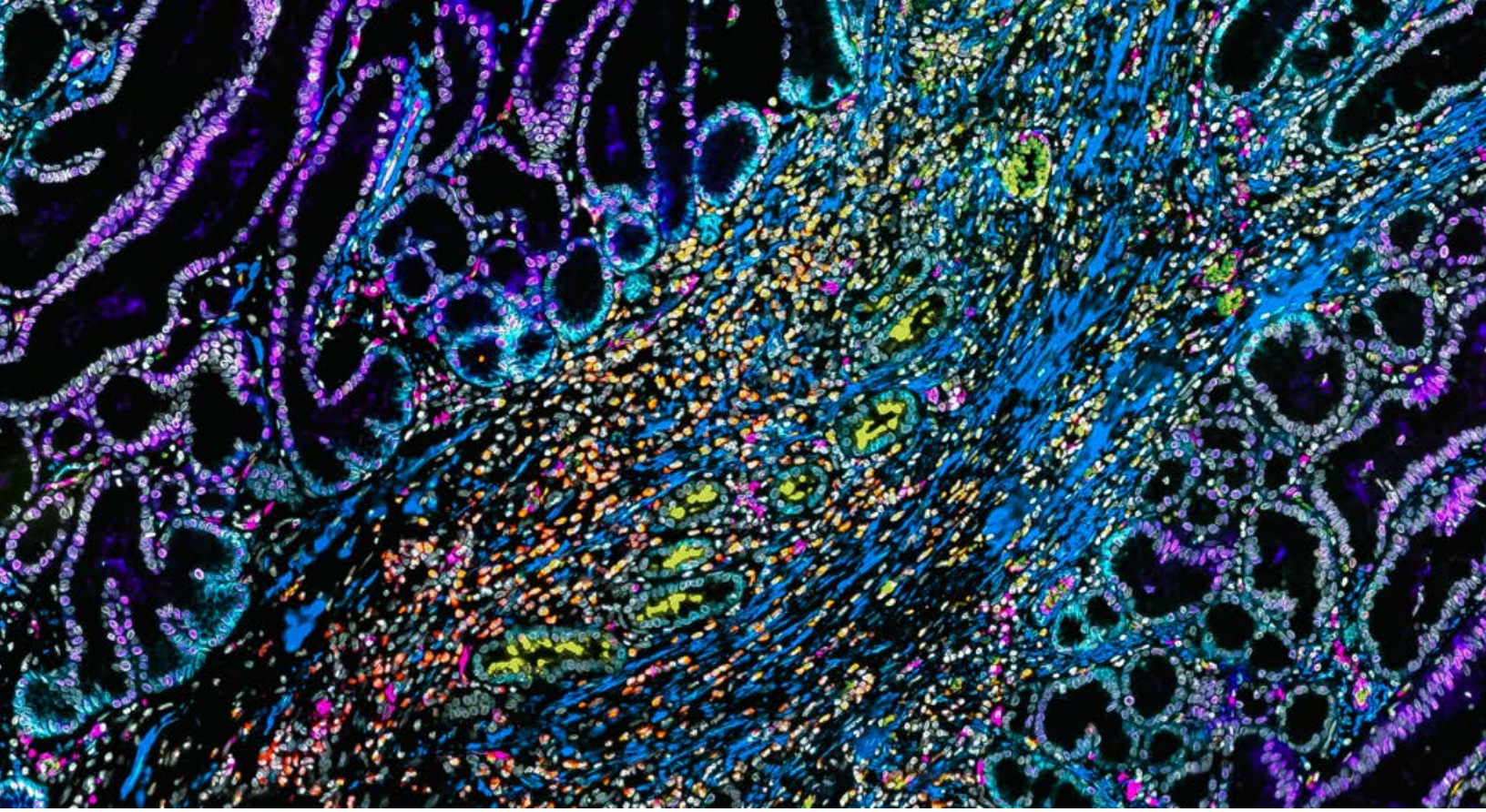

Symposium international de l'IRIC
Comprendre les cellules dans leur contexte : focus sur la biologie spatiale

IRIC International Symposium
Understanding Cells in Context: A Focus on Spatial Biology

Université de Montréal

Atrium et amphithéâtre A3502.1 campus MIL
Université de Montréal, 1375 avenue Thérèse-Lavoie-Roux
Outremont

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Vincent Trinh

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Christian Charbonneau

Noémie Desbois Mackenzie

Judith Lafaille

Lynda Landry

Melissa Lopez-Castillo

Mira-Sue Mallet

Virginie Mondin

PROGRAMME | *PROGRAM*

07:30 Accueil des participant(e)s | *Welcome of participants — Atrium*

07:50 Mot de bienvenue | *Welcome address — Salle | Room A-3502.1*

Session 1.1 — *Salle | Room A-3502.1*
Technologies de séquençage spatial – première partie
Spatial Sequencing Technologies – part 1

08:00 **Logan Walsh**, Goodman Cancer Institute, McGill University

08:50 **Faustine Gorse**, IRIC – Université de Montréal
Patterns of Expression and Activity of Estrogen Receptor, Foxa1 and Foxc1 in the Normal Mammary Gland Mirror Those in Breast Cancer Subtypes

09:05 **Loic Binan**, Lady Davis Institute – McGill University
Simultaneous Crispr Screening and Spatial Transcriptomics Reveals Intracellular, Intercellular, and Functional Transcriptional Circuits

09:55 Pause-café et présentations par affiches | *Coffee Break and poster viewing — Atrium*

Session 1.2 — *Salle | Room A-3502.1*
Technologies de séquençage spatial – deuxième partie
Spatial Sequencing Technologies – part 2

10:25 **Maya Saleh**, Institut national de la recherche scientifique (INRS)
Harnessing Spatial Biology to Define a Molecular Pathology Framework of Hepatocellular Carcinoma

11:15 **Peter Horvath**, ETH Zurich
Life Beyond the Pixels: Single-Cell Analysis Using Deep Learning and Image Analysis Methods

12:05 Dîner et présentations par affiches | *Lunch and poster viewing — Atrium*

Session 2 — *Salle | Room A-3502.1*
Analyse computationnelle en pathologie
Computational Analysis in Pathology

13:00 **Mahdi Hosseini**, Concordia University

13:50 **Pieter Goossens**, Maastricht University
Imaging Macrophage Subsets in Their Natural Habitat

14:40 **Maëlle Batardière**, IRIC – Université de Montréal
Spatial Dependencies Between Tumor Cells and Fibroblasts During Pancreatic Tumorigenesis Revealed by Multiplex Imaging

14:55 Pause-café et présentations par affiches | *Coffee Break and poster viewing — Atrium*

Session 3 — *Salle | Room A-3502.1*
Modélisation et procédés analytiques
Modeling & Analytical Pipelines

15:30 **Zixuan Cang**, North Carolina State University
Cell-cell Communication Analysis of Single-cell Data with Optimal Transport

16:20 **Helen Byrne**, University of Oxford
Mathematics Under the Microscope: Unravelling Spatial 'Omics

17:10 Mot de clôture | *Closing remarks — Salle | Room A-3502.1*

17:20 5 à 7 | Happy Hour — *Atrium*

Session 1.1
Technologies de séquençage spatial – première partie
Spatial Sequencing Technologies – part 1

Logan Walsh, PhD
Goodman Cancer Institute – McGill University

Dr Walsh is Assistant Professor at the Goodman Cancer Institute (GCI) and Department of Human Genetics at McGill University, and appointed as the *Rosalind Goodman Chair in Lung Cancer Research*. His interest in understanding responses to immunotherapy comes from his involvement in some of the seminal work in immunogenomics and biomarkers of immune checkpoint inhibitor efficacy from his postdoctoral fellowship in the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering Cancer Center. His lab currently focuses on using translational genetics and immunogenomics to develop personalized medicine strategies. He is a trained wet-lab biologist who has amassed considerable expertise in bioinformatics. This skill set provides an ideal combination to lead the efforts delineated in his research program. Dr. Walsh strongly believes that by collaborating and combining expertise of clinicians and basic scientists we will have the best chance to develop research models and strategies to help better care for cancer patients.

Faustine Gorse
PhD student
IRIC – Université de Montréal

Patterns of Expression and Activity of Estrogen Receptor, Foxa1 and Foxc1 in the Normal Mammary Gland Mirror Those in Breast Cancer Subtypes.

Breast cancer comprises clinical subtypes defined by expression of key drivers, estrogen receptor alpha (ER) and HER2/ERBB2. Triple negative breast cancer (TNBC) lacks both proteins and the progesterone receptor, an ER target. Molecular subtypes (luminal, molecular apocrine, basal) identified by transcriptome-based classifications overlap with clinical subtypes and are recapitulated by differential expression of transcription factors (TFs). We hypothesize that ER, FOXA1, and FOXC1, differentially expressed in tumors, regulate mammary epithelial differentiation and drive tumor subtype specification. Our objectives are to characterize their expression in normal and tumor tissues and their contribution to gene regulation in both contexts. Spatial RNA profiling of normal mammary glands with GeoMx revealed distinct keratin and TF expression in myoepithelial versus epithelial cells, and co-expression of luminal tumor–enriched genes in ER luminal cells. Co-immunofluorescence validated FOXA1–ER co-expression and showed mutually exclusive FOXA1–FOXC1 expression. Immunohistochemistry on tumor microarrays confirmed FOXC1 expression in TNBC (basal), while FOXA1 was present in ER, HER2, and a fraction of TNBC tumors (molecular aprocrine). Suppression of each TF in cancer models demonstrated roles in repressing myoepithelial gene programs. Our results suggest that breast cancer subtypes largely retain gene expression programs of potential cells of origin, which may select oncogenic alterations and result in subtype-specific therapeutic vulnerabilities.

Loic Binan, PhD
Assistant Professor, Department of Human Genetics, McGill University
Full time Investigator at the Lady Davis Institute for Medical Research at the Jewish General Hospital

Simultaneous Crispr Screening and Spatial Transcriptomics Reveals Intracellular, Intercellular, and Functional Transcriptional Circuits.

Research in our lab aims to develop technologies to investigate the mechanisms by which gene networks control the self-organization of cells into complex 3-D tissues during development, as well as the modifications to this organization that take place in disease. This includes approaches to collect new types of data as well as algorithms to analyze these data. The techniques we use include gene editing (CRISPR), spatial transcriptomics, single cell RNA sequencing, microscopy, and computational methods for image analysis and statistics. We develop our tools in tissues like the brain or tumors.

Loic Binan completed his PhD in biomedical engineering at Université de Montreal, then joined the broad institute for my post-doctoral research on high throughput genetic screens and spatial transcriptomics, and recently joined the Lady Davis, where I am opening my lab.

Session 1.2

Technologies de séquençage spatial – deuxième partie

Spatial Sequencing Technologies – part 2

Maya Saleh, PhD
Full Professor, Immuno-oncology
Institut National de la Recherche Scientifique (INRS)
Centre Armand Frappier Santé & Biotechnologie

Harnessing spatial biology to define a molecular pathology framework of hepatocellular carcinoma.

Dr. Saleh holds a PhD in Biochemistry from McGill University. After post-doctoral training at Merck and at the La Jolla Institute for Immunology, she became Full Professor of Medicine and William Dawson Scholar at McGill University from 2005-2019. In 2019, she relocated to France to direct oncoimmunology research at the University of Bordeaux, where she held a French Initiative of Excellence (IDEX) Senior Chair and an International-Leader-in-Oncology Chair from la Fondation ARC. In 2023, she returned to Canada as a Full Professor at INRS-Centre Armand Frappier Santé Biotechnologie.

Dr. Saleh is invested in inflammation and cancer research, in which she applies proteomics, genomics and spatial biology approaches to investigate molecular mechanisms of the disease and to identify potential therapeutic targets. She has created several local and international multi-disciplinary teams to study cancer immunology. She collaborates with oncologists, surgeons, pathologists, chemists and computational scientists to identify factors contributing to cancer progression and to better stratify patients for optimal treatments. →

Her current research program is focused on the immunological mechanisms underlying therapeutic resistance to standard of care treatments in hepatocellular carcinoma and glioblastoma. Her team is investigating the diversity of myeloid cells in the tumor microenvironment towards their rational targeting as an adjuvant immunotherapeutic approach. The Saleh team has also launched new collaborations with colleagues from STEM disciplines at INRS to develop new methods for early cancer detection towards improved clinical management.

Peter Horvath
Institute director at the Hungarian Research Network (HUN-REN)
Group leader at the AI4Health Institute in Helmholtz Center Munich
Visiting scientist as well as a Finland Distinguished Professor Fellow at the University of Helsinki (FIMM-EMBL).

Life Beyond the Pixels: Single-Cell Analysis Using Deep Learning and Image Analysis Methods.

With over 20 years of experience in image analysis and machine learning, he has conducted research at leading institutions, including ETH Zürich and INRIA Sophia Antipolis, where he earned his PhD in 2008.

His research groups focus on developing computational solutions to biological problems, integrating wet-lab techniques and light microscopy with AI-driven image analysis. His innovations in computational microscopy have contributed to the discovery of genes with essential roles in cancer, bacterial and viral infections, and diabetes. He has also introduced groundbreaking methods in single-cell research.

Horvath's scientific contributions have been published in top-tier journals, including Science, Cell, and over 20 different Nature journals, totaling 150+ peer-reviewed publications. He has secured numerous international and national grants, including funding from CZI, NIH, and EU-Horizon programs.
Currently, his research focuses on integrating AI-driven algorithms with molecular measurements to develop personalized, targeted cancer treatments and translate these advancements into real-world clinical applications. His vision is to harness single-cell manipulation technologies to improve cancer diagnostics and patient outcomes.

Peter Horvath has submitted 11 patent applications and is committed to translating scientific discoveries into practical solutions. He is the founder and CEO of Single-Cell Technologies Ltd. and the founder of mAIskin AB, a company dedicated to bringing cutting-edge research into clinical practice.

Session 2

Analyse computationnelle en pathologie

Computational Analysis in Pathology

Mahdi Hosseini, PhD
Assistant Professor, Computer Science and Software Engineering, Concordia University

Dr. Mahdi S. Hosseini is an Assistant Professor in the Department of Computer Science and Software Engineering at Concordia and a winner of the prestigious 2023 Amazon Research Award for research on auto-populating synoptic reports in histopathology. Dr. Hosseini's research is primarily advanced in foundational developments of deep learning and computer vision algorithms, which are efficiently designed for computational pathology applications. He is the director of the Atlas Analytics lab at Concordia and published several papers on related topics. Dr. Hosseini serves as an Area Chair for CVPR from 2022 to 2025, NeurIPS from 2023 to 2024 and ECCV 2024.

Pieter Goossens, PhD
Cardiovascular Research Institute Maastricht (CARIM)
Maastricht University Medical Centre

Imaging Macrophage Subsets in Their Natural Habitat.

Pieter Goossens is an Assistant Professor in the Experimental Vascular Pathology laboratory at the Maastricht University Medical Centre (The Netherlands). His research focuses on the role of immune cells in cardiovascular disease, with particular emphasis on the phenotypic and functional heterogeneity of macrophages. These cells are key regulators in chronic inflammatory disorders such as atherosclerosis and cardiomyopathies. His group investigates the presence and spatial organization of macrophage subsets within disease-specific microenvironments, and how this contributes to pathogenesis. To address these questions, his team develops and applies advanced imaging-based strategies, integrating multiple imaging modalities.

Maëlle Batardière
MSc student
IRIC – Université de Montréal

Spatial Dependencies Between Tumor Cells and Fibroblasts During Pancreatic Tumorigenesis Revealed by Multiplex Imaging.

Pancreatic cancer evolves in a complex microenvironment where cells interact influencing progression. This project aims to develop novel bioinformatic tools for the spatial characterization of tumor-stroma cellular interactions underlying pancreatic tumorigenesis. We deployed cyclic multiplex immunofluorescence covering the diversity of tumor, immune cells, and fibroblasts from 16 human samples of normal pancreas, low- and high-grade dysplasia, and invasive cancer. We implemented novel algorithms that calculate distances between cells by incorporating their spatial positions to study stromal heterogeneity in relation to proximity to tumor cells (mask-dependent radius search and closest neighbor algorithms). Fibroblast markers expression correlates with distance to tumor in pre-invasive→

stage only. The phenotype of fibroblasts located 50µm to tumor changes with adjacent epithelial subtype. For the same sub-population, the cellular association also evolves with grade. Expansion of cancer associated fibroblasts (CAFs) subtypes, especially inflammatory CAFs, marks low- to high-grade transition. Cell neighborhood analysis reveals colocalization of CAFs and certain immune populations near the tumor. Our distance-based algorithms allow the first description of the dynamics of pancreatic sub-populations according grade and distance. Identified stromal/epithelial spatial dependencies will guide in vitro functional investigation to better understand the role of the microenvironment in pancreatic tumor progression, and identify new therapeutic targets.

Session 3

Modélisation et procédés analytiques

Modeling & Analytical Pipelines

Zixuan Cang, PhD
Assistant Professor, Department of Mathematics. North Carolina State University.

Cell-cell Communication Analysis of Single-cell Data with Optimal Transport.

Zixuan Cang trained in Mathematics at the Xiamen University (B.Sc) and at Michigan State University (PhD). He then pursied a postdoctoral fellowship at the the University of California Irvine.

Zixuan Cang is an Assistant Professor at the Department of Mathematics of North Carolina State University. His research focuses on developing mathematical and computational methods for analyzing molecular and single-cell data, with an emphasis on optimal transport and topological data analysis

Helen Byrne, PhD
Professor of Applied Mathematics, University of Oxford

Mathematics Under the Microscope: Unravelling Spatial 'Omics

Helen Byrne is a Professor of Mathematical Biology at the University of Oxford where she holds a joint appointment between the Mathematical Institute, the Centre for Human Genetics and the Ludwig Institute for Cancer Research. She has made significant contributions to mathematical oncology, publishing pioneering work on multiscale and multiphase models of tumour growth. Her research combines mathematical modelling, data science, and computational biology to understand how spatial organisation influences tissue dynamics, tumour growth, and treatment response. She was awarded an Advanced Research Fellowship by the UK's Engineering and Physical Sciences Research Council (2000-2006) and the Society of Mathematical Biology's Leah Edelstein-Keshet prize (2019), became an SMB Fellow in 2020, received an honorary doctorate from Chalmers University in Sweden in June 2024 and was awarded the London Mathematical Society's Naylor Prize and Lectureship in Applied Mathematics in 2025.

1

Eve petit & Mackenzie Bates

Development and Validation of a Low Barrier-to-Entry Microfluidic Chip for High Throughput Clonal Cultures.

Functional heterogeneity is a consistent feature of most primary stem cell populations. Understanding such heterogeneous behaviour requires single cell measurements. Physical partitioning of individual cells in separate wells is frequently used to allow clonal assessment of cell function. An efficient method for this involves the use of microfluidic chips. However, production and use of these require dedicated facilities limiting their utilization. We are developing a simple-to-use and manufacture microfluidics chip based on previous gravity-partitioning designs which can allow for cell trapping and dynamic media exchange. For this, molds for a valve-free, 4-array chip were 3D-printed using a standard consumer 3D-printer and coated with parylene. Polydimethylsiloxane (PDMS) was cast in 5:1 and 15:1 ratios for the array and seal layers respectively to allow off-ratio bonding, and assembled chips were bonded into standard 6-well plates. Well depth, media loading and exchange using standard pipettes were optimized. Beads were used to test object loading, media exchange, as well as on-chip staining, demonstrating successful retention of loaded objects and on-chip staining. Cell loading and on-chip cell imaging have been validated. This will allow high-resolution time-course imaging to be performed using standard molecular biology equipment and microscopes, thus facilitating adoption in stem cell biology groups.

2

Erwan Goy

Charting the Cellular Landscape in Rare Ovarian Cancer.

Epithelial ovarian cancers (EOC) comprise distinct histological subtypes. While high-grade serous carcinoma (HGSC) is the most common (70% of cases), rare subtypes such as clear cell carcinoma (CCC), endometrioid, and mucinous carcinomas account for a smaller proportion (less than 10%) but display marked resistance to conventional chemotherapy. Their biological complexity, intra-tumoral heterogeneity, and poor therapeutic response underscore the need for a deeper understanding of their cellular and molecular landscape. We hypothesize that defining tissue composition and functional interactions at the single-cell level in rare EOC will advance our fundamental knowledge, enable biomarker discovery, and inform personalized therapeutic strategies. Our objectives are: (1) to generate a detailed cellular and molecular map of rare EOC subtypes, (2) to investigate tumor microenvironmental interactions, including immune and senescent cells, and (3) to identify novel therapeutic targets, such as antibody-drug conjugates and senolytic agents. We will leverage the pan-Canadian COEUR biobank, comprising 250 CCC, 300 endometrioid, and 100 mucinous cases, using spatial transcriptomics and proteomics. Single-nuclei RNA-seq on pilot samples from the CHUM biobank will guide probe and antibody selection. We expect to reveal spatial heterogeneity, actionable biomarkers, and clinically relevant insights to refine treatment trajectories for patients with rare EOC.

3

Faruk Akay

Elucidating the Immune Mechanisms of Glioblastoma Progression.

Glioblastoma (GB) is the most common and aggressive brain tumor in adults. Despite standard of care combining surgery, radiotherapy, and temozolomide chemotherapy, median survival remains less than 15 months, and more than 90% of patients experience recurrence. This relapse is largely attributed to invasive tumor cells, that are not fully removed by surgery, and to an unfavorable myeloid-rich tumor microenvironment, characterized by hypoxia and lactate accumulation, that promotes their persistance. To better decipher tumor-immune interactions, we implement a multimodal multiomics spatial biology approach that combines spatial transcriptomics (Xenium® and Visium®, 10x Genomics), multiplex immunofluorescence (MACSimaTM imaging and cyclic staining, Miltenyi Biotec), and mass spectrometry imaging (MSI) to identify at cellular scale resolution the metabolic signals and molecular effectors driving post-resection GB progression. Preliminary results from our lab using mouse models of GB revealed resection-induced spatiotemporal changes of the immune landscape, and unraveled specific inflammatory pathways potentially involved in tumor progression. Studying the underlying mechanisms and validating our findings in patients tumor sections will provide a better understanding of the processes that fuel recurrence and pave the way for new therapeutic strategies.

4

Gabrielle Martineau

Next-Generation UM171 Analogs for Better Selectivity and Efficacy.

Our group previously developed the small molecule UM171 as a KBTBD4-dependent molecular glue degrader of CoREST1, which enables ex vivo expansion and lymphoid rejuvenation of human hematopoietic stem and progenitor cells (HSPCs). In addition to the original UM171-like molecules, we developed a series of analogs with improved selectivity. Here, we assessed the potency, efficacy, and selectivity of the top compounds in expanding cord blood-derived CD34 HSPCs in vitro and in reconstituting the hematopoietic system in xenotransplantation models. Results to be presented at the conference will be compared to those obtained historically with UM171. We expect that these new molecules will be particularly useful in indications where HSPC rejuvenation is desirable. This includes bone marrow and mobilized peripheral blood HSCs used in auto-transplantation and in solid organ tolerization.

5

Lucas Porras

Spatial Heterogeneity of Fbp1 Expression is Associated with Epithelial Identity and Invasive Features in Er-Positive Breast Cancer Cells.

Breast tumors expressing the estrogen receptor (ER), also known as luminal tumors, constitute the majority of breast cancer cases and are generally associated with favorable short-term outcomes. However, their risk of recurrence increases over time. To better understand the spatial and phenotypic characteristics of ER-positive tumors, we analyzed transcriptomic profiles to identify genes whose expression closely correlates with ESR1, the gene encoding the estrogen receptor. Notably, FBP1, a key enzyme in gluconeogenesis, showed strong co-expression with ER as well as with FOXA1 and GATA3, two transcription factors known to shape the luminal phenotype. FBP1 expression was enriched →

in ER-positive tumors and largely absent in more aggressive subtypes. In tumor tissue microarrays, FBP1 protein detection coincided with ER expression, supporting its role in maintaining luminal identity. Its levels were notably lower in high-grade and in the invasive compartments of tumors, suggesting a spatial and temporal regulation during tumor progression. FBP1 depletion in ER-positive cell lines was associated with a shift toward more basal-like features, including increased cellular migration and a mesenchymal morphology. These observations support the role of FBP1 as both a determinant and a marker of the luminal phenotype, its regulation contributing to the observed heterogeneity of phenotypes across breast cancer subtypes.

6

Agathe Descours

Exploring the Signaling and Location Bias of Pro- and Anti-Inflammatory Fpr2 Ligands.

GPCR-mediated signaling has been classically seen as a plasma membrane event, however, increasing evidence suggests that GPCRs can also signal from other organelles. Signaling modalities initiated at the plasma membrane have been shown to be sustained in the endosomes following receptor endocytosis. Such location-biased signaling in response to different ligands has been proposed to have distinct physiological outcomes. Here, using type-2 formyl peptide receptor, we investigated the signaling pathways engaged at the plasma membrane and the early endosomes in response to 4 different FPR2 ligands. We hypothesize that the stimulation of FPR2 with different agonists will lead to distinct Gα activation and β-arrestin recruitment, with physiological consequences. This is particularly relevant for FRP2 as both pro- and anti-inflammatory actions have been described for the activation of this receptor. Using BRET-based biosensors to detect the activation of different Gα protein subtypes, we show a differential activation of the Gα proteins and β-arrestin recruitment, depending on the ligand, and receptor localization. This work establishes the potential link between FPR2 biased signaling and the pro- or anti-inflammatory properties of FPR2 ligands. Understanding what drives pro- and anti-inflammatory responses from immune cells could help develop drugs that could inhibit inflammation in diseases where this phenomenon plays important roles, ie. cancer development.

7

Paige McCallum

Understanding the Role of P-S6 in Cancer-Associated Fibroblasts in the Breast Tumor Microenvironment.

Using highly multiplexed proteomic imaging techniques, we aim to leverage the ability to identify and characterize cancer-associated fibroblasts (CAFs) and other cells of the tumor microenvironment (TME) in situ. The TME describes the complex interactions between tumor cells, endothelial cells, immune cells, adipocytes, and CAFs. CAFs are one of the most abundant stromal components of the tumor microenvironment, playing a prominent role in cancer pathogenesis and treatment resistance. CAFs are made up of a heterogeneous group of highly plastic and context-dependent cells with their phenotype and function determined by interactions between neighboring cells. Distinct phenotypic CAF subtypes have been identified through molecular profiling techniques; myofibroblastic CAFs (myCAF), inflammatory CAFs (iCAFs), antigen-presenting CAFs (apCAFs), and other less common subtypes all contribute unique functions to the TME. Additionally, the spatial organization, neighboring cell composition, and transcriptomic profiles of CAFs are unique to each subtype. More broadly, CAFs →

engage in crosstalk with neighboring cells, activating signaling pathways both within themselves and in the surrounding cells. We have observed that a subset of CAFs express pS6. We seek to understand the crosstalk between pS6-positive tumor cells and other cells in the TME, notably CAFs, and their role in promoting a pro-metastatic phenotype.

8

Serena Chan

Evaluating Input Representations and Architectures for Learning Transcriptomic Embeddings.

Gene embeddings leverage large RNA-seq datasets by capturing gene co-expression patterns, allowing deep neural networks (DNNs) to numerically characterize gene functions and regulatory roles. Given their reliance on numeric vectors or matrices as input, these models are highly sensitive to how RNA-seq data is encoded. While traditional methods use raw expression values, ranking-based approaches, as inspired by word embeddings in natural language processing (NLP), focus on relative orderings rather than absolute counts. This results in an approach that filters out stochastic noise from low- or varying-coverage experiments. This project investigates how these two representations interact with various network architectures and their impact on biological inference. Raw expression and ranked inputs were compared across tasks including cell line identification and masked token pretraining. Preliminary results indicate comparable performance for cell line identification, suggesting the task is relatively insensitive to input encoding. In contrast, raw expression profiles outperform ranked embeddings on masked pretraining tasks, with highest prediction errors for mid-ranked genes. Ongoing work aims to quantify these differences across downstream tasks and understand the complementary strengths of these embeddings to determine whether joint learning can capture relationships within transcriptomic profiles and improve prediction accuracy across diverse biological tasks.

9

Vrinda Gupta

Spatial Characterization of the Heterogeneity of Cancer-Associated Fibroblasts in the Tumour Microenvironment of β1-Integrin Deficient Breast Tumours.

Breast cancer is the most commonly diagnosed cancer across the world, consisting of tumours with varied molecular profiles. One critical area of investigation is the role of β1-integrin, which facilitates cell adhesion to the extracellular matrix (ECM) and regulation of cellular processes such as cell cycle progression, survival, and motility. In cancer-specific contexts, β1-integrin promotes binding and signal transduction between the ECM and cytoskeletal proteins, driving changes within the tumour microenvironment (TME) that support metastasis. A major component of the TME are cancer-associated fibroblasts (CAFs), a heterogenous fibroblast population that facilitates tumour growth and invasion through ECM remodeling. In a β1-integrin deficient (β1KO) breast tumour model, we see fibrosis with increased CAF infiltration and ECM deposition. Resultantly, in this study, we are interested in elucidating the integrin-mediated crosstalk between the ECM and CAFs. To do this, we use highly multiplexed fluorescent microscopy of tissues using the PhenoCycler Fusion system to characterize CAF heterogeneity and spatial organization of the TME in β1KO breast tumours, to understand and define interactions between cell types. This information is crucial for developing more effective and personalized cancer therapies, improving patient outcomes, and advancing our overall understanding of cancer.

10

Camila Kiyan

Gpcr-Mediated Erm Activation Is Dependent on Gαq/gα12/13, Rho and Kinases Slk and Lok.

Ezrin, Radixin, and Moesin (ERM) protein family acts as cross-linkers between the plasma membrane and cytoskeleton, playing a crucial role in cell motility and cancer metastases. Previous studies showed that TBXA2R enhances cell motility by modulating ERMs in cancer cells through Gαq/11 and Gα12/13. This study investigates the role of each Gα subfamily in the GPCR-mediated ERM activation and downstream effectors. Using BRET-based biosensors in HEK293 parental and Gα proteins knock-out cells, we found that oxytocin and gonadotropin-releasing hormone receptors activated ERMs through Gαq/11 activation alone; whereas serotonin and cannabinoid receptors promoted ERMs activation through Gα12/13 activation alone, validated by rescuing Gα protein in Gα knock-out cells. Using pharmacological tools, we demonstrated that GPCR-mediated ERM activation is Rho-dependent, consistent with the ability of Gαq/11 and Gα12/13 to activate this effector. We identified SLK and LOK as kinases involved in GPCR-mediated ERM activation, coherent with ERMs activation requiring phosphorylation. In contrast, Gαs- and Gαi-coupled receptors had minimal effects on ERM activation. Activation of either Gαq/11 or Gα12/13 by different GPCRs leads to Rho activation, stimulating the kinases SLK and LOK, responsible for ERM activation. This study establishes new insights into GPCRs/ERMs signaling pathway, opening potential roles of GPCRs in cancer metastasis.

11

Carl Munoz

Quantifying the Impact of Sequencing Depth Reduction and Machine-Learning-Based Denoising on Rna-Seq Data.

RNA sequencing is a technology that has advanced our understanding of cellular biology. However, this technology is also expensive ($150 per sample), thus limiting the amount of data that can be acquired given a budget. While costs were previously bottlenecked by library preparation costs, protocols such as Drug-Seq are currently leading to a drastically reduced library cost. While decreasing the sequencing depth (the number of reads sequenced per sample) also significantly reduces costs, it also decreases the quality of the data. As such, we aim to quantify the impact of low-depth RNA-seq (1M or fewer reads) and identify methods of machine-learning-based denoising to increase data quality while maintaining lower costs per sample. We have developed a neural network trained on The Cancer Genome Atlas that denoises low-depth RNA-seq. We have also identified that denoising recovers most information lost due to depth reduction, including gene expression, differentially expressed genes, and gene set enrichment analysis. Finally, we are developing a Bayesian framework as an alternate method that better captures uncertainty caused by depth reduction. Currently, following our denoising methods, the cost-benefit ratio remains competitive to full-coverage RNA-seq for 1M reads and a tenth of the price. This research has the potential to change RNA-seq standards by reducing costs for all applications, including the acquisition of large data sets or individual costs for personalized medicine.

12

Lea Kaufmann

In Silico Prediction of Chemical Compounds' Biological Activities Holds Great Potential to Accelerate the Early Steps of Drug Discovery.

Our objective was to develop a deep neural network to predict the expression profile of a target cell line treated with a compound given four modalities in input: (1) an embedding of the compound's structure, (2) an embedding of a reference cell line, (3) the expression profile of the reference line treated with the same compound, and (4) an embedding of the target cell line. Gene expression data came from the LINCS dataset (Broad Institute, 2017) and the Tahoe-100M dataset (Zhang et al., 2025). The embeddings were derived from open-source foundation models. An ablation study was conducted to identify the contribution of each of these input modalities to the model's performance. This approach enables better in silico selection of candidate compounds, bypassing high-throughput screening and going directly to validation.

13

Nicolas Jacquin

K-Meromics: Developing Methods for Reference-Free Sequencing Data Analysis.

Reference-based analyses discard non-aligning reads, overlooking biologically important elements such as alternative open reading frames and aberrantly expressed tumor-specific antigens (aeTSAs). Systematic discovery of these sequences requires not only reference-free methods but also tools that scale to the massive size of modern transcriptomic datasets. We present a reference-free framework optimized for both speed and scale. Using memory-efficient data structures, it holds billions of k-mers and their counts simultaneously and supports parallel traversal across hundreds to thousands of RNA-Seq samples. This enables rapid reconstruction of transcriptomic profiles and efficient operations across the table in a fraction of the time required by alignment-based methods. By joining a table of sequenced aeTSA peptides and one of RNASeq samples, one can rapidly find the origin of each peptide across thousands of samples at a time, completely reference free, allowing unbiased discovery of non-canonical transcripts. By combining reference independence with computational efficiency, this work lays the foundation for systematic and high-throughput identification of aeTSAs. The ability to analyze massive datasets quickly and without bias opens new opportunities for clinically relevant discoveries in immunopeptidomics and transcriptomics at large.

14

Nitya Khetarpal

Characterizing Peripheral Immune Cells in Primary Progressive Multiple Sclerosis at the Single-Cell Level.

Introduction. Multiple sclerosis (MS) is a chronic autoimmune disorder marked by peripheral immune infiltration in brain tissue. In Canada ~10% of patients present with primary progressive MS (PPMS), defined by steady neurological decline. While current disease-modifying therapies (DMTs) prevent central leukocyte invasion, they are less effective in PPMS, necessitating investigation of immune progression mechanisms. Single-cell RNA sequencing (scRNAseq) enables profiling of immune heterogeneity. I aim to compare disease-defining immune signatures in PPMS to RRMS and healthy control cells, assess gene expression relative to disease severity, and evaluate how DMT influences →

PPMS transcriptional programs via scRNAseq. **Methods**. I selected an age and sex-matched cohort (N=56) from samples collected in the CANadian PROspective COhort Study for People Living with MS (CanProCo). I made a preprocessing pipeline with six samples and 0.5-million single cells. Results. PPMS patients exhibited longer disease duration than RRMS. Disease severity via Expanded Disability Status Scale (EDSS) averaged 3.7±1.4 in PPMS versus 1.2±0.7 in RRMS. I identified 12-16 clusters per sample post-integration; batch correction and imputation are ongoing. **Conclusion**. Next, I will compare condition cluster composition, scale up the pipeline, and validate subpopulations to define cell-specific transcriptional programs in PPMS, informing potential biomarker and targeted therapeutic discovery.

15

Pedro Scarpelli Pereira

Gpcr-Mediated Sequestration of Sh2-Domain Proteins Disrupts Rtk Signaling.

SH2 (Src-Homology 2) domains are protein-protein interaction modules responsible for binding to phosphotyrosine residues. SH2-domain proteins are critical signaling mediators of Receptor Tyrosine Kinases (RTK). Although G protein-coupled receptors (GPCRs) are not known to directly interact with SH2-domains, the cross regulation of RTK signaling by GPCRs is well documented. However, the molecular mechanisms underlying such crosstalk remain incompletely understood. Given the importance of both GPCRs and RTKs in human pathophysiology and as drug targets, a better understanding of the interactions between their signalling pathways could offer new insights into targeted therapies for diseases linked to signaling dysregulation. In this study, we found that activation of a specific group of GPCRs promote the translocation of RTK effectors from the plasma membrane to the nucleus. This translocation was found to be dependent of the Rho pathway, including downstream kinases. This compartmentalization reduced their availability to RTKs at the plasma membrane, significantly decreasing RTK signaling. Our findings demonstrate GPCR activation disrupts RTK signaling by relocating SH2-domain proteins from the plasma membrane to the nucleus in a Rho dependent manner. This reveals a novel crosstalk pathway by which GPCRs inhibit RTK-mediated transcriptional activity.