology applications, including gene knockout, precise nucleotide alterations, and transcriptional modulation. At CRISPR Functional Genomics (CFG), we specialize in CRISPR-Cas technologies, and it is our mission to facilitate and accelerate research by offering flexible, cost-effective precision gene editing and high-throughput perturbation screening in user-defined cell lines.

CRISPR-Cas, gene editing, high-throughput perturbation screening

7. Poster withdrawn

8. Advancing precision medicine: humanized zebrafish models for accuracy and accelerating nanobody-based cancer therapies

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Selecting the most effective cancer treatment for an individual patient remains a major clinical challenge, potentially resulting in delayed effective therapy, unnecessary toxicity, and compromised clinical outcomes. Our laboratory uses zebrafish patient-derived tumor xenografts (zPDXs) to model tumor progression and predict treatment response. However, limited cross-species compatibility between zebrafish ligands and human receptors on tumor cells may impair signaling pathways involved in tumor growth and metastasis, potentially reducing the model's predictive accuracy. To address this limitation, I am developing humanized zebrafish models by introducing human ligands through CRISPR-Cas9-mediated genome engineering. Targeted knock-in under endogenous promoter control enables physiologically relevant ligand expression within the tumor microenvironment. As part of the EU-funded ALADDIN (Accelerated Discovery Nanobody Platform) initiative, I established a humanized zPDX platform expressing human FGF19 to evaluate nanobodies targeting its receptor, FGFR4. This platform provides a relevant, cost-effective preclinical system for drug screening and personalized therapy selection, advancing precision oncology.

precision oncology, therapeutic nanobodies, humanized zebrafish, patient-derived tumor xenograft (zPDX), CRISPR-Cas9 genome engineering.

9. High-throughput pipeline for the zebrafish embryonic cancer xenotransplantation

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Cancer modeling in the zebrafish system is increasingly used by researchers and biotechnology companies to accelerate drug discovery and personalize cancer treatment. The zebrafish embryo enables xenotransplantation studies with phenotypic evaluation of tumor growth, micrometastasis, blood vessel infiltration, and interactions between cancer cells and host macrophages. However, this rapidly developing field lacks standardized protocols for image acquisition and quantitative analysis, making it difficult to compare and evaluate results across studies.

Zebrafish xenotransplantation, Cancer modeling, High-throughput imaging, Drug discovery

10. Unlocking Functional Epigenomics from Archived Clinical Samples

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Epigenovo is developing a technology platform that unlocks functional epigenomic profiling from formalin-fixed paraffin-embedded (FFPE) specimens. FFPE archives contain millions of clinically annotated samples, but formalin fixation and paraffin embedding have traditionally limited comprehensive epigenetic analysis.

Epigenovo's technologies — FFPE-ATAC, scFFPE-ATAC, FACT-seq and scFACT-seq — enable genome-wide and single-cell profiling of chromatin accessibility and histone modifications from archived FFPE samples. Together, they transform routine pathology archives into a rich source of functional epigenetic information.

By enabling retrospective and single-cell epigenomic analysis of clinically annotated specimens, Epigenovo opens new opportunities for disease research, epigenetic biomarker discovery and precision medicine, while establishing a foundation for scalable functional epigenomics using routinely collected clinical material.

epigenetics, retrospective studies, FFPE-samples, single-cell, FFPE-ATAC

11. Using Non-Coding Constraint Mutations to find Novel Candidate Genes in Medulloblastoma: The story of FGR

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Medulloblastoma (MB) is the most common malignant pediatric tumor, with different subtypes and outcomes, requiring more efficient treatments. To uncover functionally important disease-associated mutations, we leverage evolutionary conservation scores across mammalian genomes with non-coding MB mutations. These mutations are termed Non-Coding Constraint Mutations (NCCMs). Whole-genome sequencing of 146 MB cases identified 114 genes enriched for NCCMs, among them FGR. FGR is a src-family tyrosine-kinase, normally involved in cell-growth regulation, innate-immunity and inflammation. Overexpression has been reported in e.g. leukemia, but not in brain tumors. CRISPR/Cas9 introduction of a FGR NCCM increased Dasatinib sensitivity (a src-kinase inhibitor), while FGR knockout reduced MB cell growth and tumor burden in zebrafish in vivo. FGR thus emerges as a promising biomarker and therapeutic target in MB.

Brain Tumors, Non-Coding Constraint Mutations, FGR, Medulloblastoma

12. FEGA Sweden – Repository for sharing Swedish biomedical research data

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Human genomic and phenotypic data are essential for biomedical research, but strict privacy regulations like GDPR limit how sensitive human data can be shared. FEGA Sweden solves this challenge by serving as the Swedish national node within the Federated European Genome-phenome Archive.

Operated by NBIS at SciLifeLab, FEGA Sweden provides a secure platform for the permanent deposit and controlled-access sharing of human biomedical data generated in Sweden. Data remains safely stored within national borders while managed Data Access Committees (DACs) ensure access is granted only to approved researchers. By issuing unique accession numbers, FEGA Sweden enables researchers—including those at Uppsala University—to fulfill scientific journal requirements and FAIR data standards without compromising participant privacy or legal compliance.

FAIR, respository, human data, FEGA Sweden, GDPR compliance

13. Studying cancer at the atomic level - case studies from the ISB platform

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A couple of case studies will be presented on what NMR and Mass spectrometry can contribute to the detailed understanding of cancer at atomic level. Studying prostate cancer using HR-MAS NMR on tissue samples is yet another case study presented.

NMR, Mass spectrometry, prostate cancer, metabolomics

14. Investigating HER2/HER3 activation as a predictor of response to neoadjuvant trastuzumab/pertuzumab in HER2+ breast cancer

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Although HER2-signaling is associated with aggressive clinical behavior, it can be targeted by next-generation antibody-drug conjugates. Our aim was to determine if functional measurement of HER2/HER3 activity by proximity ligation assay (PLA) is more sensitive than routine immunohistochemistry (IHC) in discriminating finer variations at the lower end of the HER2 expression spectrum, and establish a panel for measuring spatial HER2/HER3 activity and downstream signaling in the context of tumor cell proliferation and activation of the IL-6/JAK/STAT3 pathway.

Breast cancer, HER2, biomarker, PLA, spatial biology

15. Interplay Between Recycling Machinery and Growth Factor Signaling Shapes Extracellular Vesicle Release in Tumor Cells

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Extracellular vesicles (EVs) are key mediators of tumor communication. However, the impact of endosomal trafficking regulation on EV biogenesis remains poorly understood. Here, we investigated how TGF-β signaling and ErbB3-driven trafficking converge on RAB4-dependent endosomal recycling to control EV secretion in tumor cells. TGF-β upregulated endosomal regulators including ALIX, CD81, ARF6, and RAB4A in a cell type-specific manner. RAB4A acted as a negative regulator of EV secretion: its silencing enhanced multivesicular body fusion with the plasma membrane and increased EV release, whereas TGF-β-induced RAB4A expression restricted this process. TGF-β also promoted ALIX palmitoylation and ALIX-TSG101 complex formation. Consistently, ErbB3 directed Integrin β1 recycling through RAB4-positive endosomes. Additionally, loss of ErbB3 impaired recycling, redirected cargo toward degradation and EV incorporation, and increased secretion of Integrin β1-enriched EVs that enhanced recipient-cell motility. Together, our findings identify RAB4-dependent endosomal recycling as a central regulator of EV biogenesis and cancer cell communication.

TGF-beta, Erbb3, Extracellular Vesicles, Endosomes

16. A Comprehensive HNK-1 Neural Crest Migration Atlas in Chick Embryos for Neuroblastoma Research

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Background & Aim: Neuroblastoma originates from neural crest cells, making accurate developmental maps essential to study oncogenic arrest. We aim to build a continuous anatomical atlas of neural crest cell migration in chick embryos across early Hamburger-Hamilton stages through late gestation (HH7–HH25, E1–E15) as a standardized reference for disease modeling.
Methods: Harvested whole embryos fixed in 4% PFA and dissected trunk regions are processed across three scales:
(1) Thin cryosections (8–20 µm) for high-resolution 2D mapping,
(2) Intermediate tissue slices (200–500 µm) to preserve local anatomical structures
(3) Cleared whole embryos for intact 3D light-sheet fluorescence microscopy.
Significance: By connecting cellular 2D details with whole-embryo 3D architecture, this reference atlas provides a practical baseline to track neural crest migration, differentiation and neuroblastoma initiation.

neuroblastoma, neural crest migration, chick embryo, embryonic development

17. Targeting Therapy-Resistant SOX9-Positive Cells with a Cytotoxic Gene Therapy in Glioblastoma

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Glioblastoma (GBM) is an aggressive, incurable brain tumor for which treatment resistance and recurrence remain persistent clinical challenges. SOX9 has emerged as a key regulator of therapy resistance, yet no SOX9-targeted drugs exist. Using 40 patient-derived GBM cell lines, we show that SOX9 is selectively activated in resistant lines following cytotoxic stress, where it attenuates temozolomide-induced DNA damage by binding and activating DNA damage and cell-cycle arrest targets. Elevated SOX9 correlated with poor patient survival, and CRISPR-based SOX9 depletion sensitized GBM cells to standard-of-care therapy. To exploit this vulnerability, we developed a SOX9-responsive suicide gene therapy coupling Herpes Simplex Virus Thymidine Kinase (HSV-TK) to a SOX9-inducible enhancer, enabling selective ablation of SOX9-positive cells upon ganciclovir treatment. AAV-delivered therapy extended survival in immunodeficient and immunocompetent orthotopic GBM models, synergized with radiation, and induced long-term survival and immunization via a reprogrammed tumor immune microenvironment and CD8+ anti-tumor response. This first-in-class strategy targets SOX9-driven resistance and holds promise for patients with GBM.

Glioblastoma, SOX9, Therapy resistance, Gene therapy

18. Daily microbiota dynamics in pre- and postmenopausal women using long-read 16S sequencing of dried cervicovaginal fluid

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The vaginal microbiota is associated with various health conditions and is influenced by hormonal status and other host factors. We analyzed daily self-collected dried cervicovaginal fluid samples from 25 women (13 premenopausal, 12 postmenopausal) over one menstrual cycle or 28 consecutive days using full-length 16S rRNA gene sequencing on the PacBio Revio platform. While several participants maintained stable community state types (CST), others exhibited substantial temporal variation, indicating interindividual differences in microbiota stability. The cohort was well-characterized with rich clinical metadata. Although our cohort was heterogeneous, our longitudinal samples reflected the clinical information and events available. For example, one participant initiated antibiotic treatment for a sore throat on day 10, resulting in a dramatic decline in vaginal Streptococcus agalactiae, which dominated the microbiota during days 1-9. These descriptive findings demonstrate the value of high-resolution longitudinal self-sampling for characterizing vaginal microbiota dynamics and identifying microbiota features associated with reproductive aging.

full-length 16S rRNA gene sequencing, vaginal microbiota, dried cervicovaginal fluid, longitudinal self-sampling, menopause

19. Studies of the crosstalk mechanisms between growth-inhibitory vitamin D3 signaling and tumor-promoting growth factors

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Calcitriol (1α,25-dihydroxy-vitamin D3), the active form of vitamin D3, regulates gene expression through VDR and RXR and can suppress cancer cell proliferation. This project aimed to identify cell lines suitable for studying crosstalk between calcitriol and growth factors in further proteomics studies. Western blotting and qPCR were used to investigate crosstalk mechanisms, with statistical significance evaluated using two-tailed t-tests. Calcitriol suppressed EGF-induced CyclinD1 expression in KYSE150 cells, returning it to basal levels, potentially explaining its anti-proliferative effect. Conversely, EGF synergistically increased calcitriol-induced CYP24A1 expression in HaCaT and KYSE150 cells, possibly due to increased VDR levels. CYP24A1 induction was reduced in serum-depleted medium, suggesting that serum components such as proteins and lipids may contribute to calcitriol uptake. KYSE150 and HaCaT cells are suitable models for studying calcitriol–growth factor crosstalk, but culture conditions require optimization to support both calcitriol and growth factor stimulation.

Calcitriol; Vitamin D receptor (VDR); Epidermal growth factor (EGF); Crosstalk; Cancer signaling

20. Mast cell tryptase induces nuclear remodelling and reduced growth in breast cancer cells

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Mast cells are frequently found in breast cancer tissue, but their role in tumor progression remains poorly understood. This study investigated the effects of mast cell-derived tryptase on breast cancer cells. The results showed that tryptase significantly altered cancer cell morphology and inhibited tumor cell growth through both reduced proliferation and increased apoptosis. Mechanistic analyses revealed that tryptase is internalized by breast cancer cells and transported into the nucleus, where it affects chromatin organization. Tryptase induced truncation of histone H3 and reduced associated epigenetic marks, indicating substantial epigenetic remodeling. In mouse and human breast tumors, tryptase-positive mast cells were associated with localized zones of reduced cancer cell proliferation. Mast cells were also found to be more activated in breast cancer tissue than in healthy breast tissue. Supporting these findings, ATAC-seq analysis demonstrated that tryptase altered chromatin accessibility in genomic regions linked to genes involved in breast cancer growth, including CCN1 and CCN2. Overall, the study identifies a novel mechanism by which mast cell tryptase suppresses breast cancer growth.

Mast cell, tryptase, breast cancer, chromatin remodelling, histone H3 truncation.

21. A Flow Cytometry-Based Assay for Quantification of DNA Double-Strand Break Repair in Primary Human T Cells

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DNA double-strand break (DSB) repair deficiencies are associated with radiosensitivity, cancer predisposition, and immunological abnormalities, but functional assessment still relies mainly on indirect measures of repair defects. We optimized a flow cytometry-based reporter assay for direct quantification of non-homologous end joining (NHEJ) and homologous recombination (HR) in activated primary human T cells.

The assay showed good reproducibility and revealed substantial inter-individual variation in NHEJ and HR among healthy controls. Pathway specificity was supported by pharmacological inhibition, with DNA-PK inhibition reducing NHEJ and ATM inhibition reducing HR. Artemis-deficient cells also showed reduced repair activity. In patient-derived T cells, an ataxia-

telangiectasia sample showed absent HR and markedly elevated NHEJ, while FANCA and PPM1D samples remained within the control reference range. These findings demonstrate the feasibility of directly quantifying pathway-specific DSB repair in primary human T cells and support further evaluation of the assay as a functional complement for investigating suspected DNA repair deficiencies

DNA damage response; DNA double-strand break repair; NHEJ; homologous recombination; functional diagnostics

22. Mapping Non-Coding Cancer Drivers in Colorectal Cancer (CRC) through Evolutionary Constraint

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Colorectal cancer (CRC) is a leading cause of cancer mortality, yet the contribution of somatic non-coding mutations remains poorly understood. We prioritized evolutionarily constrained non-coding mutations in whole genomes from 821 non-hypermutated CRC patients. Using phyloP scores from the Zoonomia 240-mammal alignment, we identified non-coding constraint mutations (NCCMs) and quantified their burden within different flanking regions of the surrounding genes. Covariate modelling identified 57 genes with greater NCCM burden than expected (FDR < 0.1), while NCCM rate-based prioritization identified 198 genes in the top 1% and hotspot analysis revealed 127 recurrent regions present in at least 10 patients. NCCM-enriched genes showed limited overlap with coding-mutated genes and were mostly differentially expressed between CRC and adjacent normal tissue. Integrating coding and non-coding alterations strengthened CRC-related pathway enrichment and functional network connectivity, while patient-level analysis revealed significant co-mutation modules. These findings uncover recurrent regulatory alterations in CRC and nominate candidates for functional validation and biomarker development.

Non coding mutations, Evoloutionary constraint, Colorecteral cancer

23. Embedded Biosensors for Localized Cytokine Detection within 3D Microtumor Models

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Conventional cell cultures and animal models incompletely reproduce the human tumor microenvironment, motivating the development of more physiological three-dimensional models. However, cytokine signalling in these systems is typically read out from the culture supernatant, where locally secreted factors are diluted and spatially averaged. Here, we engineered antibody-coated magnetic bead biosensors, that can be embedded within 3D microtumors to enable local cytokines detection. As a proof-of-concept, IFN-γ was targeted and characterized by flow cytometry and microscopy. IFN-γ was detected at 50 pg/ml in cell derived samples. In parallel, commercial multiplex beads were incorporated into heterotypic spheroids mimicking B-cell lymphoma microenvironment. After dissociation, bead-captured signals revealed composition-dependent differences for several immunomodulatory cytokines, including IL-6 and were stronger than those obtained from matched conditioned supernatants. These results provide a basis for spatially resolved tumor-immune signalling studies in 3D tumor models and organ-on-chip systems.

3d tumor models, biosensors, spheroids, cytokines

24. Establishing a Zebrafish Xenograft Platform to Study Tumour–T Cell Interactions

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Cancer immunotherapy has transformed the treatment of several solid tumours, but only a subset of patients achieve durable responses.[1] Current biomarkers, such as PD-L1 expression, provide useful information but cannot fully predict treatment outcome,[2] because response depends on dynamic tumour–immune interactions, T-cell activity, checkpoint signalling and the suppressive tumour microenvironment.[3]

My PhD project focuses on developing zebrafish patient-derived xenograft models as fast functional platforms to study immune-oncology response. By combining patient-derived tumour cells with immune checkpoint inhibitors and/or autologous immune cells in transparent zebrafish embryos, the project aims to assess tumour burden, dissemination and tumour–immune interactions in vivo within days. This approach may support more individualized treatment selection and improve the prediction of immunotherapy response.

zebrafish patient-derived xenograft (zPDX); cancer immunotherapy; immune checkpoint inhibitors; tumour–immune interactions; precision oncology; treatment response prediction

25. Detecting the Undetectable: Multiomic Liquid Biopsy and AI-Driven Imaging for Early Ovarian Cancer Diagnosis

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Ovarian cancer is often diagnosed at advanced stages, when survival is poor. Current screening approaches lack sufficient sensitivity and specificity for population-level early detection. We aim to develop a multimodal framework integrating epigenetic liquid biopsy profiling with AI-driven ultrasound imaging, using biobanked plasma samples (n≈400). In a pilot cohort spanning benign, borderline, and malignant ovarian lesions, plasma cfDNA methylation was profiled using TAPS and analysed for differential methylation. Multiplexed histone post-translational modifications, plasma RNA sequencing, and proteomics will complement methylation profiling to provide an integrated multiomic view.

Preliminary analysis identified differentially methylated regions in CpG islands distinguishing malignant from benign samples, supporting the feasibility of epigenetic liquid biopsy biomarkers. We will integrate these biomarkers with AI-validated ultrasound features to develop a scalable multimodal approach for earlier and more accurate ovarian cancer detection.

Ovarian cancer, early detection, liquid biopsy, epigenetics

26. Comparative analysis of Olink Proximity Extension Assay and Illumina SomaSeq for blood proteome profiling in childhood acute leukemia

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High-throughput proteomics is emerging as a powerful tool for improving diagnostics and disease monitoring in hematological malignancies. We recently profiled the blood proteome of childhood acute leukemia using the Olink Explore 3,072 proximity extension assay revealing immunophenotype- and subtype-specific proteins at diagnosis. Here, we applied Illumina SomaSeq Discovery, an aptamer-based platform, to the same cohort of children with acute lymphoblastic leukemia (ALL; n=54), acute myeloid leukemia (AML; n=19), and healthy controls (n=11). Across 2,423 shared proteins, overall concordance was moderate but substantially higher for proteins significant in case vs control comparisons. Both platforms identified core leukemia-associated and immunophenotype-specific proteins, including TK1(leukemia-general) and SIGLEC15 (BCP-ALL). Within BCP-ALL, molecular subtype was reflected in the blood proteome using both platforms; CCL17 and RGMA increased in ETV6::RUNX1, whereas IL-6R and S100A167 increased in High Hyperdiploid. These findings demonstrate that the strongest leukemic signals are reproducible across affinity-based platforms, while weaker signals vary substantially.

Childhood acute leukemia, High-throughput proteomics, Biomarkers, Olink PEA, SomaSeq

27. Swedish Precision medicine Initiative for Novel Treatments and Research (SPRINTR) - Creating a Study-Ready Population including Molecular Profiling of Prostate Cancer Biopsies

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Background: To implement treatment predictive biomarkers in clinical practice, high-quality studies are needed with as few extra study specific procedures as possible in the clinical workflow. Today, there is a lack of prospective observational studies including both biobanking, molecular characterization and health economy with long-term follow-up. Further the recruitment to clinical trial is often inefficient in clinical practice.
Objectives: To create a workflow and database infrastructure for multi-omics, multi-modal analysis, to facilitate re-invitation of selected men to studies/trials based on clinical and omics data, as a basis for streamlined development, evaluation and implementation of predictive biomarkers.
Methods: Integrating the informed consent procedure in the clinical workflow for all men in the diagnostic workup in a multi-center national study. Create health-care integrated solutions for pragmatic collection of clinical data. Establish functionality in this study-ready population for selected re-invitations to clinical trials. In addition, the workflow will include protocols for high-throughput genomic and transcriptomic profiling, supported by a broad ethical approval covering longitudinal follow-up and biobanking.

Results: All university hospitals in Sweden are participating, and in addition several other diagnostic units, aiming for national coverage. A national study database infrastructure is taking shape alongside a multi-professional research group. Implementation demonstrates

feasibility within standard clinical workflows. Over 90% of invited men provide informed consent, confirming strong acceptance. Biopsies from the first 150 men are being analyzed using a DNA gene panel, RNA sequencing, and digital pathology to estimate biomarker profile outcomes, logistics and data management.

Conclusions: SPRINTR-real builds a comprehensive study infrastructure for prognostic and treatment predictive biomarkers and both evaluation of health economy and quality of life. By linking biopsy-derived and clinical data to trial eligibility, it will be able to accelerate research and personalized treatment strategies by the created study-ready population. Together this initiative has the potential to speed up inclusion into prostate cancer clinical trials in Sweden, and also to be adapted to other areas of precision medicine.

prostate cancer, molecular profiling, biopsy, precision medicine, clinical trials

28. Spatial Omics

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Anja Mezger, Anna Nilsson, Charlotte Stadler, Katarina Tiklova, Chika Yokota, SciLifeLab.

The Spatial Omics Platform offers researchers cutting-edge technologies to map the spatial organization of cells and molecules within complex tissues. By integrating profiling of transcripts, proteins, lipids, glycans, and metabolites, the platform enables comprehensive multi-modal studies. It supports projects that combine multiple spatial omics methods, providing coordinated access, expert guidance, and state-of-the-art tools to advance research in tissue biology and disease.

Spatial biology; spatial transcriptomics; spatial proteomics; spatial metabolomics

29. Pan-Neurological Disease Profiling of the Human Circulating Proteome

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Neurological disorders exhibit substantial clinical and biological heterogeneity, motivating the search for molecular signatures that capture disease-associated changes across diagnostic groups. We profiled the circulating proteome of 896 patients with Alzheimer's disease (AD), Parkinson's disease (PD), frontotemporal dementia (FTD), or amyotrophic lateral sclerosis (ALS), alongside 548 healthy controls, using the Olink HT platform. Differential abundance analyses and classification models were used to characterize disease-associated protein patterns and assess their potential for distinguishing neurological conditions from controls. Across diseases, a relatively small subset of proteins provided strong classification performance, suggesting that compact plasma-protein signatures may capture aspects of disease biology. We further examined the influence of age and sex on disease-associated proteomic patterns. Findings from PD and ALS, together with selected controls, were independently evaluated using the SomaScan 11k platform. Together, these analyses provide a cross-disease view of circulating proteomic variation in neurological disease and highlight protein signatures for further investigation.

Circulating proteome, Neurological disease, Biomarkers, Proteomic signatures, Disease classification

30. Pan-cancer atlas of cellular architecture reveals a nearest-neighbor distance-associated biomechanical-immune axis involving CD4+ memory T cells

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Linglong Huang, Arne Östman, Yunfan Sun

BACKGROUND: The systematic link between cellular spatial organization and its biomechanical consequences remains a critical knowledge gap in human oncology.
OBJECTIVE: To quantitatively map the cellular architecture of solid tumors and elucidate its mechanistic impact on mechanical signaling, immune infiltration, and patient survival.
METHODS: We developed a scalable digital pathology framework, processing 7,910 H&E whole-slide images across 21 solid tumors. A deep learning pipeline was employed to segment over 4.7 billion nuclei, enabling the calculation of cell density and nearest neighbor distance (NND) as key spatial metrics. To bridge morphology and function, we integrated these metrics with bulk RNA-seq data from 19 TCGA cohorts (n=7401) using rigorous histological matching. Furthermore, to resolve microenvironmental heterogeneity, we performed unsupervised clustering of over 60,000 T-cell transcriptomes from independent cohorts. These findings were validated through high-resolution Visium-HD spatial transcriptomics to correlate physical proximity with localized gene expression.
RESULTS: While tumors exhibited significant heterogeneity, NND, but not cell density, emerged as a primary determinant of biomechanical and immune signatures. A trend-level association was observed between lower NND and higher Hippo/YAP/TAZ pathway activity across nine cancer types (Spearman's $\rho = -0.65$, $p = 0.058$, $n = 9$). Additionally, lower NND was significantly correlated with increased CD4+ memory T-cell (CD4+ TMem cell) abundance (Spearman's $\rho = -0.86$, $p < 0.01$). Single-cell analyses confirmed that CD4+ TMem cells

intrinsically express mechanical stress signaling markers, which spatial transcriptomics localized to CD4+ TMem cell aggregation zones characterized by high pathway activity. Clinically, this spatial-mechanical-CD4+ TMem cell axis was associated with prognosis in breast, esophageal, liver, and lung adenocarcinomas, where high mechanical signaling generally predicted poor outcomes but could be modulated by CD4+ TMem infiltration levels. CONCLUSION: Our study identifies low NND as a spatial correlate of biomechanical crowding that is associated with CD4+ TMem cell programming and adverse clinical outcomes. By integrating deep learning-based spatial metrics with multi-omics, we highlight spatial mechanics as a critical, potentially targetable dimension of the tumor microenvironment for future immunotherapies.

spatial analysis; nearest neighbor distance; digital pathology; tumor microenvironment; mechanical stress; Hippo pathway; CD4 memory T-cell; survival analysis; multi-omics integration.

31. Multi-omic profiling of chemotherapy-exposed blasts reveals tetraspainin remodeling and drug-specific signatures in pediatric acute lymphoblastic leukemia

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Chemotherapy has increased survival rates for pediatric acute lymphoblastic leukemia (ALL), yet toxicity and resistance remain challenging. Emerging immunotherapies still require preconditioning chemotherapy, therefore understanding its molecular impact on blasts remains critical. We applied single-cell proteomics (Proxiome, Pixelgen Technologies) and multi-omics (MultiPro, 10X Genomics) to the ALL cell-line Reh after exposure to fludarabine, cladribine, clofarabine, melphalan, and daunorubicin. We identified remodeling of the blast proteome and transcriptome, with tetraspanins (CD82, CD53) emerging as key mediators of treatment adaptation. Each drug also induced unique molecular changes, highlighting drug-specific responses in leukemic blasts. We further applied Proxiome to four ALL cases using bone marrow and peripheral blood at diagnosis and day-2 of induction chemotherapy; we

identified remodeling of tetraspanins (CD82, CD9) on the blast proteome during day-2 of induction therapy. These findings provide novel mechanistic insight into chemotherapy responses in pediatric ALL and identify tetraspainin-remodeling as a potential mediator of treatment adaptation.

Leukemia, ALL, chemotherapy, tetraspanins, Multi-omics

32. The Swedish National Genomics Infrastructure (NGI)

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The National Genomics Infrastructure (NGI), hosted by Science for Life Laboratory (SciLifeLab), is a pioneering genomics resource in Sweden (https://ngisweden.scilifelab.se). With over 25 years of experience, NGI offers high-throughput genomics services to both academic and industrial users. NGI offers a unique combination of consultative support, biospecimen processing, and expert data handling via state-of-the art data processing, quality control, and delivery. NGI provides comprehensive services for a wide-range of -omics capabilities crucial for the development and implementation of precision medicine. NGI's services span SNP genotyping, short- and long-read sequencing, single-cell analysis, spatial transcriptomics, and high-throughput proteomics assays. In addition to providing access to cutting-edge services for genomics, a major part of NGI's operation is devoted to evaluating and introducing new methods, instruments, and protocols in collaboration with researchers and companies, or through internal development. NGI also provides comprehensive scientific support to its users and education and outreach in the form of seminars, workshops, and webinars for the Swedish research community, and participates in higher education courses. NGI is a partner in many national and international collaborative projects, and is a key part of the biomolecular research and precision medicine ecosystem in Sweden.

National Genomics Infrastructure (NGI), genomics, SNP genotyping, short-read sequencing, long-read sequencing, omics

33. Scalable Multi-Omic Profiling of Drug Responses in Pediatric Acute Lymphoblastic Leukemia

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Ex vivo drug-screening coupled with single-cell RNA-sequencing reveals heterogeneous chemotherapy responses in Acute Lymphoblastic Leukemia (ALL) yet it remains costly and difficult to scale. The AVITI24 Multi-omics Platform (Element Biosciences) offers a scalable, cost-efficient approach for simultaneous profiling of 372 RNAs, 50 proteins, and cellular morphology at single-cell resolution. We profiled the pre-B ALL cell line Reh after exposure to cladribine, fludarabine, melphalan, clofarabine, and DMSO (control) using the AVITI24 Platform. Bioinformatics analysis was performed using a Seurat-based integration pipeline, combining transcriptomic, proteomic, and morphological features. All drugs induced significant morphological and cell-cycle alterations; fludarabine and clofarabine increased cellular area by 29 μm^2 and enriched S-phase cells, whereas melphalan increased G1-phase populations. Transcriptomic and proteomic analyses revealed both drug-specific and shared responses, including concordant upregulation of CD45, IFNG, and CD279. These findings demonstrate the potential of the AVITI24 Platform for scalable, single-cell multi-omic drug screening in acute leukemia research.

Drug screening, Multi-omics, Acute lymphoblastic leukemia, Chemotherapy

34. Bioinformatic Platform

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NBIS (National Bioinformatics Infrastructure Sweden) is a distributed research infrastructure serving as the SciLifeLab bioinformatics platform and the Swedish Elixir node. With over 100 staff across six university sites, we provide comprehensive bioinformatics support, infrastructure, and training to the life science community.

Supported by the Swedish Research Council, SciLifeLab, the Knut and Alice Wallenberg Foundation, and Swedish universities, we offer expertise in omics analysis, genome assembly, biostatistics, image analysis, and data management. NBIS also hosts the Swedish node in the European Genome-phenome Archive.

Our core services include:
Consultations: Weekly online drop-ins and free study design meetings.

Project Support: Short-term assistance, long-term engagement, and extensive peer-reviewed project support.
Infrastructure: Tools, data management, and systems development.
Education: Introductory to advanced training events and a dedicated PhD mentorship program.

Bioinformatics

35. Mast Cell Density is Associated with Opposing Survival Outcomes in Lung Adenocarcinoma and Squamous Cell Carcinoma: Potential Crosstalk with M2-like Macrophages*

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Mast cells (MC) exhibit anti- and pro-tumor roles in different cancers, but their role in non-small cell lung cancer (NSCLC) remains unknown. Using multiplexed fluorescence imaging on microarrays from 294 NSCLC patients, we identified three MC subtypes: Tryptase+ (MCT), tryptase+/chymase+ (MCTC), and a non-canonical chymase+/tryptase- population (MCC). MCT predominated in the stroma of adenocarcinoma (AC) and squamous cell carcinoma (SqCC), while MCC were enriched within tumors, particularly in SqCC. MC density correlated strongly with M2-like macrophage density in both histologies. In AC, MC density was positively associated with dendritic cells, NK-, and NKT-cells, whereas in SqCC it was negatively associated with B-cells, CD4+- and CD8+-cells, reflecting distinct immune contexts. Single-cell gene expression revealed distinct MC-macrophage crosstalk: pro-tumor signalling (SPP1, MIF) in SqCC. In contrast, AC exhibited less immunosuppressive, ECM-associated interactions. Higher MC density predicted better prognosis in AC but worse prognosis in SqCC, underscoring context-dependent MC functions in NSCLC.

Mast cells, macrophages, multiplex, lung adenocarcinoma, lung squamous cell carcinoma

36. Targeting cancer-intrinsic neddylation activates cGAS/STING and overcomes acquired resistance to PD-1 blockade†

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* Selected talk, presented on stage at end of session 1
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Loss of interferon signaling or antigen presentation can drive resistance to PD-1 blockade. Using a melanoma cell line derived from a patient that acquired resistance to pembrolizumab due to a JAK2 loss-of-function mutation, we reveal that targeting neddylation can restore sensitivity to therapy.

Genetic deletion or pharmacological inhibition of the neddylation E1 enzyme increase cGAS expression and the immunogenicity of human cancer cells. In tumor-bearing mice, deletion of Jak1, Jak2 and/or B2m in cancer cells confer resistance to PD-1 blockade. Neddylation deficiency restores the response by promoting NK and dendritic cell infiltration, and polarizing macrophage towards a pro-inflammatory state. Depletion of macrophages or NK cells, as well as Cgas genetic deletion, abrogate the superior response seen in neddylation-deficient tumors.

Given the challenges of developing cGAS/STING agonists, targeting cancer-intrinsic neddylation offers an attractive alternative. Our current work focuses on developing new therapeutic strategies to target neddylation.

Immune Checkpoint Blockade, cGAS/STING, Innate Immunity, Interferon, Neddylation

37. Optimizing a SNIPR gene circuit to target metastatic tumors

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While seven CAR-T cell products are currently FDA/EMA-approved for hematological cancers, the clinical translation of CAR-T cells against solid tumors has been limited by severe treatment-related toxicities resulting from target expression in healthy tissues.

To prevent on-target, off-tumor toxicity, we generated an orthogonal gene circuit that restricts CAR expression to the tumor microenvironment, thereby sparing target-positive healthy

tissues. In our system, CAR expression is only activated when engineered T cells recognize the tumor-vascular antigen CD93 via a synthetic SNIPR receptor.

We optimized viral delivery of the gene circuit from a two- to a single-vector design to increase the efficiency of therapeutic cell production. Our resulting gene circuit has been integrated into primary human and mouse T cells and demonstrates sensitivity to CD93 antigen levels. Furthermore, we reveal that the complementarity-determining regions of the antigen binder (scFv) influence basal circuit activity, while cell-type and cell-state determine the magnitude of gene induction.

CAR-T, gene circuit, metastatic tumors, synthetic immunology

38. Targeted protein degradation reveals a cryptic NUDT5–PPAT axis governing nucleoside analog drug efficacy

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Nucleoside analog (NA) chemotherapies exploit the nucleotide requirements of proliferating cancer cells, yet the molecular determinants of NA efficacy remain poorly defined. Genome-wide screens identified the Nudix hydrolase NUDT5 as a potential enabler of thiopurine efficacy. Using targeted protein degradation (TPD), we identify a non-enzymatic NUDT5 scaffolding function governing sensitivity to NA drugs. From inhibitor-derived degraders, we developed DDD2, a potent, selective, VHL-dependent NUDT5 PROTAC, using a cell-based platform coupling a modular degradation reporter with E3 ligase engagement assays. DDD2 or NUDT5 RNAi—but not potent inhibitors—confer resistance to most NA drugs proportional to NUDT5 depletion. Mechanistically, NUDT5 loss locks purine metabolism into de novo synthesis (DNPB) via loss of interaction with phosphoribosyl amidotransferase (PPAT), the pathway's committal enzyme, misallocating phosphoribosyl pyrophosphate (PRPP) and constraining salvage flux. NUDT5-PPAT complex formation is driven by salvageable nucleotide precursors and NA drugs, establishing this axis as a key determinant of global NA drug responses.

targeted protein degradation, NUDT5, nucleoside analog drugs, metabolism

39. Customized Microfluidics: From your idea to a microchip

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Microfluidic devices are a powerful tool in cancer research enabling cancer cell behavior to be studied within tissue microenvironments in vitro. These systems offer a complementary approach to animal models, providing human-relevant experimental platforms for controlled and scalable screening. However, addressing specific research questions often requires tailor-made device designs that capture the relevant biological features and experimental conditions. Developing such devices remains challenging for many research groups as it requires access to clean room research infrastructure, and expertise in microfabrication and materials sciences. Customized Microfluidics aims to address this gap by offering a unique service with advice on design and use of microfluidic solutions to researchers in the life sciences that want to introduce new methods in their research. The facility, supported by SciLifeLab, provides full

support from scientific discussion on suitable approaches and assays to design and fabrication, as well as end-user training in our dedicated test bed.

microfluidics; organ-on-chip; 3D cell culture; cancer microenvironment; microfabrication

40. Transcriptionally defined AML cell states associate with treatment response and microenvironmental remodeling

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Acute myeloid leukemia (AML) is heterogeneous, and therapy resistance is often attributed to leukemic stem cells (LSCs). We integrated scRNA-seq and CITE-seq from diagnostic AML samples (n=6) with bulk RNA-seq (n=448), ex vivo drug sensitivity (n=124), plasma proteomics (n=38), clinical data (n=183), and longitudinal single-cell datasets to define functional AML cell states and their therapeutic and microenvironmental associations. Nine conserved states were identified spanning progenitor-like, stromal-like, monocytic, and mixed stromal/monocytic programs, with stemness distributed across multiple states. Distinct states showed differential drug sensitivity, including convergent BH3-mimetic resistance in monocytic states and selective Wee1/PLK1 inhibitor sensitivity in stress-adapted progenitors. This stress-adapted state associated with adverse clinical features and expanded after venetoclax-based therapy. Monocytic states formed immunosuppressive communication hubs, while stromal and progenitor states engaged survival and cytoprotective signaling. These findings establish functional AML states beyond the classical LSC paradigm and identify candidate vulnerabilities for state-directed therapeutic strategies.

Leukemic stem cells, Therapy resistance, Precision oncology

41. Development of molecular biology methods to facilitate cancer research

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Johan Heldin (Uppsala University), Leonie Wenson (Uppsala University) & Ola Söderberg (Uppsala University)

Over the past decades, we have developed several methods that are now widely used in medical research, including the in situ proximity ligation assay (in situ PLA). Here, we present two of our latest technologies: Sequence-Templated Erroneous End-Labeling sequencing (STEEL-seq) and Enzyme-Activated Proximity Oligonucleotide Sensing (EPOS).

STEEL-seq enables selective detection and sequencing of single-strand DNA breaks (SSBs) and is compatible with all major sequencing platforms. Using this method, we found that SSBs are enriched at promoters of actively transcribed genes, suggesting a previously unrecognized layer of genome regulation in which promoter-associated SSBs may facilitate high gene expression.

EPOS enables high-resolution mapping of endogenous protein–protein interactions. Compared with in situ PLA, it offers higher spatial resolution, greater sensitivity, and a broader dynamic range. These improvements make EPOS a powerful tool for both basic research and diagnostic applications requiring precise detection and localization of protein interactions.

Molecular biology, methods, sequencing, imaging

42. ProtLymphML: A plasma proteomics-based diagnostic tool for robust adult lymphoma classification

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We developed ProtLymphML, a machine learning model that uses plasma proteomics to classify patients into the following B-cell-derived lymphoma entities: large B-cell lymphoma (LBCL), primary central nervous system lymphoma (PCNSL), follicular lymphoma (FL), mantle cell lymphoma (MCL), and classical Hodgkin lymphoma (cHL). ProtLymphML was trained on 408 unique proteins from 376 patients and evaluated in an internal test set (n = 162) from the same Swedish discovery cohort and in serum samples from an independent Nordic high-risk LBCL trial cohort (n = 109). The model correctly classified 80% and 83% of patients in the test and external validation cohorts, respectively. Misclassifications often reflected biological similarities across lymphomas, further highlighting the potential of the circulating proteome as a complementary diagnostic approach.

Lymphoma, plasma proteomics, classification

43. Tree and space-aware optimal transport for single-cell and spatial transcriptomics data integration*

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The spatial organization of evolving cell populations in tumors influences how they progress and respond to treatment. Spatially-resolved transcriptomics data may be used to examine the locations of these diverse cell states in tumor sections. However, these technologies often lack single-cell resolution and instead capture groups of cells in spatial spots, making it difficult to obtain accurate clonal identities and build phylogenetic trees. In contrast, full-length single-cell transcriptomics data are better suited to obtain cell lineages but do not capture their spatial locations in tissue. We present SpOTr, an optimal transport and statistical model designed to quantify the concordance between the evolutionary tree and the spatial distribution of cancer cells by integrating single-cell and spatial transcriptomics data from tumors.

SpOTr uses Fused Gromov-Wasserstein optimal transport to leverage the tree-based cell distances from one modality and spatial neighborhoods from the other to map single cells to spatial locations. The method learns clone-specific concordances with spatial structure, which can be used to investigate lineage-specific zonation patterns. We validate SpOTr on simulated and real spatial lineage tracing data from a mouse model of breast cancer lung metastasis and show that it recovers spatial locations of subclones better than alternative methods that ignore the tree structure.

scRNA-seq, spatial, data integration, optimal transport, cancer

* Selected talk, presented on stage at end of session 1

44. Small Molecule-based Dendritic Cell Reprogramming for Cancer Immunotherapy

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Type 1 conventional dendritic cells (cDC1s) are essential for cross-priming CD8+ T cells and initiating anti-tumor immunity, and their intratumoral abundance correlates with improved clinical outcomes. We previously showed that PU.1, IRF8, and BATF3 (PIB) can reprogram cancer cells into cDC1-like cells in vivo, but TFs and viral vectors pose challenges for clinical application. Here, we sought to chemically reprogram tumor cells into cDC1s by identifying small molecules that substitute for these TFs. Using Clec9a-tdTomato reporter MEFs transduced with insufficient two-TF combinations, we screened small-molecule libraries and identified compounds that activated the Clec9a reporter in the absence of individual TFs. Concurrently, computational RNA-seq analysis further nominated compound combinations inducing dendritic cell-associated markers. These ongoing studies support small molecule-based reprogramming to induce cDC1 traits in non-hematopoietic cells.

cell reprogramming, chemical reprogramming, small molecules, cancer immunotherapy, dendritic cell

45. An Innervated and Vascularized HNSCC-on-a-Chip Model Built on Defined and Tunable Engineered Extracellular Matrices

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Understanding and targeting the tumor microenvironment requires human experimental models that capture its cellular, vascular, neural, and extracellular matrix complexity. Here, we present an all-human, innervated and vascularized head and neck squamous cell carcinoma (HNSCC)-on-a-chip platform built with fully defined and tunable engineered extracellular matrices (eECMs). Patient-derived HNSCC cells, cancer-associated fibroblasts, and endothelial cells exhibited eECM-dependent transcriptional states, multicellular organization, and sensitivity to cisplatin. Integration into a cancer–vascular interface enabled analysis of matrix-dependent directional migration and invasion, while incorporation of 3D human bioengineered trigeminal ganglia established a functional tumor–nerve–vascular tri-interface. By reconstructing key determinants of the human HNSCC microenvironment within a controllable and patient-relevant system, this platform provides a framework for dissecting mechanisms of tumor progression and for evaluating therapeutic responses under conditions that more closely reflect human disease.

Organ-on-a-chip; Extracellular matrix; 3D Cancer models; Innervation; Vasculature

46. Deciphering the Molecular Mechanism of Action of Nelarabine for Improved Clinical Efficacy in the Treatment of T-cell lymphoblastic leukemia

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Nelarabine, a deoxyguanosine analogue, is an antimetabolite found to selectively target T-cell lymphoblastic malignancies, leading to its wider adoption in protocols for refractory T-ALL. The Rudd and Herold groups have identified the dNTP triphosphohydrolase SAMHD1 as a novel vulnerability dictating cellular sensitivity to nucleoside analogues such as nelarabine. However, this does not fully explain the variation in patient responses nor account for the cellular phenotypes observed in vitro.

We have integrated transcriptomics, proteomics and CRISPR knockout screening from patient biobank material to identify novel regulators of nelarabine sensitivity. Our preliminary functional validations have led to a comprehensive time-resolved picture of nelarabine's effect on cellular redox flux and proteostasis.

These latest findings provide a novel perspective on the mechanism of action of nelarabine and will serve as a starting point for better stratification of responders and predictive molecular biomarkers, as well as constitute a blueprint for studying other clinically relevant antimetabolites.

T-cell lymphoblastic leukemia, nucleotide metabolism, drug mechanism of action, nelarabine

47. scFFPE-ATAC enables high-throughput single cell chromatin accessibility profiling in formalin-fixed paraffin-embedded samples

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Formalin-fixed paraffin-embedded (FFPE) samples are the gold standard for tissue preservation in clinical and research settings. Current single-cell chromatin accessibility technologies cannot resolve cell-type-specific epigenetic profiles in FFPE tissues due to extensive DNA damage. We present scFFPE-ATAC, a high-throughput single-cell chromatin accessibility assay for FFPE samples that integrates an FFPE-adapted Tn5 transposase, ultra-high-throughput DNA barcoding (>56 million barcodes per run), T7 promoter-mediated DNA damage repair, and in vitro transcription. We benchmark scFFPE-ATAC on FFPE mouse spleen and validate its performance against fresh tissue. We apply it to human lymph node samples archived for 8–12 years and to lung cancer FFPE tissues, revealing distinct regulatory trajectories between tumor center and invasive edge. Analysis of archived follicular lymphoma and transformed diffuse large B-cell lymphoma samples identifies relapse- and transformation-associated epigenetic dynamics. scFFPE-ATAC enables retrospective, spatial, and mechanistic epigenetic studies in long-term archived specimens.

scFFPE-ATAC; Single-cell chromatin accessibility; FFPE tissue; Single-cell epigenomics; Cancer epigenetics

48. SciLifeLab Cellular & Molecular Imaging Platform

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Cellular and molecular imaging enables the visualization of biological systems from atomistic to tissue levels. Typical methods involve the transmission, absorption, reflection, or refraction of a focused beam of visible light or electrons by a microscopic sample of interest. In the life sciences, such samples may be biological macromolecules, cells, small organs or organisms of interest to biomedical or planetary biology research. At SciLifeLab, imaging staff assist users from academic, industry, and clinical settings to identify and implement relevant techniques

for sample preparation and for the collection, processing, analysis, and sharing of imaging data, with a focus on methods and instruments not generally accessible to individual research groups or local facilities. Key SciLifeLab imaging services include cryogenic electronic microscopy (cryo-EM) and tomography (cryo-ET), super-resolution and other advanced methods in fluorescence microscopy, focused ion-beam milling scanning electron microscopy (FIB-SEM), correlative array tomography (CAT) and nanoscale secondary ion mass spectrometry (nanoSIMS), along with a range of imaging modalities in support of structural biology and spatial omics.

imaging, cryo-EM, tomography, fluorescence, nanoSIMS

49. From Cancer Biology to Therapeutic Opportunity: Enabling Academic Drug Discovery at SciLifeLab

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Rebecka Klintenberg, Per Arvidsson, Kristian Sandberg, Drug Discovery and Development Platform, SciLifeLab

Rapid advances in cancer biology reveal new disease mechanisms and therapeutic vulnerabilities, yet translating these discoveries into viable drug discovery programs remains challenging. The Drug Discovery and Development (DDD) Platform at SciLifeLab bridges this gap by providing academic researchers with integrated expertise in areas such as target validation, assay development and screening, medicinal and computational chemistry, biophysics, drug metabolism, pharmacokinetics, and pharmacology. DDD supports drug discovery across small molecules, human antibodies, oligonucleotides, and emerging therapeutic modalities.

Academic Drug Discovery, New modalities, Translational Drug Discovery

50. Rapid diagnostics of actionable mutations in acute myeloid leukemia using amplicon nanopore sequencing

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Rapid genetic characterization of acute myeloid leukemia (AML) is critical for timely risk stratification and treatment selection. We developed and clinically implemented a targeted amplicon panel based on Oxford Nanopore Technologies (ONT) long-read sequencing (LRS) for simultaneous analysis of NPM1, FLT3, IDH1, IDH2 and TP53.
The assay was evaluated in 36 patients carrying 64 variants previously identified by standard methods, including variants with allele frequencies (VAF) of 1–83% and FLT3-ITDs ranging from 18–176 bp. ONT detected 63 of 64 variants (98.4% sensitivity), leading to clinical reporting thresholds of 0.05 allelic ratio for FLT3-ITDs and 0.05 variant allele frequency for other variants. In a separate cohort of 18 patients with multiple TP53 variants, all variants were detected and successfully phased, enabling reliable assessment of TP53 allelic status. Prospective validation in 26 patients showed 100% sensitivity and specificity versus standard-of-care diagnostics, with an average turnaround time of 31.7 hours from sequencing to reporting.

Precision diagnostics, AML

51. Lymphotoxin alpha expression alters the tumor microenvironment in murine glioma

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Glioblastoma is the most common malignant primary brain tumor. Characteristically, these tumors exhibit abnormal vascularization and an immune suppressive tumor microenvironment (TME). Lymphotoxin alpha (LTα) has previously been implicated in regulating formation of high endothelial venules (HEVs) and tertiary lymphoid structures (TLS) in autoimmunity and cancer. Here, we aim to understand the effects of LTα on the TME of murine glioma.
Stimulation of human brain vascular endothelial cells (HBMVECs) with LTα in vitro upregulated adhesion molecules without concurrent upregulation of immune cell suppressive molecules. Overexpression of LTα in orthotopic CT-2A glioma cells led to significantly prolonged survival and induced changes in both the vascular and immune cell phenotypes. Whereby, LTα overexpression increased the proportion of intra-tumoral MAdCAM-1+ HEVs but did not induce TLS formation. Our ongoing work aims at investigating the crosstalk between the different TME components and thereby evaluate the potential benefit of LTα expression as a therapeutic approach.

Glioblastoma, Lymphotoxin alpha, High endothelial venules, Tertiary lymphoid structures

52. Myofibroblastic cancer-associated fibroblasts are associated with glioblastoma progression*

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Glioblastoma (GBM) is the most common primary malignant brain tumour in adults and is associated with high mortality due to inevitable tumour recurrence. In various solid epithelial tumours, different subtypes of cancer-associated fibroblasts (CAFs) have been identified within the tumour microenvironment, either promoting or inhibiting tumour growth. However, normal fibroblasts have recently been found in the adult human brain, raising questions about their potential role in GBM biology. To explore this, we analysed the transcriptome profiles of fibroblasts in human and murine GBM tumours using single-cell and spatial transcriptomic data. Remarkably, we discovered several fibroblast subtypes, including myofibroblastic and inflammatory CAFs, which shared genomic profiles with CAF subtypes previously described in epithelial tumours. Further analysis suggested that myofibroblastic CAFs originate from perivascular fibroblasts in the normal brain. These perivascular fibroblasts with myofibroblastic features appear to reside in or near hypoxic areas and are associated with poorer disease outcomes (OS: hazard ratio (HR) > 1.41, $p < 0.02$; DSS: HR > 1.58, $p < 0.01$; PFI: HR > 1.66). Spatial transcriptomics revealed a strong association, particularly in recurrent GBM samples, between macrophages and astrocytes in peri-hypoxic areas. Further analysis of 91 paired primary and recurrent GBM samples demonstrated a significant increase in myofibroblastic CAFs at disease recurrence. Overall, our findings highlight the diversity of fibroblasts in GBM, which could have implications for developing directed therapies that specifically target stromal cell types within the tumour microenvironment.

Glioblastoma, Tumor Microenvironment, Fibroblasts

53. Quantitative Liquid Biopsy Epigenomics Using EpiFinder:tm: cNUC: Multi Mark Profiling from Limited Plasma Input

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Background: Liquid biopsy approaches based on circulating cell free DNA (cfDNA) capture genetic alterations but miss the regulatory epigenetic layer that shapes cellular identity and disease biology. Circulating nucleosomes (cNUCs) retain histone modifications and DNA

* Selected talk, presented on stage at end of session 3

methylation from their cell of origin, providing direct access to chromatin states in cancer. We evaluated EpiFinder:tm: cNUC, a multiplexed and quantitative platform for epigenetic profiling from plasma, in a colorectal cancer (CRC) cohort.
Methods: Twenty four plasma samples (12 CRC, 12 controls) were processed in a single pooled workflow using 200 µL plasma per sample. Five epigenetic features—H3K4me3, H3K27ac, H3K27me3, H3K9me3, and CpG DNA methylation—were profiled in parallel, alongside an input library for copy number analysis. Data were analyzed using differential region calling, feature selection, PCA, and gene level functional enrichment.
Results: All libraries yielded robust genome wide profiles, confirming that early pooling preserves quantitative relationships across samples. CRC samples showed higher levels of tumor derived nucleosomes than controls. PCA demonstrated clear separation of CRC and healthy samples across multiple epigenetic layers. Simultaneous profiling of promoters, enhancers, and gene associated regions revealed CRC linked regulatory programs. Gene Ontology analysis highlighted pathways related to epithelial differentiation, transcriptional regulation, and immune and leukocyte biology. Epigenetic signatures remained informative even in samples lacking copy number alterations.
Conclusion: EpiFinder:tm: cNUC enables scalable, multiplexed epigenetic profiling directly from plasma, revealing disease associated chromatin signatures and supporting liquid biopsy–based discovery, early detection, and translational research.

Liquid Biopsy, Epigenetic profiling, nucleosomes, DNA methylation, Histone modifications, plasma epigenetics, cfDNA, fragmentoics, CVA

54. Sensitive gene fusion detection and comprehensive transcriptome profiling from degraded FFPE samples

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Background: RNA sequencing (RNA-seq) of Formalin-Fixed Paraffin-Embedded (FFPE) tissue is essential for oncology research but is challenged by RNA degradation, chemical modifications, and inconsistent library quality. We developed a streamlined workflow to improve transcriptome profiling from low-input, degraded FFPE samples.
Methods: The truCOVER Total RNA Library Prep workflow combines Covaris Adaptive Focused Acoustics (AFA:registered:) Technology for mechanical shearing with optimized rRNA depletion. Performance was evaluated using 50 ng FFPE-derived RNA and benchmarked against leading commercial kits using the Seraseq:registered: FFPE Tumor Fusion RNA Reference Material. Metrics included rRNA depletion efficiency, alignment rates, library quality, and fusion detection sensitivity.

FFPE RNA Sequencing, Transcriptomics, Gene Fusion Detection, Library Preparation

55. Spatial metabolomic changes in the tumorigenesis of adenocarcinoma of the lung

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The progression from adenocarcinoma in situ (AIS) to invasive lung adenocarcinoma is associated with metabolic adaptation.
Whole-tissue sections from 7 samples (6 patients) were analyzed by MALDI-2 timsTOF flex mass spectrometer (Bruker Daltonics) using two matrices (NEDC, FMP10), with annotation of four categories: normal lung, AIS, AC, and immune-rich regions.
Joint UMAP analysis showed that metabolic variation was dominated by patient identity, without slide-level clustering. Histological compartments remained distinguishable within individual patients; therefore, within-patient comparisons were used, applying one-versus-rest and neoplastic-versus-non-neoplastic tests.
Lipid-associated metabolites dominated in normal lung, AIS, and immune-rich regions, while polyamine metabolites were highest in AC. Spermine, putrescine, and phosphatidylglycerol were significantly elevated compared with normal tissue (FDR < 0.05; 6/7 each), and all three increased progressively from normal through AIS to AC; however, they did not reach statistical significance (p > 0.05). Our established pipeline will now be extended to additional patient samples and tissue collections.

spatial metabolomics, lung adenocarcinoma, tumorigenesis

56. Exploring the abundance and therapeutic potential of lipid droplets in Multiple Myeloma

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Multiple myeloma (MM) is a heterogeneous haematological malignancy originating from the bone marrow. Cancer cells meet their increased energetic demands needed to maintain a high proliferative rate by enhancing lipid synthesis and storage within LDs. Herein, we identified increased abundance of LDs in MM cells by LD-BTD1 staining. By utilizing RNA-seq data from newly diagnosed MM patients within the MMRF cohort, we demonstrated that the transcription factors SREBPs which regulate the expression of the de novo lipogenesis

enzymes are overexpressed in MM and associated with worse prognosis. Interestingly, combinatorial treatment with bortezomib, the standard-of-care for newly diagnosed MM patients, and fatostatin (SREBPsi) significantly increased cell death and apoptosis in human and murine MM cells compared to control and single treatments. To investigate the therapeutic potential of the combinatorial treatment in vivo, we will evaluate its effect on tumour growth and mouse survival in the 5T33MM immunocompetent syngeneic murine MM model.

Multiple myeloma, lipid metabolism, lipid droplets, bortezomib and fatostatin

57. BioImage Informatics, SciLifeLab, Sweden: Providing support on Bioimage data

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The BioImage Informatics unit (BIIF) develops new computational technologies and provides access to expertise and state-of-the art software for processing and quantitative analysis of all kinds of microscopy image data, primarily for applications in the life sciences. BIIF is a SciLifelab unit, and part of the National Bioinformatics Infrastructure Sweden NBIS. We are active within the GloBIAS and EuroBioImaging networks. We offer - i) advice on best-practice and guidance on overall experimental design for research involving microscopy imaging and quantitative data analysis, ii) guidance on image analysis assay development, including image processing algorithm development and software engineering to address challenging project goal, iii) advice on best-practice and guidance on high throughput/large-scale image processing using computing clusters, including data transfer and storage during the activity of the project, iv) guidance on large-scale data analysis and visualization and dissemination of bioimage analysis knowledge in courses and workshops.

58. Cells as Tokens: A Language-Inspired Framework for Nuclei Morphology and Spatial Context in Colorectal Adenocarcinoma

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Tianhui Xu, Linglong Huang

Background & Objective: Inspired by natural language, we propose a novel framework that treats each nucleus as a "morphological token" and tissue as a "spatial language," aiming to systematically decode the structural architecture and cell type composition of the tumor microenvironment.
Methods
Our pipeline consists of three sequential stages: (i) nuclear shape encoding using 20-harmonic elliptic Fourier descriptors (EFD-20) derived from boundary-sampled spots; (ii) morphological tokenization via a two-level clustering strategy (K-means over-clustering into 200 groups, followed by silhouette-optimized sub-clustering) on the COAD cohort, yielding a fixed and transferable morphological classifier; (iii) spatial context modeling, in which the types of the

neighboring nuclei assigned by the classifier are recorded as an ordered sequence for each nucleus, analogous to contextual windows in language.
Results
Clustering of these contextual sequences revealed ten recurrent spatial "patterns" across tissues. Notably, Pattern 2 consistently corresponded to tumor cells, while the remaining nine patterns represented various stromal components, demonstrating that morphological "grammar" can robustly discriminate malignancy from its microenvironment.
Conclusion
This tokenization-and-context approach transforms histological images into a spatial language, offering a structured, interpretable, and quantitative framework for AI pathology.

AI pathology, tumor biology

59. Development of an optimized workflow for sensitive variant detection in FFPE-damaged samples

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NGS of FFPE samples allows for detailed characterization of cancer from routinely collected clinical specimens. However, the preservation process often leads to significant damage and degradation of genetic material, complicating library preparation.

Using the Twist TrueAmp library preparation kit and target enrichment workflow, we demonstrate library conversion of severely damaged (DIN<2) FFPE with as little as 5ng input mass. Compared to other workflows, an increase in library complexity is observed. Importantly, the enzymatic fragmentation of input DNA can be tuned to provide larger insert sizes that are appropriate for sequencing with longer read length. Coupled with target enrichment, more target sites are captured and the uniformity is significantly improved. These improvements are driven by the incorporation of Twist TrueAmp polymerase, an engineered polymerase with a low error rate capable of amplifying through GC extremes to recover challenging genomic regions. In summary, our optimized library preparation kit built on engineered enzymes emerges as a valuable asset for the deployment of NGS-based FFPE assays.

Spatial biology; spatial transcriptomics; spatial proteomics; spatial metabolomics

60. Single cell analysis reveals molecular traits of paediatric lymphoma resistant subclones

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Paediatric lymphoma accounts for 10-15% of childhood cancer. Accumulating evidence underscores paediatric lymphoma being a unique entity from its adult counterpart. However, traits unique to paediatric lymphoid landscape and how it affects lymphomagenesis is unclear. Here, we applied single cell RNA sequencing (scRNA-seq) and immune receptor sequencing (scVDJ-seq) on freshly acquired paediatric non-Hodgkin lymphoma (pNHL n=12) and 10 reactive lymph nodes from adults or children (a/pReLy). We discovered that pReLy harboured a paediatric niche (PN) that allowed development of marginal zone precursor (MZP) cells and stem T cells (Tsc). Surprisingly, we observed that multiple types of paediatric lymphoma/leukaemia developed subclones that competed for the PN. Combining chromosomal copy number variation inference (inferCNV) and single nucleotide variation (SNV, via SComatic), we observed that paediatric lymphoma evolved towards the PN-like status to acquire drug-resistance. Finally, we identified MSI2 as a potential target to intercept this transition, paving ways to treatments preventing relapse/refractory in paediatric lymphoma.

Pediatric; lymphoma; evolution; chemoresistance

61. Defining a “one-two-punch” strategy against KRAS-driven cancers

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Recent advances in targeting the previously undruggable RAS oncogenes have transformed lung cancer treatment, yet resistance almost invariably emerges, limiting durable responses. Growing evidence shows that non-genetic adaptations and cellular plasticity enable cancer cells to rapidly and reversibly enter a drug-tolerant state following KRAS inhibition (KRASi). This transient state allows cancer cells to evade initial therapy, facilitating the emergence of resistant clones and, ultimately, driving relapse. Targeting this pool of KRASi-tolerant cells may therefore provide a strategy to achieve more durable responses in KRAS-mutant cancers. Inspired by the “one-two-punch” concept, in which sequential administration of two drugs maximizes treatment efficacy by eliminating the cells that survive initial therapy, we have implemented a high-throughput phenotypic screening workflow to identify compounds that selectively kill KRASi-tolerant cancer cells. Here, we present our screening results and characterize candidate vulnerabilities that emerge following KRAS inhibition, revealing new opportunities for targeting drug-tolerant cancer cell states.

phenotypic screening, lung cancer, drug-tolerant persister cells

62. Effects of Sex Hormone Biology on Endometrial Cancer Risk

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Endometrial cancer (EC) is one of the most common gynaecological cancers. Circulating sex hormones are strongly associated with its development, but whether their causal effects vary across menopausal and hormone replacement therapy (HRT) groups remains unclear. Using UK Biobank women stratified by menopausal status and HRT use, we performed genome-wide association studies (GWAS) of oestradiol, testosterone, and sex hormone-binding globulin (SHBG) followed by univariable, multivariable, and clustered Mendelian randomization (MR) of EC risk. GWAS identified a total of 10, 130, and 188 independent genetic loci associated with oestradiol, testosterone, and SHBG, respectively, across all menopausal and HRT strata. Univariable MR showed positive testosterone and inverse SHBG associations with EC across non-HRT menopausal strata; after multivariable adjustment, testosterone estimates attenuated towards the null, whereas SHBG remained inverse in direction. Positive association of oestradiol was only observed in the context of HRT use, driven by a single instrument at the CYP3A7 locus.

Endometrial cancer, Sex hormones, GWAS, Menopause, HRT