Faculté de médecine
Département de biochimie
et médecine moléculaire
Université de Montréal

TISSEZ UN LIEN AVEC VOTRE COMMUNAUTE SCIENTIFIQUE!

RENCONTRE SCIENTIFIQUE LOUIS-PHILIPPE-BOUTHILLIER

14 ET 15 MAI 2026

ESTRIMONT SUITES & SPA - ORFORD

PRESENTATIONS ORALES - SPEED TALK - COMPETITION PAR AFFICHES - ACTIVITE PLEIN-AIR

PROGRAMMATION DE L'ÉVÉNEMENT
EVENT PROGRAM

MOT DE BIENVENUE

C’est avec plaisir que nous vous souhaitons la bienvenue à cette édition 2026 de la rencontre Louis-Philippe-Bouthillier du Département de biochimie de l’Université de Montréal. Le professeur Louis-Philippe Bouthillier, biochimiste de grande qualité, est décédé le 22 juillet 1994 à l'âge de 81 ans. Après avoir obtenu un Ph.D. à l'Université du Wisconsin à Madison, il s'est joint au corps professoral du Département de biochimie de l'Université. Dès son arrivée, il a su attirer dans ses laboratoires de nombreux étudiants désireux de se familiariser avec les techniques et les procédures les plus avant-gardistes. Plusieurs d'entre eux ont par la suite entrepris des carrières remarquables dont le lancement a été en grande partie catalysé par la formation reçue chez Bouthillier.

Cette rencontre est maintenant devenue une tradition qui permet de rassembler tous les membres et intervenants en recherche de notre département et de permettre ainsi à chacun de bénéficier de ce forum privilégié pour prendre connaissance et discuter des différents projets de recherche.

Nous remercions tous les conférenciers et les présentateurs d’affiches d’avoir accepté de prendre de leur temps pour partager avec nous le fruit de leurs recherches des dernières années. Enfin, un remerciement sincère à tous les participants, qui assureront la qualité des interactions, garantes du succès de cet événement dont nous sommes fiers.

Bonne retraite!

Le comité organisateur

REMERCIEMENTS

Le comité organisateur tient à exprimer sa gratitude envers tous ceux et celles qui ont participé, de près ou de loin, à la préparation de cet événement. Leur aide et leurs encouragements ont été fort appréciés. Ceci inclut également nos partenaires financiers, regroupés à la fin de ce prospectus, sans qui, toute cette entreprise n’aurait pu être réalisée.

MERCI!

Votre comité organisateur

Malik Chaker-Margot	Audrey Noël
Pascale Legault	Benoit Bessette
Gerardo Ferbeyre	Emmanuel Bajon
Philipe Lampron	Yani Bouaziz
Elaine Meunier	Justina Chu

Conception du programme : *Yani Bouaziz et Philipe Lampron*

JEUDI LE 14 MAI 2026

9h00	**ARRIVÉE DES PARTICIPANTS** *ARRIVAL OF PARTICIPANTS*
10h30	**CÉRÉMONIE D'OUVERTURE** *OPENING CEREMONY* **Pascale Legault, Directrice**

SESSION – Chercheurs du département
Modératrice: Pascale Legault

10h40	**Jean Benoit LALANNE** Multi-scale epistatic profiling of sequence-to-function maps in mammalian transcriptional regulation
11h20	**El Bachir AFFAR** Liquid phase separation explains chromatin condensation during apoptosis
12h00	**LUNCH**

SESSION 1
ARN / *RNA*
Modérateur : Pascal Chartrand

13h40	**Hebatallah Samy SAAD – Labo Legault** Insights into miRNA biogenesis regulation by the Zika virus capsid protein
14h00	**Justina CHU – Labo Zenklusen** Investigating real-time spatio-temporal progression of ribosome biogenesis using single-molecule resolution microscopy
14h20	**Mouna FERDEBOUH – Labo Chartrand** Impact des mutations de POT1 et de la voie ATR sur le recrutement de la télomérase
14h40	**Carl MUNOZ – Labo Lemieux** Quantifier l'impact du séquençage de basse profondeur et du débruitage par réseaux de neurones de données RNA-seq
15h00	**Simon CHASLES – Labo Major** The RNA Interaction Maps (RIMaps): Introducing RIMap-RISC as a tool to model miRNA:mRNA interactions

PRÉSENTATIONS RAPIDES - SPEED TALKS

15h20	**Davoud AMIRI MEHR – Labo Ferbeyre** Role of Nucleolus-Associated Chromatin Domains in Cellular Senescence and Cancer

Audrey LANGLOIS – Labo Ferbeyre
Mitochondrial Iron Sensitizes Senescent Cancer Cells to Ferroptosis

Marine GUELLE – Labo Archambault
Phosphorégulation du nucléole par la protéine phosphatase 1 (PP1)

Malana LOXAM – Labo Strauss
De nouvelles cibles pour le traitement du poliovirus grâce aux interactions entre VP4 et l'ARN

Léo MILLOT – Labo Archambault
Rôle de la phosphatase PP2A-B56 dans la régulation des centrosomes

Helena DE CASTRO ALVARENGA – Labo Strauss
Structural insights into chromatin organization in situ

Charles-Éric BRY – Labo François
Ancestral state reconstruction using branched optimal transport.

Mina ANADOLU – Labo Legault
The role of long non-coding RNAs in modulating the alpha-synuclein microRNA regulatory pathway in Parkinson's Disease

Nicolas POUDEROUS – Labo Ferbeyre
Étude du rôle des ARN non codants nucléolaires dans le cancer du pancréas dans l'induction de la senescence par thérapie

Rini Ravindran PATEL – Labo Serohijos
Transcriptome-informed prediction of protein interaction network rewiring in breast cancer models

Mélanie LEMAIRE – Labo Major
Understanding The Roles Of RNA Structural Dynamics And RNA-Binding Protein Interactions In The Biogenesis Of miR-125a, miR-128-1, and miR-188

16h30	**COMPÉTITION PAR AFFICHES organisée conjointement avec l'AEECSBUM et l'AÉBINUM** *POSTER COMPETITION organized jointly with AEECSBUM and AEBINUM* **AFFICHES IMPAIRES: 16h30 à 17h45** **AFFICHES PAIRES: 17h15 à 18h30** **FINALE: 18h30 à 19h30**
19h30	**BANQUET** *DINNER*
20h30	**PRÉSENTATION SPÉCIALE** *SPECIAL PRESENTATION*
21h00	**REMISE DE PRIX** *AWARDS*

21h30	**SOIRÉE, JEUX ET DANSE** *PARTY, GAMES AND DANCING*

VENDREDI LE 15 MAI 2026

7h30	**PETIT DÉJEUNER** (pour les participants résidants à l'hôtel seulement) *BREAKFAST (only for participants residing at the hotel)*

SESSION 2
Signalisation
Modérateur : Gerardo Ferbeyre

9h00	**Gerardo Raul DIEZ RODRIGUEZ – Labo Ferbeyre** S6K Inhibition as a therapeutic strategy to target relapse cells in pancreatic ductal adenocarcinoma
9h20	**Maria CHEMROUK – Labo Roy** Signalisation JAK/STAT lors de la régénération du membre chez l'axolotl
9h40	**Laura CHASTANT – Labo Archambault** BAF protège contre la réponse cGAS-STING aux ponts de chromatine
10h00	**Romain VILLOT – Labo Mallette** CH25H drives the senescence-associated secretory phenotype and promotes retinopathy
10h20	**Asmaa Toumi – Labo Rossignol** Plateforme de validation fonctionnelle intégrant le FLIM-FRET pour disséquer les troubles neurodéveloppementaux associées à TRIO

10h40	**PAUSE CAFÉ**

SESSION 3
Bio-informatique et évolution / *Bioinformatics and Evolution*
Modérateur : Sébastien Lemieux

11h10	**Viktoria MOCHULSKA – Labo François** Generative landscape models of cellular differentiation
11h30	**Léa KAUFMANN – Labo Lemieux** Transcriptomes as an experimentally measured proxy for small molecule representation enables generalization across biological activity measures

11h50	**Matthew SCICLUNA – Labo Hussin** PHATE-Derived Ancestry Coordinates Capture Continuous Population Structure in Human Genomic Data
12h10	**Jacob BEAULAC – Labo Serohijos** A universal translator of transcriptomes to protein interactomes for molecular interpretation of cell and tissue models
12h30	**LUNCH**
14h00	**ACTIVITÉ EDI**
	SESSION 4 **Biologie structurale /** *Structural biology* **Modérateur :** Malik Chaker-Margot
14h40	**Mohamed Mourad KENFAOUI – Labo Chaker-Margot** Functional Role of OGDH in Metabolic Regulation: A Structural and Molecular Approach
15h00	**Harry MCFARLANE – Labo Strauss** Structural investigation of Cardiovirus rueckerti receptor interactions.
15h20	**Guillaume BEAUCAIRE – Labo Omichinski** Spécificité de MerB et transfert du produit vers MerA chez E. coli
	SESSION - Boursiers Robert Cedergren 2026-2027 **Modératrice:** Pascale Legault
15h55	**Boursier – Programme de bio-informatique**
16h15	**Boursier – Programme de biochimie**
16h40	**MOT DE CLÔTURE /** *CLOSING WORD* Gerardo Ferbeyre
17h00	**ACTIVITÉ** – **Randonnée Parc du Mont-Orford et souper Micro-Brasserie** *ACTIVITY – Mont-Orford Park hike and Micro-Brasserie dinner*

SOYEZ DES NÔTRES POUR L'ÉDITION 2028 !

ABSTRACTS / RÉSUMÉS

Rencontre Louis-Philippe-Bouthillier 2026

PRÉSENTATIONS ORALES / ORAL PRESENTATIONS

SESSION - Chercheurs du département

Jean-Benoit Lalanne

Multi-scale epistatic profiling of sequence-to-function maps in mammalian transcriptional regulation

Transcriptional regulation is dictated by interactions between transcription factors (TF), chromatin remodelers, and co-factors. These interactions are encoded in the DNA sequence of control elements (often cis-regulatory elements or CREs). I will present three ongoing projects which map out epistasis at different genetic scales within and between CREs. First, we performed combinatorial gain-of-function profiling of the top point mutations across multiple CREs. This represents the first comprehensive assessment of high-order epistasis within CREs. Second, we constructed thousands of bottom-up synthetic arrays of TF binding sites, finding strong biological activity and evidence of TF-to-TF synergies. Third, we developed a new double-barcode reporter assay to query enhancer-promoter communication in a fully multiplex manner and identify pervasive short-range activity decay. Together, these chart a phenomenology for transcriptional sequence-to-function maps with actionable insights for synthetic biology and biomedical engineering applications.

El Bachir Affar

Liquid phase separation explains chromatin condensation during apoptosis

Phase separation is a physicochemical process increasingly recognized for its critical function in biological processes. During apoptosis, the nucleus undergoes a series of cytological changes that result in a highly compacted chromatin state, often referred to as chromatin hypercondensation. First observed in dying cells in the late 19th century, the molecular underpinnings of chromatin hypercondensation have remained elusive. We now demonstrate that, during apoptosis, chromatin undergoes mesoscale phase separation analogous to spinodal decomposition-mediated demixing. The apoptotic chromatin undergoes a regulated process of coacervation and coalescence involving the ordered action of caspases and the proteasome, culminating in the formation of a singular terminal condensate known as the pyknotic nucleus. Our study resolves a longstanding debate regarding how chromatin hypercondensation is orchestrated during apoptosis, and provide a mechanism that might explain the manner in which dying cells limit the release of immunogenic genomic DNA.

SESSION 1 - ARN

Hebatallah Samy Saad - Labo Legault

Insights into miRNA biogenesis regulation by the Zika virus capsid protein

MicroRNAs (miRNAs) are key regulators for gene expression. They are transcribed in precursor forms that are processed by Dicer to generate the mature miRNAs. Interestingly, the activity of Dicer is inhibited by the Zika virus capsid protein (ZVCP), which resulted in a global decrease in the miRNA levels in neural stem cells. This interaction is likely the cause of the severe neurological complications associated with Zika infection. However, the mechanism of Dicer regulation by the ZVCP is not well understood. Here, we employed biochemical tools, enzyme kinetics, cryo-EM, confocal microscopy methods to investigate the interaction between Dicer and the ZVCP. Enzymatic assays showed a potent inhibition of Dicer by the ZVCP. This inhibition is not explained by substrate sequestration. However, the ZVCP-Dicer interactions lead to biomolecular condensates, creating a microenvironment incompatible with Dicer activity. Our findings reveal a previously unrecognized mechanism of host Dicer regulation via biomolecular condensation, which can guide future therapeutic approaches aiming to combat the Zika infection.

Justina CHU - Labo Zenklusen

Investigating real-time spatio-temporal progression of ribosome biogenesis using single-molecule resolution microscopy

Ribosome biogenesis requires the interplay of hundreds of ribosome biogenesis factors (RBFs), ribosomal proteins (RPs) and rRNAs, and occurs mainly in the nucleolus, a multilayered condensate. Despite extensive research, the spatio-temporal progression of ribosome biogenesis remains poorly understood, in part because of technical limitations due to its rapidly changing dynamics. To overcome some of these limitations, we used live-cell single-molecule microscopy to elucidate the spatial progression of ribosome biogenesis in real time. Using Halo-tagged RPs/RBFs as proxies for the maturing subunits, fast imaging enabled us to monitor the dynamic behaviour of single proteins within nucleolar subcompartments at ~50nm resolution. Single-particle movement analysis of pre-ribosome-bound RPs reveals confined dwell times and lateral movement within nucleolar subcompartments. Taken together, live-cell single-molecule microscopy allows us to further study the spatial-temporal behaviour of maturing ribosomal subunits.

Mouna Ferdebouh - Labo Chartrand

Impact des mutations de POT1 et de la voie ATR sur le recrutement de la télomérase

La longueur des télomères est maintenue par la télomérase, dont l'expression diminue dans les cellules somatiques, entraînant leur raccourcissement et la sénescence. À l'inverse, elle est réactivée dans près de 90 % des cancers, favorisant l'immortalisation cellulaire. L'homéostasie des télomères est régulée par le complexe shelterin, incluant POT1, qui se lie à l'ADN télomérique simple brin et contrôle la télomérase ainsi que la voie ATR. Des mutations de POT1, associées à plusieurs cancers, induisent une élongation anormale des télomères via des mécanismes encore mal compris. Par imagerie en molécules uniques de l'ARN de la télomérase (hTR) et analyse par CoPixie, nous avons montré que certains mutants de POT1 augmentent l'accès et la durée des interactions de la télomérase aux télomères. De plus, l'inhibition de ATR réduit ces interactions, suggérant un rôle clé de cette voie dans leur régulation. Ces résultats mettent en évidence une interaction fonctionnelle entre POT1 et ATR dans le contrôle du recrutement de la télomérase.

Carl Munoz - Labo Lemieux

Quantifier l'impact du séquençage de basse profondeur et du débruitage par réseaux de neurones de données RNA-seq

Le RNA-seq est une technologie permettant une compréhension approfondie de l'activité cellulaire, mais son coût demeure élevé (environ 150 $ par échantillon bulk). Réduire la profondeur de séquençage permet de diminuer ces coûts, mais entraîne aussi une perte de qualité des données. Nous visons donc à quantifier l'impact de cette réduction de profondeur et à identifier des méthodes de débruitage pouvant augmenter la qualité de ces données. Nous avons développé des modèles d'apprentissage automatique et d'inférence bayésienne capables de reconstruire des données RNA-seq de pleine profondeur à partir de données de basse profondeur. Ces approches permettent de récupérer une grande partie de l'information biologique perdue, notamment la classification des types et sous-types de cancer, ainsi que l'identification des gènes différentiellement exprimés. Cette recherche pourrait contribuer à modifier les standards du RNA-seq, tant pour la médecine personnalisée que pour l'acquisition de larges volumes de données auparavant inaccessibles.

Simon Chasles - Labo Major

The RNA Interaction Maps (RIMaps): Introducing RIMap-RISC as a tool to model miRNA:mRNA interactions

Nos travaux visent à comprendre et à concevoir des systèmes de régulation basés sur l'ARN grâce à des approches de modélisation structurelle et intégrative. Nous développons des outils informatiques permettant d'élucider comment la structure de l'ARN gouverne les interactions avec des facteurs régulateurs, avec un accent particulier sur les microARN (miARN) et les protéines liant l'ARN (RBP). Premièrement, à travers la plateforme RIMap-RISC, nous modélisons le ciblage des miARN à l'échelle du transcriptome en intégrant l'accessibilité structurale, les paramètres énergétiques de liaison, incluant les constantes de dissociation (Kd), ainsi que le contexte de séquence (Chasles et al. 2026). Cette approche permet d'identifier des sites cibles fonctionnels et soutient la conception rationnelle d'ARN régulateurs synthétiques capables de moduler de manière coordonnée plusieurs cibles au sein de réseaux géniques. Deuxièmement, nous étudions les déterminants structuraux de la biogenèse des miARN en nous concentrant sur les paysages de repliement des pri-miARN (Lemaire et al., en préparation). Nous cherchons à identifier des caractéristiques d'accessibilité et des motifs ARN qui régulent l'efficacité du clivage par le microprocesseur. Ces travaux apportent un éclairage sur la manière dont la dynamique structurale façonne la maturation et l'expression des miARN. Ensemble, ces projets établissent un lien entre la biologie fondamentale de l'ARN et sa modélisation structurelle et intégrative, ouvrant la voie à la prédiction des interactions régulatrices et au développement d'outils ARN programmables pour étudier et contrôler l'expression génique.

SESSION 2 - Signalisation

Gerardo Raul Diez Rodriguez - Labo Ferbeyre

S6K Inhibition as a therapeutic strategy to target relapse cells in pancreatic ductal adenocarcinoma

Cellular senescence is a stress-induced state characterized by stable cell-cycle arrest, extensive metabolic reprogramming, and acquisition of a pro-inflammatory senescence-associated secretory phenotype (SASP). In pancreatic ductal adenocarcinoma (PDAC), the chemotherapy regimen FOLFIRINOX is a potent inducer of therapy-induced senescence. However, clinical responses are frequently transient, and tumor relapse remains a major therapeutic challenge. To model relapse in vitro, we generated KP4 relapse-derived cells through five consecutive cycles of FOLFIRINOX treatment (R5 cells). Compared to parental KP4 cells, R5 cells exhibited accelerated relapse kinetics, enhanced proliferative capacity following treatment withdrawal, and reduced sensitivity to FOLFIRINOX rechallenge. Integrated transcriptomic (RNA-seq) and proteomic (mass spectrometry) analyses identified S6K-dependent signaling as a recurrent and actionable vulnerability in R5 cells. Pharmacological inhibition of S6K, in combination with FOLFIRINOX, maintained the senescent state and prevented the re-emergence of proliferative tumor cells in vitro. By defining the S6K-dependent signaling axis and its downstream effectors, this work aims to uncover targetable vulnerabilities in relapse-driving cells and to inform rational combination therapies designed to enhance the durability of FOLFIRINOX responses and limit tumor recurrence in PDAC.

Maria Chemrouk - Labo Roy

Signalisation JAK/STAT lors de la régénération du membre chez l'axolotl

La capacité de régénération tissulaire varie considérablement selon les espèces. Contrairement aux mammifères qui cicatrisent leurs blessures en formant du tissu fibreux, l'axolotl régénère des structures complexes telles que ses membres. Comprendre les mécanismes moléculaires à la base de cette capacité représente une avenue prometteuse pour la médecine régénérative. La phase de préparation de la régénération du membre est principalement régulée par la voie TGF-b qui transmet son signal via Smad2 et Smad3. Des analyses sur des blastèmes en régénération indiquent une activation préférentielle pour Smad2, associé à la prolifération cellulaire, par rapport à Smad3, davantage lié à la fibrose. Les mécanismes responsables de cette activation différentielle restent inexpliqués. L'hypothèse de ce projet est que STAT3, activé par la réponse inflammatoire post-amputation, inhibe l'activation de Smad3, favorisant ainsi la régénération. Pour tester cette hypothèse, des axolotls sont traités avec des inhibiteurs de la voie JAK/STAT afin d'évaluer leurs effets sur la régénération et sur l'activation différentielle de Smad2 et Smad3, par des approches histologiques, d'immunobuvardage et qPCR.

Laura Chastant - Labo Archambault

BAF protège contre la réponse cGAS-STING aux ponts de chromatine

Des défauts mitotiques peuvent induire l'activation de réponses immunitaires innées. Parmi eux, les micronoyaux ont été proposés comme capables d'activer la voie pro-inflammatoire cGAS-STING. Cependant, la contribution des micronoyaux ou d'autres défauts post-mitotiques à la réponse cGAS-STING reste incertaine. Nous avons comparé la capacité de défauts post-mitotiques résultants de l'inhibition du point de contrôle d'assemblage du fuseau mitotique (par inhibition de MPS1) ou d'une perturbation du réassemblage nucléaire (par inactivation de BAF) à induire la réponse cGAS-STING. Combiner ces deux perturbations renforce de façon synergique la réponse cGAS-STING. Cet effet n'est pas dû à une induction de micronoyaux, mais est corrélé à une augmentation des ponts de chromatine déstabilisés, aboutissant à des structures qui recrutent fortement cGAS. Nos résultats suggèrent qu'en stabilisant les ponts de chromatine, BAF contribue à prévenir la dégénérescence de ces ponts en structures de chromatine activant cGAS. Ce travail permet de comprendre comment l'immunité innée détecte les défauts mitotiques

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Romain Villot - Labo Mallette

CH25H drives the senescence-associated secretory phenotype and promotes retinopathy

Cellular senescence is a biological response to stress associated with numerous pathological conditions, including ischemic retinopathies. Clearance of senescent cells or limiting their senescence-associated secretory phenotype (SASP) improved vascular phenotypes in mouse models of retinopathies and vision in human clinical trials for diabetic eye disease. However, the molecular mechanisms underlying the secretory phenotype of senescent cells in ischemic retinopathy remain unclear. Using a mouse model of retinopathy (oxygen-induced retinopathy, OIR), we identify a central role for cholesterol 25-hydroxylase (CH25H)—the enzyme that produces 25-hydroxycholesterol (25-HC)—in driving cellular senescence. The level of CH25H is high in senescent cells and its depletion limits stress-induced senescence. In addition, 25-HC triggers cellular senescence and the SASP through calcineurin-mediated activation of lysosome-associated transcription factors. In a mouse model of retinopathy, CH25H deletion decreases the senescence burden within the retina leading to improved physiological revascularization of the retina. Thus, CH25H and the oxysterol 25-HC are critical mediators of cellular senescence contributing to ischemic retinopathies.

Asmaa Toumi - Labo Rossignol

Plateforme de validation fonctionnelle intégrant le FLIM-FRET pour disséquer les troubles neurodéveloppementaux associées à TRIO

Les mutations perte ou gain de fonction du gène TRIO sont associées à un large spectre de troubles du neurodéveloppement (NDDs). TRIO code une Rho-guanine nucléotide exchange factor (RhoGEF) connue pour activer Rac1 et RhoA, deux RhoGTPases impliqués dans la migration cellulaire. Des données récentes de notre groupe indiquent que la délétion conditionnelle de Trio dans les interneurones GABAergiques (INs) altère le développement morphologique et la migration de ces INs, entraînant une réduction de l'inhibition corticale, des comportements de type autistique et de l'épilepsie chez les souris TriocKO. Pour tester si les troubles associés à TRIO résultent d'une telle altération du développement et de la migration des INs, nous avons conçu une plateforme de validation fonctionnelle permettant d'exprimer un ADNc mutant (MT), portant des variants dérivés de patients, ou l'ADNc sauvage (WT) dans des explants de l'éminence ganglionnaire médiane (MGE) d'embryons TriocKO à e13.5. Nous avons étudié la dynamique migratoire et le développement morphologique des INs à l'aide d'imagerie time-lapse haute résolution et quantifié la morphologie cellulaire 3D avec Neurolucida. Nos résultants montrent que les mutations situées dans le domaine GEFD1, ne restaure ni le retard migratoire ni la morphologie aberrante des INs TriocKO. En outre, à l'aide d'essais FLIM-FRET, nous démontrons que ces mutations entraînent une réduction de l'activité de Rac1.

SESSION 3 - Bio-informatique et évolution / Bioinformatics and Evolution

Viktoria MOCHULSKA - Labo François

Generative landscape models of cellular differentiation

Cellular differentiation is a process by which cells become specialized to perform a particular function in the body. It is often envisioned as a "Waddington landscape", where cells, like balls, roll downhill and end up in one of the deep valleys – one of the possible cell fates. Thanks to recent advances in single-cell technologies, this metaphor can be turned into a quantitative model, opening an avenue for understanding, predicting, and guiding cell fate decisions. We propose Evoscape, a method for the systematic generation of such landscape models based on data. For constructing the landscape, we combine simple building blocks such as hills and valleys, creating a flexible yet interpretable model. This allows us to optimize both the topography (location and depth of features) and topology (the routes taken by the cells). To fit landscapes to data, we use an algorithm that mimics evolution and apply our method to different biological examples. From hundreds of optimized landscapes, we identify a small number of distinct possible solutions. These solutions, however, share a common topography, which shows how the landscape is constrained by the data, allowing for the systematic generation of interpretable and predictive models.

Léa KAUFMANN - Labo Lemieux

TRANSCRIPTOMES AS AN EXPERIMENTALLY MEASURED PROXY FOR SMALL MOLECULE REPRESENTATION ENABLES GENERALIZATION ACROSS BIOLOGICAL ACTIVITY MEASURES

AI holds promise for in silico drug screening, but approaches relying solely on chemical structure fail to capture the complex biological interactions within the cell (Moshkov et al 2023). We hypothesize that the transcriptomic response of a reference cell line to a treatment, measured as changes in gene expression (delta profile), is a meaningful representation of that treatment, implicitly encoding the compound's activity, dose, and exposure time. The target cell line is represented by its untreated expression profile. We developed a deep neural network predicting the delta profile of a target cell line given the delta profile of a reference cell line exposed to the same treatment, and the untreated profile of the target cell line. We further investigate structural embeddings from molecular foundation models as an additional compound representation. Gene expression data came from LINCS (Broad Institute 2017) and Tahoe-100M (Zhang et al 2025). Our model predicts Tahoe delta profiles with a Pearson correlation exceeding 0.7 with the ground truth. On LINCS, results are preliminary, and work is ongoing. Structural embeddings from foundation models yield no improvement, consistent with recent literature. These findings suggest that delta profiles are effective representations of compound activity, with promise for generalizing predictions across cell lines.

Matthew Scicluna - Labo Hussin

PHATE-Derived Ancestry Coordinates Capture Continuous Population Structure in Human Genomic Data

Large-scale human genomic datasets are commonly visualized using low-dimensional embeddings as ancestry coordinates, yet widely used methods often fail to faithfully represent continuous population structure. Linear approaches such as PCA capture global variation but miss fine-scale structure, while nonlinear methods like t-SNE and UMAP preserve local relationships at the expense of global coherence, often producing disconnected clusters. Here, we demonstrate how PHATE, a diffusion-based manifold learning method, can recover both local and global structure when appropriately tuned. We show that neighborhood scale plays a critical role: small values lead to disconnected representations, while larger values enable recovery of continuous geographic and admixture patterns. Using both synthetic data and real-world cohorts, including the 1000 Genomes Project, HGDP, UK Biobank, and All of Us, we demonstrate that PHATE more faithfully captures population structure than existing approaches. These results highlight the importance of parameter selection and sampling design, and support the use of diffusion geometry for constructing interpretable ancestry coordinates.

Jacob Beaulac - Labo Serohijos

A universal translator of transcriptomes to protein interactomes for molecular interpretation of cell and tissue models

Identifying molecular representations that capture distinct cellular states is a central challenge in biology. Protein–protein interaction (PPI) networks reflect variation in cell types and biochemical pathways, yet measuring them at scale remains impractical. We reasoned that PPI affinity and complex abundance could be predicted from transcript levels, given the evolutionary coupling between protein abundance and gene expression. We present UTTOPIA (Universal Translators of Transcriptomes to Protein Interactomes Algorithms). By combining RNA-seq data with protein turnover and localization variables, UTTOPIA estimates PPI fraction bound and binding affinity with a level of accuracy comparable to experimental measurements. This framework enables the molecular characterization of cells and tissues, facilitates mapping of functional transitions, and supports the interpretation of genetic variation.

SESSION 4 - Biologie structurale / Structural Biology

Mohamed Mourad KENFAOUI - Labo Chaker-Margot

Functional Role of OGDH in Metabolic Regulation: A Structural and Molecular Approach

Cells must dynamically reprogram their metabolism to match energy demand, nutrient availability, and redox state. The tricarboxylic acid (TCA) cycle lies at the heart of this adaptive process, acting as a central hub that integrates metabolic inputs within mitochondria. Disruption of this regulation is now recognized as a unifying feature of diverse diseases, including cancer and type 2 diabetes, highlighting the need to understand how metabolic control is achieved at the molecular level. The α-ketoglutarate dehydrogenase complex (OGDHc) occupies a strategic position within the TCA cycle by catalyzing an irreversible reaction that directly links carbon flux to mitochondrial redox balance. OGDH responds to key metabolic signals such as calcium, ATP, ADP, and NADH, allowing it to function as a metabolic sensor. Despite decades of biochemical studies, how these signals are structurally integrated to control OGDH activity remains largely unknown, particularly in the human enzyme. This project aims to define how allosteric regulation controls OGDH activity by directly visualizing ligand-induced conformational changes using cryo-electron microscopy (cryo-EM). Preliminary results establish both feasibility and novelty. Human E1 subunit was produced and purified, and structural analysis revealed that the enzyme functions as a stable dimer whose regulation is mediated by subtle, ligand-dependent conformational changes rather than large-scale rearrangements. 3.0 Å resolution cryo-EM structures identified an ATP-binding pocket located away from the catalytic site, providing direct structural evidence for allosteric control. Building on these findings, the project will systematically map the binding sites for adenine nucleotides, α-ketoglutarate, and NADH, and determine how each regulator reshapes OGDH conformation. These structural states will be directly linked to enzymatic activity using functional assays, and key regulatory residues will be validated through targeted mutagenesis. By combining high-resolution structural biology with functional analysis, this work will generate a coherent molecular model of how energy status, substrate availability, and redox signals converge on OGDH to control metabolic flux. Beyond advancing fundamental understanding of mitochondrial metabolism, this project will provide a structural framework that can be applied to broader questions of metabolic dysregulation in human disease.

Harry McFarlane - Labo Strauss

Structural investigation of Cardiovirus rueckerti receptor interactions.

Current understanding of viral cell entry in picornaviruses is limited, preventing the development of effective therapies. Cardiovirus rueckerti (EMCV) infects a diverse range of mammalian hosts, such as mice, primates, pigs, lions, elephants, and humans. EMCV infection results in a wide variety of symptoms in its different hosts, such as myocarditis, encephalitis, reproductive failure, and diabetes. While serious infection in humans is rare, usually resulting in asymptomatic or mild disease, this virus presents a serious risk of recombination and zoonotic transmission. EMCV cell entry occurs through receptor-mediated endocytosis, and to date 2 receptors have been identified, VCAM1 in mice and ADAM9 in humans. Despite the seemingly unrelated predicted structure of these two receptors both allow infection, implying a degree of flexibility in the required receptor-capsid interaction. Using single particle cryo-electron microscopy we have obtained high-resolution structures of EMCV in complex with human and mouse ADAM9.

Guillaume Beaucaire - Labo Omichinski

Spécificité de MerB et transfert du produit vers MerA chez E. coli

Le mercure est un contaminant environnemental dont certaines formes, notamment le méthylmercure ($MeHg^+$), sont toxiques. Chez les bactéries, la résistance au $MeHg^+$ repose sur l'opéron mer, dans lequel MerB et MerA jouent un rôle central. MerB catalyse le clivage de la liaison carbone–mercure du $MeHg^+$, produisant du Hg^{2+}, ensuite réduit en mercure élémentaire (Hg^0) par MerA. Bien que ces réactions soient bien décrites, le mécanisme de transfert du Hg^{2+} de MerB vers MerA demeure peu compris chez Escherichia coli. Des travaux du laboratoire du Dr Omichinski ont suggéré que la région N terminale de MerB jouait un rôle dans la spécificité de substrat de MerB et le transfert du produit vers la région N terminale de MerA. Afin d'étudier ce rôle, une version sans N-terminal de MerB (ΔN MerB), MerB de type sauvage et la région N terminale de MerA ont été produites et purifiées. Les expériences d'extinction de fluorescence ont montré que ΔN MerB conserve son activité catalytique et ont suggéré l'implication de la région N terminale de MerA dans le retrait du Hg^{2+} du site actif. La structure cristallographique de ΔN MerB révèle un réarrangement des cystéines du site actif qui suggérant le transfert du produit vers MerA. Une meilleure compréhension de ces mécanismes pourrait contribuer au développement d'approches de bioremédiation.

PRÉSENTATIONS RAPIDES / SPEED TALKS

Davoud Amiri Mehr - Labo Ferbeyre

Role of Nucleolus-Associated Chromatin Domains in Cellular Senescence and Cancer

Cellular senescence is a permanent cell-cycle arrest that contributes to tumor suppression, tissue repair, and aging. A defining feature of senescence is genome-wide chromatin remodelling, yet the role of nucleolus-associated chromatin domains (NADs) ,heterochromatin-rich, gene-poor regions around the nucleolus, remains poorly defined. This project examines whether NAD reorganization is a mechanistic component of senescence and a potential link to cancer development. We analyzed ATAC-seq data from IMR-90 undergoing RAS versus proliferating controls. The ATACseq peaks were intersected with NAD coordinates to define accessibility changes within NADs. Senescent cells displayed strong chromatin opening within NADs. Open regions in NADs (OpenSenNADs) were present on nearly all chromosomes. Approximately 80% mapped to intronic or intergenic regions, while fewer localized to promoters. We also observed ectopic expression of several genes located downstream of openSenNADs. This finding supports the idea that NAD opening can act as a regulatory event in senescence by enabling activation of nearby genes that are normally repressed. Next, we will perturb selected NAD loci using CRISPRi, including multiplex strategies with truncated guides

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Audrey Langlois - Labo Ferbeyre

Mitochondrial Iron Sensitizes Senescent Cancer Cells to Ferroptosis

Le FOLFIRINOX est la chimiothérapie de première ligne dans le traitement de l'adénocarcinome canalaire pancréatique (PDAC). Malgré un bénéfice sur la survie, la majorité des patients développent une résistance et rechutent. Notre laboratoire a montré que le FOLFIRINOX induit la sénescence cellulaire dans des lignées PDAC, menant à un relapse (Rowell et al., 2023). Un criblage CRISPR-Cas9 a identifié la glutathionne peroxydase 4 (GPX4), enzyme clé contre la ferroptose, comme une vulnérabilité des cellules sénescentes. Nous proposons une stratégie « one-two punch » : induire la sénescence par FOLFIRINOX, puis inhiber GPX4 pour éliminer ces cellules par ferroptose. Nous observons une accumulation de fer mitochondrial et une augmentation des transporteurs SLC25A28 et SLC25A37 dans les cellules PDAC sénescentes, absentes dans les cellules saines. Ce projet vise à définir le rôle du métabolisme du fer mitochondrial dans la sensibilité à la ferroptose. Nous avons également confirmé dans un modèle murin, avec un shARN inductible contre GPX4, l'efficacité de cette stratégie.

Marine Guelle - Labo Archambault

Phosphorégulation du nucléole par la protéine phosphatase 1 (PP1)

Le nucléole est un compartiment nucléaire dont la fonction principale est la biogenèse des ribosomes. Son assemblage repose sur la séparation de phase dépendante des interactions entre ARN et protéines nucléolaires. La phosphorylation réversible de ces protéines pourrait moduler ces interactions et l'organisation du nucléole. La phosphatase PP1 se localise au nucléole, mais son rôle et ses substrats restent mal définis. Chez la drosophile, il existe quatre PP1 dont deux, PP1-87B et PP1-96A, sont localisées au nucléole. L'analyse de leurs interacteurs a identifié Nnp-1, une sous-unité régulatrice responsable de cette localisation. Des approches de phosphoprotéomique ont permis d'identifier des substrats nucléolaires potentiels du complexe Nnp-1–PP1, dont NHK-1. La mutation de ses sites phosphorylables entraîne la perte de sa localisation nucléolaire. La déplétion ou mutation de Nnp-1 provoque des anomalies nucléolaires, suggérant un rôle de PP1 dans le maintien de l'intégrité du nucléole.

Malana Loxam - Labo Strauss

De nouvelles cibles pour le traitement du poliovirus grâce aux interactions entre VP4 et l'ARN

Bien que la vaccination généralisée contre le poliovirus ait fait progresser les efforts d'éradication, la partie de l'objectif qui reste est un traitement pour le poliovirus après l'infection. Ce projet de recherche examinera la protéine virion quatre (VP4) du poliovirus, à la fois indépendamment et en relation avec les interactions ARN. VP4 est la plus petite (7,5 kDa) et la seule des quatre protéines structurelles sans structure et fonction confirmées dans tous les états environnementaux. VP4 est logé à l'intérieur de la capside et devient externalisé lors des événements d'infection. VP4 est suspecté de s'oligomériser, se diviser en membrane cellulaire et former un pore à travers lequel l'ARN peut passer dans la cellule hôte. En comprenant mieux VP4, des informations sur l'administration du génome du poliovirus seront acquises, ce qui peut conduire au développement de médicaments à partir du ciblage thérapeutique et à la prévention de la propagation du poliovirus dans tout le corps après une infection.

Léo Millot - Labo Archambault

Rôle de la phosphatase PP2A-B56 dans la régulation des centrosomes

La mitose est régulée par des kinases et des phosphatases. Ce projet étudie l'enzyme PP2A-B56, un hétérotrimère jouant divers rôles durant la mitose, en interagissant avec ses substrats via un motif SLiM. Chez D. melanogaster, deux orthologues de B56 existent : Widerborst et Well-rounded. Les centrosomes sont régulés par des kinases, mais le rôle des phosphatases y reste peu connu. Nous utilisons D. melanogaster pour mieux comprendre la phosphorégulation des centrosomes. Nos travaux montrent que les B56 se localisent aux centrosomes et interagissent avec des protéines centrosomales. Leur codéplétion réduit le nombre de centrosomes en mitose, et des mutations dans le domaine de reconnaissance du SLiM en abolissent la localisation. Nos résultats suggèrent que PP2A-B56 déphosphoryle des protéines centrosomales. Les recherches futures viseront à élucider le mécanisme moléculaire de recrutement de cette phosphatase

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Helena de Castro Alvarenga - Labo Strauss

Structural insights into chromatin organization in situ

The eukaryotic cell nucleus has a high order genomic organization that permits gene regulation. One of the key components of this organization is chromatin, a biological assembly composed of nucleosomes arranged along DNA strands. Conventional Electron Microscopy (EM) requires heavy-metal staining of resin-embedded samples for enough contrast, which obscures finer details in the structure. Alternatively to conventional EM, which relies on elastic scattering (no energy exchange), Electron Energy Loss Spectroscopy (EELS) records inelastic signal, where electrons lose energy characteristic to the element they interact with. By coupling Scanning Transmission EM (STEM) with EELS, there is no required use of heavy-metals stains and we can have the energy loss information per pixel of the image. STEM-EELS used in combination with electron tomography can spatially map the elemental distribution of cell sections in 3D. Since nucleic acids are enriched in phosphorus, but proteins are typically not, by analyzing phosphorus and nitrogen maps of cell nuclei we gain structural insight into chromatin organization without the use of stains.

Charles-Éric Bry - Labo François

Ancestral state reconstruction using branched optimal transport.

In evolutionary biology, phenotypic traits evolve in time and change the physical appearance of species, and we can represent them as drifting particles in a phenotypic parameter space. Most models today [Revell, 2024] use the Brownian motion model to reconstruct ancestral states, optimizing the likelihood of the real-life outcome. Our method instead relies on concepts coming from the machine learning community like optimal transport. In particular, branched optimal transport is a variant that allows optimization by finding the shortest path between points in a phenotypic parameter space. The result is a phylogenetic tree that links every species studied and determines when their paths separate, localising ancestor species in the phenotype space. This study is powered by a dataset supplied by the Ehab Abouheif research team as McGill university containing allometric data from 17 species of ants. The goal is then to use this data to predict the physical appearance of ancestors, represented as nodes in the tree.

Mina Anadolu - Labo Legault

The role of long non-coding RNAs in modulating the alpha-synuclein microRNA regulatory pathway in Parkison's Disease

Parkinson's Disease is a progressive, incurable disorder marked by the cumulative loss of dopaminergic neurons and the toxic accumulation of α-synuclein (α-syn) protein in neuronal cells. α-Syn levels are post-transcriptionally controlled by microRNAs (miRNAs) that bind the 3'UTR of α-syn mRNA to repress its translation. Recent evidence suggests that long non-coding RNAs (lncRNAs) act as sponges to sequester miRNAs from doing their job. However, little is known about the mechanism. Our goal is to define how lncRNAs control α-syn-targeting miRNAs and impact α-syn levels in human neuronal and dopaminergic cells. For this, we use custom miRNA baits modeled after known α-syn-targeting miRNAs to pull down interacting lncRNAs and characterize them through RNA-seq. We will then perturb the identified lncRNAs through knockdown and examine the impact on miRNAs and α-syn levels. By defining the lncRNA–miRNA–α-synuclein axis, we aim to identify druggable lncRNAs and develop liquid-biopsy RNA biomarkers for early diagnosis and treatment monitoring.

Nicolas Pouderous - Labo Ferbeyre

Étude du rôle des ARN non codants nucléolaires dans le cancer du pancréas dans l'induction de la senescence par thérapie.

L'adénocarcinome canalaire pancréatique (PDAC) demeure l'un des cancers les plus létaux, avec le FOLFIRINOX (FX) comme traitement standard. La prolifération tumorale est étroitement liée à la biogenèse des ribosomes, processus nucléolaire impliquant plus de 600 facteurs. Notre laboratoire a démontré que sa perturbation induit la sénescence cellulaire, caractérisée par l'activation des voies p53/p21 et p16/pRB, une activité SA-β-galactosidase, un SASP pro-inflammatoire, ainsi que des défauts ribosomiques (SARD) et des foyers nucléolaires (SANF). Certaines cellules cancéreuses peuvent néanmoins échapper à ce processus, contribuant à la rechute tumorale. Nous émettons l'hypothèse que les ARN non codants nucléolaires (ncARN), incluant snoARN, lncARN et ARN-IGS, constituent un niveau clé de régulation de ce processus. Nous montrons que le FX induit la sénescence dans les cellules KP4, confirmée par SA-β-gal, SASP, p21, Ki67 et réorganisation nucléolaire. Des nucléoles purifiés ont été soumis à un séquençage ARN, révélant une signature de ncARN dérégulés.

Rini Ravindran Patel - Labo Serohijos

Transcriptome-informed prediction of protein interaction network rewiring in breast cancer models

Breast cancer progression is driven by coordinated changes in gene expression, yet how these alterations translate into functional protein interaction networks remains poorly understood. In this study, we adopt a transcriptome-driven approach to investigate how interaction networks are remodeled across a breast cancer progression model. We hypothesize that shifts in RNA abundance give rise to measurable changes in protein complex formation and interaction probabilities that ultimately drive tumorigenic phenotypes. To test this, we integrate RNA-seq data with PPI networks generated using UTTOPIA, a tool developed in our lab, to identify condition-specific interaction changes. By intersecting differential gene expression with PPI data, we predict network rewiring events, which we then validate using proximity-based assays and link to phenotypic outputs. Overall, by bridging transcriptomics and interactomics into a unified, predictive model of cellular state, this study provides a foundation for identifying context-specific therapeutic vulnerabilities and advances a systems-level understanding of breast cancer.

Mélanie Lemaire - Labo Major

Understanding The Roles Of RNA Structural Dynamics And RNA-Binding Protein Interactions In The Biogenesis Of miR-125a, miR-128-1, and miR-188

MicroARN (miRNA) maturation initiates through microprocessor-mediated cleavage of primary miRNAs (pri-miRNAs). However, single nucleotide polymorphism (SNP) within pri-miRNA sequences can disrupt this process and lead to dysregulation and subsequently disease. The mechanisms underlying this loss of maturation remain unresolved. We hypothesize that SNPs disrupt structural dynamic and affect interactions with RNA-binding proteins (RBPs) thus decreasing pri-miRNA maturation. Methods and results: To identify key interaction sites and RNA-binding proteins involved in pri-miRNA maturation, we study SNP-induced loss-of-maturation. SNPs affecting structural dynamic and blocking maturation of miR-125a, miR-128-1 and -188 were predicted using bioinformatic, RT-qPCRs and northern blots. Those pri-miRNAs proteome were identified by RNA pull-down and mass spectrometry analysis (LC-MS/MS). SRSF3 and ADAR1 knockdowns induced a decrease of miR-128-1 biogenesis in Hs578T suggesting a role as positive regulators of miR-128-1 biogenesis in this cell line. Using our machine learning tool, D-ORB, three interaction sites in miR-125a potentially required for efficient maturation were predicted. Their functional relevance is currently being assessed by evaluating the impact of their disruption on biogenesis using RT-qPCR. Finally, to determine whether the SNP affecting miR-125a biogenesis also alters processing of its co-clustered miRNAs (miR-99b and let-7e), the SNP was introduced endogenously in MDA-MB-453 cells using CRISPR/Cas9, recapitulating its effect in a genomic context. Effects on miR-99b and let-7e maturation are currently being assessed by RT-qPCR. Conclusion and impact: These findings could help identify RBPs and key interactions sites involved in miR-125a, -128-1 and -188 biogenesis and predict the impact of genetic variation on miRNA maturation efficiency.

PRÉSENTATIONS PAR AFFICHES / POSTER PRESENTATIONS

Poster #01 **Jessica Adams** - *Phd* - Labo Ferbeyre

Intégration du signal oncogénique par la régulation de la chromatine : Implication des domaines associées nucléolaires dans la sénescence

La sénescence cellulaire est un arrêt irréversible du cycle cellulaire agissant comme barrière antitumorale. Le laboratoire Ferbeyre a établi que la sénescence induite par l'oncogène RAS (OIS) s'accompagne d'un remodelage chromatinien majeur, marqué par l'ouverture des domaines associés au nucléole (NADs), riches en séquences non codantes. Les facteurs de transcription ETV4 et RUNX1, effecteurs de RAS, sont recrutés au noyau et suffisent individuellement à déclencher la sénescence. Mon projet vise à déterminer si la modulation de la chromatine au niveau des NADs est le déclencheur critique de l'OIS. Premièrement, je validerai la capacité d'ETV4 et RUNX1 à remodeler la chromatine en utilisant des protéines de fusion combinant leur domaine de liaison à l'ADN au répresseur KRAB. Deuxièmement, j'utiliserai la technologie CRISPRi pour cibler des régions spécifiques identifiées comme différentiellement accessibles. L'objectif est de distinguer si la sénescence découle de l'ouverture globale des NADs ou de la modulation de loci précis. Enfin, l'impact de ce remodelage sera évalué dans un contexte de cellules cancéreuses pour en tester le potentiel thérapeutique.

Poster #02 **Isra Alaya** - *MSc* - Labo Affar

Rôle des complexes Polycomb dans la régulation épigénétique des sarcomes à résolution cellule unique

Le sarcome est un cancer rare pour lequel les options thérapeutiques restent limitées, en grande partie à cause du manque de données annotées et de connaissances mécanistiques. Les complexes Polycomb, acteurs clés de la régulation épigénétique, jouent un rôle majeur dans la plasticité cellulaire et la tumorigenèse, mais leur implication précise dans le sarcome demeure peu explorée.Ce projet vise à étudier l'impact des complexes Polycomb dans le sarcome à travers l'analyse de données single-cell RNA-seq, permettant de caractériser la régulation génique à haute résolution. Sur le plan méthodologique, nous développerons un pipeline intégrant des approches de deep learning,pour apprendre des représentations biologiques compressées, combinées à des modèles supervisés entraînés sur d'autres cancers où les réponses thérapeutiques sont connues.L'objectif final est de transférer ces connaissances vers le sarcome afin de proposer des prédictions thérapeutiques et d'ouvrir de nouvelles perspectives de traitement pour cette pathologie rare

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Poster #03 **Davoud Amiri Mehr** - *PhD* - Labo Ferbeyre

Role of Nucleolus-Associated Chromatin Domains in Cellular Senescence and Cancer

Cellular senescence is a permanent cell-cycle arrest that contributes to tumor suppression, tissue repair, and aging. A defining feature of senescence is genome-wide chromatin remodelling, yet the role of nucleolus-associated chromatin domains (NADs) ,heterochromatin-rich, gene-poor regions around the nucleolus, remains poorly defined. This project examines whether NAD reorganization is a mechanistic component of senescence and a potential link to cancer development. We analyzed ATAC-seq data from IMR-90 undergoing RAS versus proliferating controls. The ATACseq peaks were intersected with NAD coordinates to define accessibility changes within NADs. Senescent cells displayed strong chromatin opening within NADs. Open regions in NADs (OpenSenNADs) were present on nearly all chromosomes. Approximately 80% mapped to intronic or intergenic regions, while fewer localized to promoters. We also observed ectopic expression of several genes located downstream of openSenNADs. This finding supports the idea that NAD opening can act as a regulatory event in senescence by enabling activation of nearby genes that are normally repressed. Next, we will perturb selected NAD loci using CRISPRi, including multiplex strategies with truncated guides, and also test whether these loci are enriched for somatic mutations across cancer genomes.

Poster #04 **Mina Anadolu** - *Postdoc* - Labo Legault

The role of long non-coding RNAs in modulating the alpha-synuclein microRNA regulatory pathway in Parkison's Disease

Parkinson's Disease is a progressive, incurable disorder marked by the cumulative loss of dopaminergic neurons and the toxic accumulation of α-synuclein (α-syn) protein in neuronal cells. α-Syn levels are post-transcriptionally controlled by microRNAs (miRNAs) that bind the 3'UTR of α-syn mRNA to repress its translation. Recent evidence suggests that long non-coding RNAs (lncRNAs) act as sponges to sequester miRNAs from doing their job. However, little is known about the mechanism. Our goal is to define how lncRNAs control α-syn-targeting miRNAs and impact α-syn levels in human neuronal and dopaminergic cells. For this, we use custom miRNA baits modeled after known α-syn-targeting miRNAs to pull down interacting lncRNAs and characterize them through RNA-seq. We will then perturb the identified lncRNAs through knockdown and examine the impact on miRNAs and α-syn levels. By defining the lncRNA–miRNA–α-synuclein axis, we aim to identify druggable lncRNAs and develop liquid-biopsy RNA biomarkers for early diagnosis and treatment monitoring.

Poster #05 **Yani Bouaziz** - *PhD* - Labo Chartrand

Arx1/Alb1 define a non-canonical nuclear export pathway for telomerase RNA in Saccharomyces cerevisiae.

Telomerase biogenesis in Saccharomyces cerevisiae requires the nuclear export of its RNA component, telomerase RNA (TLC1), followed by re-import and maturation. Nuclear export of the 3' unprocessed TLC1 RNA precursor requires the exportins Xpo1 and Mex67, while its nuclear re-import involves the importins Kap122 and Mtr10. Once in the nucleus, nuclear retention of the telomerase RNP requires the interaction between TLC1 and the yKu complex. The requirement for Xpo1 and Mex67 in TLC1 RNA export has led to the model that telomerase uses the snRNPs biogenesis pathway. However, since the TLC1 RNA is larger than other snRNAs, other export pathways may also be required for telomerase RNA trafficking. Indeed, we found that the Arx1/Alb1 complex, which acts as a nuclear export factor for the pre-60s ribosomal subunit, is also required for TLC1 RNA nuclear export. Using single molecule RNA FISH, we quantified the nucleo-cytoplasmic distribution of telomerase RNA in jjj1Δ, arx1Δ, and alb1Δ strains. In a yku70Δ background, which disrupts nuclear retention of telomerase RNA, loss of Jjj1, Arx1, or Alb1 led to a decrease in cytoplasmic localization, consistent with a defect in nuclear export. Co-immunoprecipitation followed by RT-qPCR showed that Arx1 and Alb1 associate with the 3'unprocessed telomerase RNA in vivo, supporting a role for this complex in TLC1 RNA trafficking. In parallel, RT-qPCR analysis revealed an accumulation of the 3'precursor forms of telomerase RNA in jjj1Δ, arx1Δ, and alb1Δ strains, suggesting that this pathway also contributes to RNA maturation. Southern blot analysis further revealed telomere shortening in these mutants, linking defects in telomerase RNA trafficking and processing to impaired telomerase function. We aim to map the Arx1/Alb1 binding sites on telomerase RNA using RIPiT-seq. In addition, we are assessing the nucleocytoplasmic localization of newly synthesized telomerase RNA using the TLC1 MS2-IN system to further characterize its trafficking dynamics. These results support a model in which the Arx1/Alb1–Jjj1 pathway defines a non-canonical nuclear export route for telomerase RNA and couples its trafficking to maturation. This work reveals a link between ribosome biogenesis and telomerase biogenesis in S. cerevisiae. Interestingly, mutations in the Hsp40 co-chaperone DNAJC21, the human ortholog of Jjj1, cause bone marrow failure syndrome and are linked to telomere shortening, suggesting a connection between ribosome biogenesis and telomerase function.

Poster #06 **Charles-Éric Bry** - *MSc* - Labo François

Ancestral state reconstruction using branched optimal transport

In evolutionary biology, phenotypic traits evolve in time and change the physical appearance of species, and we can represent them as drifting particles in a phenotypic parameter space. Most models today [Revell, 2024] use the Brownian motion model to reconstruct ancestral states, optimizing the likelihood of the real-life outcome. Our method instead relies on concepts coming from the machine learning community like optimal transport. In particular, branched optimal transport is a variant that allows optimization by finding the shortest path between points in a phenotypic parameter space. The result is a phylogenetic tree that links every species studied and determines when their paths separate, localising ancestor species in the phenotype space. This study is powered by a dataset supplied by the Ehab Abouheif research team as McGill university containing allometric data from 17 species of ants. The goal is then to use this data to predict the physical appearance of ancestors, represented as nodes in the tree.

Poster #07 **Catherine Champagne** - *MSc* - Labo Chartrand

Imaging Telomerase-Telomeres Interactions in Live Cells

The recruitment of telomerase to telomeres is a tightly regulated process critical for maintaining telomere length and ensuring genomic stability. Dysregulation of this recruitment mechanism has been implicated in various pathological conditions, particularly in cancer cells. Studying the dynamic of telomerase to telomeres in vivo is therefore crucial for a better understanding of these diseases. Telomerase can be visualized through its RNA component, hTR, which serves as a reliable marker of the enzyme. Live-cell imaging of hTR enables direct observation of telomerase behavior at telomeres in real time. Single-molecule tracking reveals transient and long-lived interactions, allowing quantitative measurement of colocalization and residence time of telomerase to telomeres. These results demonstrate that RNA dynamics can serve as a functional readout of enzymatic activity in living cells, here, providing insight into the regulation of telomeres maintenance at the molecular level in cancer cells.

Poster #08 **Simon Chasles** - *PhD* - Labo Major

The RNA Interaction Maps (RIMaps): Introducing RIMap-RISC as a tool to model miRNA:mRNA interactions

Nos travaux visent à comprendre et à concevoir des systèmes de régulation basés sur l'ARN grâce à des approches de modélisation structurelle et intégrative. Nous développons des outils informatiques permettant d'élucider comment la structure de l'ARN gouverne les interactions avec des facteurs régulateurs, avec un accent particulier sur les microARN (miARN) et les protéines liant l'ARN (RBP). À travers la plateforme RIMap-RISC, nous modélisons le ciblage des miARN à l'échelle du transcriptome en intégrant l'accessibilité structurale, les paramètres énergétiques de liaison, incluant les constantes de dissociation (Kd), ainsi que le contexte de séquence (Chasles et al. 2026). Cette approche permet d'identifier des sites cibles fonctionnels et soutient la conception rationnelle d'ARN régulateurs synthétiques capables de moduler de manière coordonnée plusieurs cibles au sein de réseaux géniques.

Poster #09 **Laura Chastant** - *PhD* - Labo Archambault

BAF protège contre la réponse cGAS-STING aux ponts de chromatine

Des défauts mitotiques peuvent induire l'activation de réponses immunitaires innées. Parmi eux, les micronoyaux ont été proposés comme capables d'activer la voie pro-inflammatoire cGAS-STING. Cependant, la contribution des micronoyaux ou d'autres défauts post-mitotiques à la réponse cGAS-STING reste incertaine. Nous avons comparé la capacité de défauts post-mitotiques résultants de l'inhibition du point de contrôle d'assemblage du fuseau mitotique (par inhibition de MPS1) ou d'une perturbation du réassemblage nucléaire (par inactivation de BAF) à induire la réponse cGAS-STING. Combiner ces deux perturbations renforce de façon synergique la réponse cGAS-STING. Cet effet n'est pas dû à une induction de micronoyaux, mais est corrélé à une augmentation des ponts de chromatine déstabilisés, aboutissant à des structures qui recrutent fortement cGAS. Nos résultats suggèrent qu'en stabilisant les ponts de chromatine, BAF contribue à prévenir la dégénérescence de ces ponts en structures de chromatine activant cGAS. Ce travail permet de comprendre comment l'immunité innée détecte les défauts mitotiques

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Poster #10 **Maria Chemrouk** - *MSc* - Labo Roy

Signalisation JAK/STAT lors de la régénération du membre chez l'axolotl

La capacité de régénération tissulaire varie considérablement selon les espèces. Contrairement aux mammifères qui cicatrisent leurs blessures en formant du tissu fibreux, l'axolotl régénère des structures complexes telles que ses membres. Comprendre les mécanismes moléculaires à la base de cette capacité représente une avenue prometteuse pour la médecine régénérative. La phase de préparation de la régénération du membre est principalement régulée par la voie TGF-b qui transmet son signal via Smad2 et Smad3. Des analyses sur des blastèmes en régénération indiquent une activation préférentielle pour Smad2, associé à la prolifération cellulaire, par rapport à Smad3, davantage lié à la fibrose. Les mécanismes responsables de cette activation différentielle restent inexpliqués. L'hypothèse de ce projet est que STAT3, activé par la réponse inflammatoire post-amputation, inhibe l'activation de Smad3, favorisant ainsi la régénération. Pour tester cette hypothèse, des axolotls sont traités avec des inhibiteurs de la voie JAK/STAT afin d'évaluer leurs effets sur la régénération et sur l'activation différentielle de Smad2 et Smad3, par des approches histologiques, d'immunobuvardage et qPCR.

Poster #11 **Justina Chu** - *PhD* - Labo Zenklusen

Investigating real-time spatio-temporal progression of ribosome biogenesis using single-molecule resolution microscopy

Ribosome biogenesis requires the interplay of hundreds of ribosome biogenesis factors (RBFs), ribosomal proteins (RPs) and rRNAs, and occurs mainly in the nucleolus, a multilayered condensate. Despite extensive research, the spatio-temporal progression of ribosome biogenesis remains poorly understood, in part because of technical limitations due to its rapidly changing dynamics. To overcome some of these limitations, we used live-cell single-molecule microscopy to elucidate the spatial progression of ribosome biogenesis in real time. Using Halo-tagged RPs/RBFs as proxies for the maturing subunits, fast imaging enabled us to monitor the dynamic behaviour of single proteins within nucleolar subcompartments at ~50nm resolution. Single-particle movement analysis of pre-ribosome-bound RPs reveals confined dwell times and lateral movement within nucleolar subcompartments. Taken together, live-cell single-molecule microscopy allows us to further study the spatial-temporal behaviour of maturing ribosomal subunits.

Poster #12 **Cassandre Clermont** - *MSc* - Labo Serohijos

Developing a High-Throughput Approach for Screening In Vivo Non-Coding RNA-Protein Interactions

Problem and hypothesis : Non-coding RNAs (ncRNAs) have emerged as key regulators, participating in transcriptional and post-transcriptional control of gene expression1. Despite representing the vast majority of the transcriptome, the molecular functions of many ncRNAs remain largely unknown2. In contrast, proteins are generally much better characterized. Therefore, by identifying which proteins a given ncRNA interacts with, we can try to infer its potential function3. Mapping these RNA-protein interactions (RPIs) at scale is therefore essential to uncover the functional landscape of ncRNAs. However, despite significant advances, many limitations remain to study RPIs at scale4,5. High-throughput methods for studying RPIs can be separated into protein-centered and RNA-centered approaches. Protein-centered methods isolate a protein of interest to identify the RNAs bound to it by sequencing. RNA-centered methods use an RNA of interest as bait to capture interacting proteins, which are then identified by mass spectrometry (MS)4. These approaches generally rely on one of two strategies: without cross-linking, where cells are lysed and then complexes are isolated, or with cross-linking, where complexes are stabilized in the cell before lysis. Both strategies can introduce biases. Without cross-linking, interactions are more preserved in their native form but the lysis and washing steps can be harsh and disrupt fragile complexes and introduce a strong bias toward abundant molecules6. Cross-linking methods can stabilize complexes before lysis by creating covalent bonds, reducing some of these artifacts7. However, they introduce strong sequence and amino acid composition biases8. For example, UV cross-linking occurs mainly through uridine residues, and amino acids like cysteine, tyrosine, tryptophan, phenylalanine, and lysine react preferentially with pyrimidines8. Also, RNA-centered approaches that depend on MS face other issues. While powerful, MS has significant limitations for large scale screening. It often requires large amounts of biological material, favors the identification of abundant complexes over lower or transient interactions, and can remains costly10. All together, these limitations compromise quantitation, reduce the detection of certain interactions such as transient ones, can fail to capture complexes at their endogenous expression levels and need cell lysis to detect the interaction. These challenges reduce sensitivity and accuracy, highlighting the need for alternative high-throughput methods for mapping RPIs. To overcome these challenges, we propose adapting the murine dihydrofolate reductase (mrDHFR) based Protein Complementation Assay (PCA), originally developed for protein-protein interactions (PPIs), to the study of RPIs. In this system, the mrDHFR enzyme is split into two inactive fragments, each fused to a different protein. When these proteins interact, the fragments are brought into proximity, allowing the enzyme to refold and regain activity11. In the presence of methotrexate (MTX), which inhibits endogenous DHFR but not the murine version, only cells with reconstituted mrDHFR can grow, allowing the interaction to be quantitatively measured by monitoring growth under MTX selection11. This offers several advantages demonstrated in PPI studies: it avoids cell lysis to capture interaction, can detect both transient and abundant interactions, and is sensitive enough to capture interactions as few as 25–100 complexes per cell12. In our adapted system, we plan to use MS2 tagging to bridge the RNA and protein partners to the PCA fragments13. The ncRNA of interest will be tagged with MS2 loops, bound by an MS2 coat protein fused to one mrDHFR fragment, while the RNA-binding protein (RBP) will be fused to the other fragment of the DHFR. If the RBP binds the RNA, the two fragments will be brought together, restoring mrDHFR activity. Our hypothesis is that the mrDHFR-based PCA system, originally designed for PPIs, can be adapted to detect RPIs in vivo with high sensitivity and accuracy, enabling the study of interactions under endogenous conditions, and ultimately supporting large-scale RNA-centric screening. Aims: The project is structured around three main objectives: (1) testing the assay on the well-characterized Aco1 and IRE interaction, a validated heterologous system previously used to study RPIs in yeast13; (2) adapting the system to endogenously expressed components, using She2p protein and ASH1 RNA as a model14; and (3) performing a genome-wide RNA-centric screen using the yeast telomerase RNA, a common benchmark for RPIs studies15. Methodology: For the first aim, the IRE RNA will be tagged with MS2 stem-loops. The MS2 coat protein will be fused to the DHFR(1,2) fragment, while the protein Aco1 will be fused to the DHFR(3) fragment. As a negative control, Aco1 will be replaced by YFP, which is not expected to bind to IRE and should therefore fail to support growth under MTX selection. The system will initially be tested using three separate plasmids, each encoding one component of the assay. This configuration allow flexibility to test different promoter, fusion orientations, and tag arrangements, enabling rapid optimization. Growth assays will be performed in the presence and absence of MTX to confirm assay specificity. Once the synthetic system is optimized, we will adapt it to study RPI under endogenous expression levels. Components will be integrated into the yeast genome by CRISPR/Cas9, except for the MS2 coat and DHFR(1,2) fusion, which will remain on plasmid to allow adjustable expression. The She2p protein and ASH1 interaction will serve as a testing model and will be put under MTX selection to verify that results align with published data. For genome-wide screening, we will use an existing yeast library from our laboratory in which each protein coding gene is tagged with DHFR(3) and a genomic barcode. The yeast telomerase RNA will be endogenously tagged with MS2 stem-loops, and the MS2 coat protein and DHFR(1,2) fusion will be expressed in all strains, either from a plasmid or integrated at a neutral genomic locus. Interaction readout will be again based on growth under MTX selection, and strains showing significantly different growth compared to negative controls will be classified as positive interactors.

Poster #13 **Daphnée Couture** - *BSc* - Labo Affar

Caractérisation du rôle de l'interaction BAP1-FOXKs dans la prolifération et le métabolisme cellulaire chez la souris

BAP1 est un suppresseur de tumeurs muté dans de nombreux cancers. Cette déubiquitinase de l'histone H2AK119 joue un rôle dans la régulation de la transcription, la prolifération cellulaire, l'apoptose et la réparation de l'ADN. BAP1 interagit, via sa thréonine 492 phosphorylée, avec les facteurs de transcription FOXK1 et FOXK2, également impliqués dans la prolifération, la différenciation et le métabolisme cellulaire. Toutefois, les fonctions métaboliques de cette interaction restent peu caractérisées. Ce projet visait à déterminer si la perte d'interaction entre BAP1 et les FOXKs affecte le métabolisme et les fonctions cellulaires associées. Des souris KI T492A présentent une létalité partielle et un faible poids, suggérant un rôle physiologique important. Des cellules MEFs WT et T492A ont été comparées pour la prolifération, la sénescence, la différenciation et la réponse au stress. Aucune différence significative n'a été observée. Ces résultats suggèrent que l'interaction BAP1–FOXK1/2 exercerait des effets dépendants du type cellulaire ou du contexte physiologique. Des études dans des cellules souches myogéniques, ainsi que des analyses RNA-seq, pourraient permettre d'identifier les voies métaboliques impliquées.

Poster #14 **Helena de Castro Alvarenga** - *PhD* - Labo Strauss

Structural insights into chromatin organization in situ

The eukaryotic cell nucleus has a high order genomic organization that permits gene regulation. One of the key components of this organization is chromatin, a biological assembly composed of nucleosomes arranged along DNA strands. Conventional Electron Microscopy (EM) requires heavy-metal staining of resin-embedded samples for enough contrast, which obscures finer details in the structure. Alternatively to conventional EM, which relies on elastic scattering (no energy exchange), Electron Energy Loss Spectroscopy (EELS) records inelastic signal, where electrons lose energy characteristic to the element they interact with. By coupling Scanning Transmission EM (STEM) with EELS, there is no required use of heavy-metals stains and we can have the energy loss information per pixel of the image. STEM-EELS used in combination with electron tomography can spatially map the elemental distribution of cell sections in 3D. Since nucleic acids are enriched in phosphorus, but proteins are typically not, by analyzing phosphorus and nitrogen maps of cell nuclei we gain structural insight into chromatin organization without the use of stains.

Poster #15 **Normand Cyr** - *Hors concours* - Labo Plateformes

Plateforme de biologie structurale - Institut Courtois d'innovation biomédicale

La plateforme de biologie structurale de l'Institut Courtois d'innovation biomédicale (CI2B) de l'Université de Montréal offre un accès à des instruments de pointe et un environnement intégré pour l'étude structurale et biophysique des biomolécules, de la caractérisation en solution à l'analyse structurale avancée. Elle comprend trois spectromètres de résonance magnétique nucléaire (RMN) à haut champ (500, 600 avec cryosonde et 700 MHz) permettant notamment la détermination structurale en solution ainsi que l'étude des interactions biomoléculaires et des dynamiques moléculaires. Un instrument de BioSAXS (diffusion des rayons X aux petits angles), doté d'un système robotisé pour le criblage à haut débit et compatible avec des montages de type SEC-SAXS, est également disponible pour l'analyse de systèmes dynamiques ou hétérogènes. Un spectromètre de masse (Refeyn TwoMP) permet la caractérisation de biomolécules, incluant l'analyse de masse intacte et la détection d'hétérogénéité. D'autres instruments complètent l'offre en caractérisation biophysique, notamment un système de diffusion de la lumière multi-angle (SEC-MALS) pour l'étude de l'oligomérisation et de l'homogénéité des échantillons, ainsi qu'un calorimètre de titrage isotherme (ITC) pour la mesure des constantes d'affinité. Des robots permettent également le criblage de conditions de cristallisation. Un nouveau pôle de cryo-microscopie électronique (cryo-EM) est en cours de déploiement, avec l'arrivée de trois microscopes électroniques de pointe (Thermo Fisher Talos, JEOL cryoARM200 et Thermo Fisher Krios). Ces instruments permettront la détermination de structures 3D à haute résolution de complexes macromoléculaires, ainsi que l'analyse de la variabilité conformationnelle et la visualisation d'assemblages hétérogènes. Finalement, une équipe hautement qualifiée assure la formation et l'accompagnement des utilisateurs afin de maximiser la qualité des résultats, notamment par la validation de la qualité et de la stabilité des échantillons. Des services de consultation scientifique sont également offerts sur demande.

Poster #16 **Christian Denis** - *PhD* - Labo François

Dynamical model and geometric insights in the discontinuity theory of immunity

The ability to distinguish between immunogenic and non-immunogenic challenges is a fundamental function of the immune system. Discontinuity theory, proposed by Pradeu and Vivier, suggests that the immune system identifies threats based on the rate of change in the concentration of an immune challenge. While fast growing challenges are considered immunogenic, slow-growing ones are tolerated. In this study, we present a biologically realistic ODE-based model of the adaptive immune system, that naturally accounts for and explains discontinuity theory. Our dynamical model can differentiate between acute and chronic infections based on the growth rate of the immune challenge, and we further show that the qualitative properties of our model are generic i.e. associated with a small number of hypotheses irrespective of the model details. Importantly, we examine the impact of multiple concurrent challenges and demonstrate the occurrence of antagonism, wherein, in some parameter regimes, slow-growing challenge can impinge acute response to fast growing ones. These findings provide a quantitative framework for justifying and studying discontinuity theory, and encourage further investigation into multi-agent infections.

Poster #17 **Alexandre Devaux** - *Postdoc* - Labo Chaker-Margot

LncRNA-protein interaction in colorectal cancer tumorigenesis

Colorectal cancer (CRC) is one of the deadliest cancer worldwide. With low survival rate five years from the diagnosis and high metastastic capacity, this cancer is also characterized by a high resistance to chemotherapeutic agents. Thoses abilities are driven by a transition state termed as 'epithelial-mesenchymal transition' and the activation/inhibition of factors in several pathways promoting pro-oncogenic functions. It has been suggested that several factors involved in CRC tumorigeneiss are impacted by long non coding RNAs (lncRNA). In CRC, several lncRNA are known to be higly expressed but majority of their interactions with protein remains poorly understood. Our project aims to discover new uncharacterized lncRNA-protein interactions involved in CRC tumorigenesis. By taking seven specificly highly expressed lncRNAs in CRC, we have established two indepedent methods, MS2 pulldown and O-MAP (définition), to find new interactors. Those complentary approaches will help us to find direct and indirect interactions of these lncRNAs as well as validate their functions further regarding their RNA binding activity and phenotype in tumorigenesis. Our long term goal is characteried the mecanism of lncRNA roles in CRC tumorigenesis and evaluate their potential as therapeutic target.

Poster #18 **Geneviève Di Tomasso** - *Hors concours* - Labo Legault

Unraveling the role of RNA-binding proteins in let-7 regulation through protein-protein interaction network

MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression by inhibiting translation or promoting the degradation of target mRNAs. Their biogenesis is tightly controlled, in part by RNA-binding proteins (RBPs), which modulate miRNA levels and thereby influence numerous cellular processes. Understanding the protein-protein interaction (PPI) networks involving RBPs is therefore essential to elucidate the mechanisms governing miRNA regulation. In this study, affinity purification coupled with mass spectrometry (AP-MS) was applied to the human let-7 miRNA family, a group of 12 conserved miRNAs with key roles in development, differentiation, and tumor suppression. While this approach identified a substantial set of associated proteins, it likely represents only a subset of a broader regulatory network. To address this limitation, we employed computational approaches to expand and characterize the underlying PPI network. This integrative analysis revealed an extended network consistent with the AP-MS dataset while uncovering additional candidate interactions. Network centrality analyses, combined with randomization approaches, identified key proteins likely involved in regulating let-7 levels. Selected candidates were evaluated using cell-based and in vitro assays to validate their roles in miRNA maturation, providing new insights into the regulatory landscape of let-7 biogenesis. Further characterization of two RBPs, SOX2 and LARP7, through binding and kinetic assays combined with pseudotime analysis of single-cell RNA-seq data to reconstruct developmental trajectories in early mouse embryogenesis, enables us to propose new roles for these proteins in let-7 regulation.

Poster #19 **Melissa Dupuig** - *MSc* - Labo Michnick

Exploring allosteric protein regulation in live cells using the Structural Dynamics

Response assay Protein function is mainly regulated by several mechanisms, but one of the most important is allostery, a process in which the binding of a molecule at one site induces changes in the structure of a protein, affecting its activity. This process plays a central role in how cells respond to their environment and regulate metabolic pathways. However, studying allostery remains challenging, because most available methods rely on in vitro systems and fail to capture protein behavior in living cells. Our hypothesis is that there is widespread allosteric regulation of proteins at the proteome scale. In this study, we aimed to determine whether ligand binding allosteric regulation can be detected directly in living cells using the Structural Dynamics Response (SDR) assay. This method has previously been shown in vitro to detect ligand binding through changes in luminescent signal. In this system, a small fragment of NanoLuc (SmBiT) is fused to the (N) or (C) terminus of the protein of interest, while the complementary fragment (LgBiT) is expressed from a separate plasmid. In this work, we applied the SDR assay in Saccharomyces cerevisiae using both plasmid based expression and endogenous tagging. We then tested the system under different metabolic conditions, including treatment with 2 deoxyglucose, to explore how ligand binding events can be detected in a cellular context. We first confirmed that the SDR assay behaves as expected in living cells, where inhibitor binding leads to an increase in luminescent signal while enzymatic activity decreases. Importantly, this was achieved without the need for cell lysis, demonstrating that the assay can be applied in vivo. Using endogenous tagging, we further showed that the system is functional in 9 yeast proteins. Finally, under 2 deoxyglucose conditions, we observed an increase in SDR signal in hexokinases, consistent with the accumulation of 2-DG-6P acting as a product inhibitor. In conclusion, these results show that the SDR assay can be used to detect ligand binding allosteric regulation directly in living cells. This approach provides a new way to study protein regulation in its native cellular context and reveals how metabolic perturbations can influence protein behavior.

Poster #20 **Cassandra Gbaboua** - *PhD* - Labo Wilhelm

Régulation de l'épissage alternatif de NCOR2 par MBNL1 dans les leucémies myéloïdes aiguës KMT2A-réarrangées

La leucémie myéloïde aiguë (LMA) est une hémopathie maligne caractérisée par une grande hétérogénéité moléculaire, qui entrave la compréhension de ses mécanismes et le développement de thérapies ciblées. Parmi ses sous-types, les LMA KMT2A-réarrangées représentent environ 20–25 % des cas pédiatriques et sont associées à un pronostic défavorable. L'épissage alternatif, fréquemment dérégulé dans les cancers, contribue à cette diversité transcriptionnelle. Dans les LMA KMT2A-réarrangées, MBNL1 apparaît comme un régulateur clé de l'épissage. Nous montrons qu'une forte expression de MBNL1 est associée à une sélection préférentielle de la forme courte de l'exon 45 de NCOR2, isoforme dépourvue d'un domaine d'interaction aux récepteurs nucléaires (RID), suggérant une altération de sa fonction de corépresseur transcriptionnel. Nous cherchons à comprendre les déterminants de cette préférence isoforme-spécifique et, pour cela, caractérisons les conséquences transcriptomiques induites par l'inclusion forcée de la forme longue de l'exon 45.

Poster #21 **Marine Guelle** - *PhD* - Labo Archambault

Phosphorégulation du nucléole par la protéine phosphatase 1 (PP1)

Le nucléole est un compartiment nucléaire dont la fonction principale est la biogenèse des ribosomes. Son assemblage repose sur la séparation de phase dépendante des interactions entre ARN et protéines nucléolaires. La phosphorylation réversible de ces protéines pourrait moduler ces interactions et l'organisation du nucléole. La phosphatase PP1 se localise au nucléole, mais son rôle et ses substrats restent mal définis. Chez la drosophile, il existe quatre PP1 dont deux, PP1-87B et PP1-96A, sont localisées au nucléole. L'analyse de leurs interacteurs a identifié Nnp-1, une sous-unité régulatrice responsable de cette localisation. Des approches de phosphoprotéomique ont permis d'identifier des substrats nucléolaires potentiels du complexe Nnp-1–PP1, dont NHK-1. La mutation de ses sites phosphorylables entraîne la perte de sa localisation nucléolaire. La déplétion ou mutation de Nnp-1 provoque des anomalies nucléolaires, suggérant un rôle de PP1 dans le maintien de l'intégrité du nucléole.

Poster #22 **David Hamelin** - *PhD* - Labo Hussin

Modeling Viral Evolution and T Cell Evasion through HLA-Informed Deep Learning Understanding how viral evolution interacts with human immunity is critical for pandemic preparedness

Human variation in HLA class I genes shapes T cell responses by determining which viral epitopes are presented. As a result, viral mutations can disrupt epitope presentation in an HLA-dependent manner. Importantly, variations in HLA profiles across human populations, may lead to varying immune escape risks. We present an AI-driven framework to study viral mutations and HLA variability. First, we used machine learning to assess and visualize HLA diversity across global cohorts. Next, we quantified HLA-specific susceptibility to T cell evasion across six HLA alleles in UK Biobank and 1000 Genomes data, identifying up to six affected epitopes in individuals with HLA-B07:02 and HLA-A03:01. This was achieved using a combination of measured as well as predicted T cell evasion events. Our results were replicated in the RECOVER-2 cohort (n=576, HLA-typed by nanopore sequencing). Finally, we developed a deep learning model that leverages Protein Language Modelling (ESM-2) to interrogate the epistasis-dependant evolutionary plausibility of immune-evading mutations. This framework supports more inclusive public health strategies and vaccine design.

Poster #23 **Gabin Felix Kere** - *PhD* - Labo Mallette

Impact du 25-hydroxycholestérol sur la traduction dans la sénescence cellulaire

La rétinopathie est une affection rétinienne caractérisée par la dégénérescence des vaisseaux sanguins de l'œil, qui s'accompagne d'un phénomène d'angiogenèse pathologique. Le laboratoire du Dr Mallette a montré que les cellules rétiniennes dans cette maladie entrent davantage dans un état de sénescence cellulaire : un processus biologique caractérisé par l'arrêt de la prolifération, de nombreux réarrangements métaboliques et la sécrétion de diverses molécules pro-inflammatoires : phénotype sécrétoire associé à la sénescence (PSAS). Le PSAS est un aspect incoutournable de la sénescence cellulaire et présente un pouvoir paracrine, permettant de propager la sénescence aux cellules environnantes. En utilisant des modèles de souris rétinopathiques, le groupe du Dr Mallette a montré que l'inhibition pharmacologique du PSAS limite l'angiogenèse pathologique tout en favorisant la revascularisation de la rétine. Actuellement, des données transcriptomiques indiquent que l'enzyme cholestérol 25-hydroxylase (CH25H) augmente dans les rétines de souris rétinopathiques ainsi que durant la sénescence cellulaire. CH25H est impliquée dans la synthèse du 25-hydroxycholestérol (25-HC), et nos travaux montrent que le 25-HC déclenche la sénescence cellulaire et un fort phénotype sécrétoire, entre autres, via la régulation transcriptionnelle de RagB et RagD, connues pour stimuler la voie mTOR. Puisqu'il a été rapporté que RagB était impliqué dans la régulation traductionnelle des molécules du PSAS, nous proposons que le 25-HC pourrait être un acteur clé de la traduction de molécules sécrétées par les cellules sénescentes. Pour cela, des expériences de fractionnement de polysomes seront mises en place et utilisées sur des cellules traitées au 25-HC suivies du séquençage d'ARN. Par ces expériences, nous souhaitons identifier les ARNm activement traduits à la suite d'un traitement au 25-HC afin de mieux comprendre l'impact de cet oxystérol sur la progression de la rétinopathie.

Poster #24 **André Laezza** - *PhD* - Labo Chartrand

Exploring the proteome of pathogenic RNAs with nucleotide repeat expansions

Plusieurs troubles neuro-musculaires dégénératifs actuellement incurables sont causés par des expansions de répétitions nucléotidiques (i.e CAG, CTG, CGG,...), entraînant la production de molécules d'ARN toxiques qui s'accumulent dans des foyers nucléaires sous forme de granules d'ARN ou foci. Ces granules d'ARN répétés agissent comme des éponges moléculaires capables de séquestrer certaines protéines liant l'ARN (RNA-Binding Proteins ou RBPs) et perturbent profondément leurs fonctions normales dans la régulation post-transcriptionnelle des gènes. Cependant, il demeure incertain si différents types d'ARN qui ont les nucléotides répétés influencent les mêmes RBPs ou ont des effets similaires sur la régulation post-transcriptionnelle. Une des maladies causées par l'expansion d'ARN toxique est la dystrophie myotonique de type 1, qui fait l'objet d'une étude approfondie. La Dystrophie Myotonique de type 1 (DM1) est une maladie génétique autosomale dominante qui affecte principalement les muscles, mais aussi d'autres tissus du corps. La DM1 est causée par une expansion instable des répétitions du triplet nucléotidique CTG dans la région 3' non traduite du gène DMPK (Protéine Kinase de la Dystrophie Myotonique). Cette expansion de triplet entraîne un dysfonctionnement global au niveau cellulaire, notamment par des effets toxiques sur l'ARNm, conduisant à une perturbation de l'épissage alternatif de nombreux gènes. Plusieurs protéines impliquées dans l'épissage alternatif et la biogenèse des ribosomes, tel que la famille MBNL1-3, sont directement affectées par l'expansion CUG dans l'ARNm DMPK, ce qui ouvre la voie à de futures recherches pour comprendre les liens entre ces processus et les anomalies systémiques observées dans la DM1. En collaboration avec le laboratoire du Dr Lécuyer à l'IRCM, un criblage par imagerie à haut débit a été effectué afin d'identifier les protéines liant l'ARN (RBP) susceptibles de colocaliser avec les foyers d'ARN contenant une expansion de triplets CUG dans des cellules HeLa exprimant un ARN porteur de répétitions CUG. Dans le but de valider les résultats du criblage, nous avons d'abord détecté l'ARNm DMPK contenant des répétitions de triplets CUG dans des myoblastes de patients DM1 à l'aide de la technique de smFISH (single-molecule fluorescence in situ hybridization), une méthode permettant la détection sensible des ARN. Nous avons ensuite réalisé des expériences d'immunofluorescence (IF) afin de

visualiser les protéines d'intérêt. Nous avons ensuite appliqué cette approche combinée de smFISH-IF à d'autres RBP identifiées lors du criblage, notamment PUM1 (régulateur post-transcriptionnel impliqué dans le contrôle de la stabilité et de la traduction des ARNm) et RBM25 (facteur d'épissage participant à la régulation de l'épissage alternatif). Afin de consolider la robustesse de nos observations, nous avons également analysé Gemin5, CSTF2 et SC35 (pour cibler SRSF2) comme contrôles supplémentaires. Nos données indiquent un enrichissement de RBM25 à proximité des foyers d'ARN contenant des répétitions CUG dans les myoblastes DM1, ainsi qu'une colocalisation plus modeste de PUM1. La colocalisation observée par smFISH-IF sera quantifiée à l'aide d'approches bioinformatiques d'analyse d'images, notamment "Napari", "Cellpose" et "big_FISH". Nous utiliserons aussi la technique O-MAP-MS (Oligonucleotide-directed Proximity-Interactome Mapping coupled to mass spectrometry) afin d'identifier des interactions entre les ARN avec triplets CUG et des RBPs, ainsi qu'avec des protéines autres que des RBPs. Les protéines identifiées seront validées par des approches de co-immunoprécipitation et RT-qPCR, et leur rôle dans la formation des foci d'ARN avec répétitions CUG sera évalué par déplétion avec siARNs. Cette approche innovante fournira de nouvelles perspectives sur les mécanismes moléculaires impliqués et sur les voies protéiques affectées par les ARN avec triplets CUG, ouvrant ainsi la voie à de nouveaux développements thérapeutiques.

Poster #25 **Audrey Langlois** - *PhD* - Labo Ferbeyre

Mitochondrial Iron Sensitizes Senescent Cancer Cells to Ferroptosis

Le FOLFIRINOX est la chimiothérapie de première ligne dans le traitement de l'adénocarcinome canalaire pancréatique (PDAC). Malgré un bénéfice sur la survie, la majorité des patients développent une résistance et rechutent. Notre laboratoire a montré que le FOLFIRINOX induit la sénescence cellulaire dans des lignées PDAC, menant à un relapse (Rowell et al., 2023). Un criblage CRISPR-Cas9 a identifié la glutathionne peroxydase 4 (GPX4), enzyme clé contre la ferroptose, comme une vulnérabilité des cellules sénescentes. Nous proposons une stratégie « one-two punch » : induire la sénescence par FOLFIRINOX, puis inhiber GPX4 pour éliminer ces cellules par ferroptose. Nous observons une accumulation de fer mitochondrial et une augmentation des transporteurs SLC25A28 et SLC25A37 dans les cellules PDAC sénescentes, absentes dans les cellules saines. Ce projet vise à définir le rôle du métabolisme du fer mitochondrial dans la sensibilité à la ferroptose. Nous avons également confirmé dans un modèle murin, avec un shARN inductible contre GPX4, l'efficacité de cette stratégie.

Poster #26 **Léanne Leclerc** - *MSc* - Labo Chaker-Margot

The hydride transfer complex (HTC) and its implication in cancer metabolism: a structural approach

Senescence is a defence mechanism by which the cell cycle stops. Indeed, this mechanism acts as a protection against cancer development. By preventing cell division, it precludes cells from transferring mutations to the next generation. When a cell enters senescence, it undergoes a metabolic rewiring and sometimes exhibits specific characteristics such as mitochondrial dysfunctions. Those are characterized by a depreciation of the NAD+/NADH ratio, which leads to a reduction of the metabolic activity. In some cases, cells have the capacity to escape senescence and resume cellular replication. One mechanism involves the migration of PC into the cytoplasm and its interactions with MDH1 and ME1. Those enzymes form a metabolon called the hydride transfer complex (HTC) that replenishes the cells with NAD+ and NADPH. Therefore, providing enough cofactors to resume cell replication, counteract the ROS and thus support cell migration and metastasis. The HTC and its importance in cancer development have been mostly studied in-cellulo. However, no structural or enzymatic information has been provided in the literature. Wherefore, we sought to assemble the complex using in-vitro techniques and define the structure using a combination of Cryo-EM and cross-linking MS. Defining the structure and the enzymatic activity of the HTC could help understand how the interactions occur and provide key information for future therapeutic development.

Poster #27 **Mélanie Lemaire** - *PhD* - Labo Major

Understanding The Roles Of RNA Structural Dynamics And RNA-Binding Protein Interactions In The Biogenesis Of miR-125a, miR-128-1, and miR-188

MicroARN (miRNA) maturation initiates through microprocessor-mediated cleavage of primary miRNAs (pri-miRNAs). However, single nucleotide polymorphism (SNP) within pri-miRNA sequences can disrupt this process and lead to dysregulation and subsequently disease. The mechanisms underlying this loss of maturation remain unresolved. We hypothesize that SNPs disrupt structural dynamic and affect interactions with RNA-binding proteins (RBPs) thus decreasing pri-miRNA maturation. Methods and results: To identify key interaction sites and RNA-binding proteins involved in pri-miRNA maturation, we study SNP-induced loss-of-maturation. SNPs affecting structural dynamic and blocking maturation of miR-125a, miR-128-1 and -188 were predicted using bioinformatic, RT-qPCRs and northern blots. Those pri-miRNAs proteome were identified by RNA pull-down and mass spectrometry analysis (LC-MS/MS). SRSF3 and ADAR1 knockdowns induced a decrease of miR-128-1 biogenesis in Hs578T suggesting a role as positive regulators of miR-128-1 biogenesis in this cell line. Using our machine learning tool, D-ORB, three interaction sites in miR-125a potentially required for efficient maturation were predicted. Their functional relevance is currently being assessed by evaluating the impact of their disruption on biogenesis using RT-qPCR. Finally, to determine whether the SNP affecting miR-125a biogenesis also alters processing of its co-clustered miRNAs (miR-99b and let-7e), the SNP was introduced endogenously in MDA-MB-453 cells using CRISPR/Cas9, recapitulating its effect in a genomic context. Effects on miR-99b and let-7e maturation are currently being assessed by RT-qPCR. Conclusion and impact: These findings could help identify RBPs and key interactions sites involved in miR-125a, -128-1 and -188 biogenesis and predict the impact of genetic variation on miRNA maturation efficiency.

Poster #28 **Malana Loxam** - *MSc* - Labo Strauss

De nouvelles cibles pour le traitement du poliovirus grâce aux interactions entre VP4 et l'ARN

Bien que la vaccination généralisée contre le poliovirus ait fait progresser les efforts d'éradication, la partie de l'objectif qui reste est un traitement pour le poliovirus après l'infection. Ce projet de recherche examinera la protéine virion quatre (VP4) du poliovirus, à la fois indépendamment et en relation avec les interactions ARN. VP4 est la plus petite (7,5 kDa) et la seule des quatre protéines structurelles sans structure et fonction confirmées dans tous les états environnementaux. VP4 est logé à l'intérieur de la capside et devient externalisé lors des événements d'infection. VP4 est suspecté de s'oligomériser, se diviser en membrane cellulaire et former un pore à travers lequel l'ARN peut passer dans la cellule hôte. En comprenant mieux VP4, des informations sur l'administration du génome du poliovirus seront acquises, ce qui peut conduire au développement de médicaments à partir du ciblage thérapeutique et à la prévention de la propagation du poliovirus dans tout le corps après une infection.

Poster #29 **Hoai Thinh Luu** - *MSc* - Labo Zenklusen

Investigating features of intron lariat biology and its relationship with innate immune signaling

Investigating features of intron lariat biology and its relationship with innate immune signaling Hoai Thinh Luu (1), Mathilda McGirr (1), Gerald Raffl (2), Pascal Raymond (1), Stefan Ameres (2) and Daniel Zenklusen (1) 1. Département de biochimie et médecine moléculaire, Université de Montréal 2. Max Perutz Labs, University of Vienna, Vienna BioCenter (VBC), 1030 Vienna, Austria Introns are spliced from pre-mRNA into a 2'-5' lariat and the lariat debranching enzyme DBR1 is currently the only known 2'-5' phosphodiester bond hydrolyzing enzyme that linearizes lariats for degradation. Mutations in DBR1 have been associated with an increased susceptibility to brainstem viral infections through poorly understood mechanisms, a phenotype reminiscent of defects in components of the innate immune system. We hypothesize that stabilized lariats interact with cytoplasmic sensors for double stranded RNA via their inverted and repeated Alu elements. Since introns are nuclear retention elements, interactions could only occur through mitosis since, at the end of prophase, the nuclear envelope breaks down. To study intron lariats biology, we established a degron-based cellular system for rapid depletion of DBR1 in HCT116 cells and probed intron lariat behaviour using RNA sequencing and single-molecule resolution imaging approaches. Together, these studies will lead to a better mechanistic understanding of intron lariat biology and pathologies related to DBR1 mutations and lariat stabilization.

Poster #30 **Saad Menggad** - *PhD* - Labo Ferbeyre

RUNX1 and ETV4: Orchestrators of a Senescence Program Disrupted in Pancreatic Cancer

Cancer arises when cells evade normal control mechanisms that limit their growth. One such mechanism is cellular senescence, a natural process in which damaged or stressed cells permanently stop dividing. Senescence acts as a powerful defense against cancer but the persistent accumulation of senescent cells with age can disrupt tissue homeostasis and promote chronic inflammation, thereby contributing to age-related diseases such as cancer. Understanding how this process works at the molecular level could lead to strategies that either activate or eliminate senescent cells, depending on the clinical context. My research focuses on two proteins, RUNX1 and ETV4, recently identified in our lab as key regulators of the senescence program. These proteins help “open” the DNA structure (chromatin) and activate genes that stop cell division. Interestingly, their expression is lost in pancreatic cancer cells, suggesting that shutting down this protective mechanism may help cancer progress. By studying how RUNX1 and ETV4 remodel chromatin to trigger senescence, we aim to uncover new drug targets capable of reactivating this fail-safe program in cancer cells. Our preliminary data show that overexpression of RUNX1 or ETV4 in normal IMR90 fibroblasts and normal HPNE pancreatic cells induces senescence but not in KP4 pancreatic cancer cells. Moreover the observed senescence in IMR90 seems independently of DNA damage, accompanied by increased expression of the cell cycle inhibitor p15 (CDKN2B), decreased heterochromatin marks (H3K27me3, H3K9me3, H3K9me2) and EZH2 (PRC2 methyltransferase). In contrast, chemoresistant KP4 pancreatic cancer cells treated with Folfirinox upregulate RUNX1, ETV4, EZH2, and H3K27me3, suggesting chromatin closure rather than relaxation, in contrast to normal cells. These findings indicate that PRC2-mediated repression may contribute to senescence escape and therapy resistance. We are currently testing whether targeting EZH2 or HDAC, via inhibitors such as Tazmetostat or shRNA, can restore chromatin accessibility and induce senescence in cancer cells. Our data show that Tazmetostat enhances slightly the antiproliferative effect of Folfirinox on KP4 cells, supporting the concept of combining epigenetic therapy with chemotherapy. Our ultimate goal is to develop new epigenetic therapies that restore chromatin openness, reengage the senescence program, and block cancer cell growth. This research will improve our understanding of how healthy cells prevent cancer and support the development of innovative therapies for pancreatic cancer, one of the deadliest forms of the disease.

Poster #31 **Clemence Messmer** - *PhD* - Labo Affar

The ASXL2-BAP1-KDM1B complex in epigenetic regulation through methylation-ubiquitination crosstalk

ASXL1 and ASXL2 are essential epigenetic regulators that function as transcriptional activators or repressors depending on their binding partners. They assemble into multiprotein complexes with the deubiquitinase BAP1, the methyltransferases MLL3/4, and the histone demethylase KDM1B, and these complexes are frequently deregulated in cancer. Rationale and Hypothesis: Our laboratory demonstrated that ASXL1/2–BAP1 interactions are mutually exclusive: binding to ASXL1/2 stabilizes these proteins and enhances BAP1’s catalytic activity, which removes ubiquitin from histone H2AK119 to activate Polycomb target genes. IP-MS analyses further revealed that KDM1B specifically associates with the ASXL2–BAP1 subcomplex. We hypothesize that ASXL2 serves as a regulatory platform coordinating BAP1 and KDM1B engagement to drive transcriptional activation. Our aim is 1) to determine how ASXL2–KDM1B binding alters H3K4 and H2AK119 modification landscapes at enhancers and promoters. And 2) to elucidate the functional consequences of this interaction in vivo using a knock-in (KI) mouse model. Results: To date, we identified a 20-amino-acid motif in ASXL2 (residues 1113–1134) that is necessary and sufficient for KDM1B binding and generated an ASXL2ΔKDM1B mutant. Sequence homology with NPAC, a known coactivator of KDM1B, suggests direct competition for the same KDM1B interface, a notion corroborated by both in vitro and in cellulo assays. Interestingly, enzymatic assays on purified nucleosomes show that, unlike NPAC, ASXL2 fails to stimulate—and even inhibits—KDM1B demethylase activity on H3K4me1/2 by sequestering KDM1B away from NPAC. Furthermore, we could not observe any activity towards other methylated histones. Finally, ASXL2ΔKDM1B KI mice have been generated, validated by IP-MS, and homozygous MEFs are in hand for RNA-seq and ChIP-seq analyses. Together, these studies will clarify how ASXL2–KDM1B interactions shape chromatin landscapes and regulate transcription.

Poster #32 **Léo Millot** - *MSc* - Labo Archambault

Rôle de la phosphatase PP2A-B56 dans la régulation des centrosomes

La mitose est régulée par des kinases et des phosphatases. Ce projet étudie l'enzyme PP2A-B56, un hétérotrimère jouant divers rôles durant la mitose, en interagissant avec ses substrats via un motif SLiM. Chez D. melanogaster, deux orthologues de B56 existent : Widerborst et Well-rounded. Les centrosomes sont régulés par des kinases, mais le rôle des phosphatases y reste peu connu. Nous utilisons D. melanogaster pour mieux comprendre la phosphorégulation des centrosomes. Nos travaux montrent que les B56 se localisent aux centrosomes et interagissent avec des protéines centrosomales. Leur codéplétion réduit le nombre de centrosomes en mitose, et des mutations dans le domaine de reconnaissance du SLiM en abolissent la localisation. Nos résultats suggèrent que PP2A-B56 déphosphoryle des protéines centrosomales. Les recherches futures viseront à élucider le mécanisme moléculaire de recrutement de cette phosphatase

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Poster #33 **Viktoria Mochulska** - *PhD* - Labo François

Generative landscape models of cellular differentiation

Cellular differentiation is a process by which cells become specialized to perform a particular function in the body. It is often envisioned as a "Waddington landscape", where cells, like balls, roll downhill and end up in one of the deep valleys – one of the possible cell fates. Thanks to recent advances in single-cell technologies, this metaphor can be turned into a quantitative model, opening an avenue for understanding, predicting, and guiding cell fate decisions. We propose Evoscape, a method for the systematic generation of such landscape models based on data. For constructing the landscape, we combine simple building blocks such as hills and valleys, creating a flexible yet interpretable model. This allows us to optimize both the topography (location and depth of features) and topology (the routes taken by the cells). To fit landscapes to data, we use an algorithm that mimics evolution and apply our method to different biological examples. From hundreds of optimized landscapes, we identify a small number of distinct possible solutions. These solutions, however, share a common topography, which shows how the landscape is constrained by the data, allowing for the systematic generation of interpretable and predictive models.

Poster #34 **Carl Munoz** - *PhD* - Labo Lemieux

Quantifier l'impact du séquençage de basse profondeur et du débruitage par réseaux de neurones de données RNA-seq

Le RNA-seq est une technologie permettant une compréhension approfondie de l'activité cellulaire, mais son coût demeure élevé (environ 150 $ par échantillon bulk). Réduire la profondeur de séquençage permet de diminuer ces coûts, mais entraîne aussi une perte de qualité des données. Nous visons donc à quantifier l'impact de cette réduction de profondeur et à identifier des méthodes de débruitage pouvant augmenter la qualité de ces données. Nous avons développé des modèles d'apprentissage automatique et d'inférence bayésienne capables de reconstruire des données RNA-seq de pleine profondeur à partir de données de basse profondeur. Ces approches permettent de récupérer une grande partie de l'information biologique perdue, notamment la classification des types et sous-types de cancer, ainsi que l'identification des gènes différentiellement exprimés. Cette recherche pourrait contribuer à modifier les standards du RNA-seq, tant pour la médecine personnalisée que pour l'acquisition de larges volumes de données auparavant inaccessibles.

Poster #35 **Gilberto Muñoz Nieto** - *MSc* - Labo Ferbeyre

SENESCENCE AND PREMATURE AGING IN AN INDUCIBLE MODEL OF IMPAIRED RIBOSOME BIOGENESIS IN VIVO

Ribogenesis, the process by which a cell makes new ribosomes, is a tightly regulated process that is impaired in senescence, a state of stable cell cycle arrest. Our laboratory has shown that impairing ribogenesis through a knock-down of its key factor RSL1D1 can also cause a cell to enter senescence in a p53-independent manner. Most of the work that has brought information on the link between ribogenesis and senescence has been done on cell lines. Knowing that an accumulation of senescent cells in vivo is linked with signs of aging and pathologies, we wish to investigate the effects of impaired ribogenesis on a live organism. To do so, our laboratory has developed a murine model of a conditional knockdown of RSL1D1 that affects all tissues except the brain. Starting after 3 months of induction, the animals present clinical signs of aging including alopecia and kyphoscoliosis. They also become more likely to develop pathologies linked to aging such as dermatitis and blepharitis. Upon necropsy, they tend to present with splenomegaly, a sign of deficient bone marrow hematopoiesis. SA-B-galactosidase assay of extracted tissues shows accumulation of SA-B-gal+ cells in high-turnover tissues like skin and testis. Preliminary IHC results show accumulation of p21+ cells in the pancreas. We have so far concluded that impairing ribogenesis leads to accumulation of senescent cells and signs of accelerated aging in mice.

Poster #36 **Maya Nikolova** - *PhD* - Labo Ferbeyre

Investigating the Anti-Senescence Function of Extracellular Vesicles from Mesenchymal Stem Cells

Mesenchymal stem cells (MSCs) are adult stem cells that have great therapeutic potential due to their functions in promoting tissue repair and limiting inflammation. MSCs have rejuvenating effects when transplanted in animal models of aging and can reduce senescent cell burden. The function of MSCs is mainly mediated by secreted factors, including extracellular vesicles (EVs) which are important mediators of cellular communication. Indeed, MSC-EVs can reduce cellular senescence in recipient cells, however, the precise contexts and mechanisms of this anti-senescence effect have yet to be elucidated. In this project, we propose to characterize the function of EVs from human MSCs (hMSCs) by (i) isolating hMSC-EVs and evaluating their effect on senescent fibroblasts, (ii) characterizing the RNA and protein content of hMSC-EVs with the hope of identifying EV-loaded factors mediating the observed effect, and (iii) evaluating the effect of hMSC-EVs in mouse models of senescence. We hope that the proposed research will advance aging research, allowing for the development of novel therapies for the treatment of age-related diseases.

Poster #37 **Nicolas Pouderous** - *PhD* - Labo Ferbeyre

Étude du rôle des ARN non codants nucléolaires dans le cancer du pancréas dans l'induction de la senescence par thérapie.

L'adénocarcinome canalaire pancréatique (PDAC) demeure l'un des cancers les plus létaux, avec le FOLFIRINOX (FX) comme traitement standard. La prolifération tumorale est étroitement liée à la biogenèse des ribosomes, processus nucléolaire impliquant plus de 600 facteurs. Notre laboratoire a démontré que sa perturbation induit la sénescence cellulaire, caractérisée par l'activation des voies p53/p21 et p16/pRB, une activité SA-β-galactosidase, un SASP pro-inflammatoire, ainsi que des défauts ribosomiques (SARD) et des foyers nucléolaires (SANF). Certaines cellules cancéreuses peuvent néanmoins échapper à ce processus, contribuant à la rechute tumorale. Nous émettons l'hypothèse que les ARN non codants nucléolaires (ncARN), incluant snoARN, lncARN et ARN-IGS, constituent un niveau clé de régulation de ce processus. Nous montrons que le FX induit la sénescence dans les cellules KP4, confirmée par SA-β-gal, SASP, p21, Ki67 et réorganisation nucléolaire. Des nucléoles purifiés ont été soumis à un séquençage ARN, révélant une signature de ncARN dérégulés.

Poster #38 **Hebatallah Samy Saad** - *PhD* - Labo Legault

The regulation of miRNA biogenesis by the Zika virus capsid protein

MicroRNAs (miRNAs) are key regulators for gene expression. They are transcribed in precursor forms that are processed by Dicer to generate the mature miRNAs. Interestingly, the activity of Dicer is inhibited by the Zika virus capsid protein (ZVCP), which resulted in a global decrease in the miRNA levels in neural stem cells. This interaction is likely the cause of the severe neurological complications associated with Zika infection. However, the mechanism of Dicer regulation by the ZVCP is not well understood. Here, we employed biochemical tools, enzyme kinetics, cryo-EM, confocal microscopy methods to investigate the interaction between Dicer and the ZVCP. Enzymatic assays showed a potent inhibition of Dicer by the ZVCP. This inhibition is not explained by substrate sequestration. However, the ZVCP-Dicer interactions lead to biomolecular condensates, creating a microenvironment incompatible with Dicer activity. Our findings reveal a previously unrecognized mechanism of host Dicer regulation via biomolecular condensation, which can guide future therapeutic approaches aiming to combat the Zika infection.

Poster #39 **Issam Saadie** - *MSc* - Labo Hussin

Evaluating the Performance of Peptide-HLA Binding Predictors Reveals Gaps in Current Tools

Computational tools for predicting immune responses have become indispensable to immunological research, an impact made even more evident in the wake of the COVID-19 pandemic. Among those tools are those that predict the binding that occurs between a pathogen's peptide, called an epitope, and the human leukocyte antigen (HLA), getting us a step closer to detecting cytotoxic T-cell's immune response to virus infections. We aim to use these tools to predict immunogenic SARS-CoV-2 epitopes. Toward that goal, we evaluate the performance of widely used peptide-HLA binding predictors including NetMHCpan and MHCFlurry. We conducted a series of comprehensive benchmarks using data from the immune epitope database (IEDB), giving us the current state of the art dataset to select the best performing tools. These benchmarks uncover a major weakness in the tools' ability to predict novel SARS-CoV-2 epitopes and show variable performance depending on epitope origin, viral- or cancer-based. We conclude by underscoring the need for more specialized tools tailored to viral epitopes and for more diverse, better-annotated immunological datasets to support future development.

Poster #40 **Matthew Scicluna** - *PhD* - Labo Hussin

PHATE-Derived Ancestry Coordinates Capture Continuous Population Structure in Human Genomic Data

Large-scale human genomic datasets are commonly visualized using low-dimensional embeddings as ancestry coordinates, yet widely used methods often fail to faithfully represent continuous population structure. Linear approaches such as PCA capture global variation but miss fine-scale structure, while nonlinear methods like t-SNE and UMAP preserve local relationships at the expense of global coherence, often producing disconnected clusters. Here, we demonstrate how PHATE, a diffusion-based manifold learning method, can recover both local and global structure when appropriately tuned. We show that neighborhood scale plays a critical role: small values lead to disconnected representations, while larger values enable recovery of continuous geographic and admixture patterns. Using both synthetic data and real-world cohorts, including the 1000 Genomes Project, HGDP, UK Biobank, and All of Us, we demonstrate that PHATE more faithfully captures population structure than existing approaches. These results highlight the importance of parameter selection and sampling design, and support the use of diffusion geometry for constructing interpretable ancestry coordinates.

Poster #41 **William Tamburri** - *PhD* - Labo Chartrand

Nucleolar Trafficking in Saccharomyces Cerevisiae Telomerase Biogenesis

Telomeres protect the ends of linear chromosomes, acting as important buffer regions regulating cell division. Cancers achieve replicative immortality via the disregulation of telomere length, most frequently through the erroneous reexpression of the telomere lengthening enzyme telomerase, an enzyme absent from somatic cells in adults. The pathway for biogenesis of telomerase is broadly conserved between the model organism Saccharomyces Cerevisiae and Homo Sapiens, but remains poorly understood, particularly with regards to the role of the nucleolus in the trafficking of the telomerase RNA component (TERC, TLC1 in Sacc. Cerevisiae). Developments in live cell imaging, advanced microscopy techniques, and image analysis pipelines enable the study of mislocalization of TERC in the context of genetic perturbations to ascertain the role of key factors in the construction of the immortality enzyme. Emerging evidence links the ubiquitous nucleolar Nsr1, an RNA binding protein and budding yeast homologue of human nucleolin, as a candidate regulator responsible for nucleolar shuttling of TLC1 RNA during the creation of the telomerase holoenzyme. Nsr1 has previously been studied in its role in promoting the stability of the genome and processivity of transcription of ribosomal DNA via shuttling of Top1 topoisomerase to the nucleolus. Interestingly, protein polyphosphorylation, a novel post-translational modification involving the addition of inorganic polyphosphate chains to proteins, has been identified as a regulatory mechanism for the localization and trafficking of Nsr1, nucleolar proteins, and potential binding partners in the nucleolus. Tgs1, a conserved nucleolar methyltransferase, confers TLC1 RNA a trimethylguanosine cap in the nucleolus during telomerase biogenesis, a process which is not only required for nuclear retenion, abrogating the erroneous export of completed telomerase holoenzyme to the cytoplasm, but also required for nucleolar transit of TLC1 RNA. Deletion of Nsr1 causes telomerase-dependent telomere elongation and mislocalization of TLC1 to the nucleolus, implicating Nsr1 in quality-control step of RNA maturation beyond its established roles in rRNA processing and rDNA topology. Further, preliminary coimmunoprecipitation results suggest TLC1 RNA interacts with Nsr1. Deletions of Nsr1, Tgs1 and Vtc4, the Vacuolar membrane polyphosphate polymerase and originator of all cellular polyphosphates, localize Tlc1 RNA to the nucleolus, and analysis of single molecule fluorescence in situ hybridization (smFISH) microscopy data show an increase in TLC1 RNA foci, suggesting increased expression of telomerase RNA and impaired biogenesis of telomerase. Preliminary data also indicates deletions of Nsr1 and Tgs1 swell the nucleolus, suggesting an accumulation of pre-ribosomal RNA. Given the mounting evidence of Nsr1 as a propose a model for nucleolar trafficking of telomerase RNA wherein Nsr1 enables the shuttling and capping of TLC1 RNA through the nucleolus via interactions with TLC1 RNA and Tgs1 regulated by the presence of inorganic polyphosphates. In sum, our study aims to dissect how nucleolar protein modifications integrate with RNA trafficking to control telomerase maturation, thereby addressing a barrier to understanding a pathway whose misregulation drives the proliferation of most cancers.

Poster #42 **Asmaa Toumi** - *PhD* - Labo Rossignol

Plateforme de validation fonctionnelle intégrant le FLIM-FRET pour disséquer les troubles neurodéveloppementaux associées à TRIO

Les mutations perte ou gain de fonction du gène TRIO sont associées à un large spectre de troubles du neurodéveloppement (NDDs). TRIO code une Rho-guanine nucléotide exchange factor (RhoGEF) connue pour activer Rac1 et RhoA, deux RhoGTPases impliqués dans la migration cellulaire. Des données récentes de notre groupe indiquent que la délétion conditionnelle de Trio dans les interneurones GABAergiques (INs) altère le développement morphologique et la migration de ces INs, entraînant une réduction de l'inhibition corticale, des comportements de type autistique et de l'épilepsie chez les souris TriocKO. Pour tester si les troubles associés à TRIO résultent d'une telle altération du développement et de la migration des INs, nous avons conçu une plateforme de validation fonctionnelle permettant d'exprimer un ADNc mutant (MT), portant des variants dérivés de patients, ou l'ADNc sauvage (WT) dans des explants de l'éminence ganglionnaire médiane (MGE) d'embryons TriocKO à e13.5. Nous avons étudié la dynamique migratoire et le développement morphologique des INs à l'aide d'imagerie time-lapse haute résolution et quantifié la morphologie cellulaire 3D avec Neurolucida. Nos résultants montrent que les mutations situées dans le domaine GEFD1, ne restaure ni le retard migratoire ni la morphologie aberrante des INs TriocKO. En outre, à l'aide d'essais FLIM-FRET, nous démontrons que ces mutations entraînent une réduction de l'activité de Rac1.

Poster #43 **Natalia Uzcategui** - *MSc* - Labo Lécuyer

Deregulation of RNA localization in myotonic dystrophy type I

Myotonic dystrophy type I (DM1) is a multisystemic neuromuscular disorder caused by a CTG repeat expansion in the DMPK gene. The mutant mRNA accumulates in the nucleus in repeat RNA foci, which act as RNA-protein interaction hotspots. Some RNA binding proteins (RBPs) tend to be functionally disrupted by their sequestration within them, most notably MBNL1, an RBP involved in mRNA regulation. The impact of CUG repeat RNA on the functional properties of RBPs remains unclear. To evaluate the impact of the repeat expansion on the subcellular distribution of the transcriptome, we sequenced RNA extracted from subcellular compartments of healthy versus diseased myoblasts. We observed compartment-specific differences in RNA expression, features and RBP binding site enrichment. Mislocalized genes were also enriched in disease-relevant functions and displayed splicing events in patient biopsies, some of which may be clinically relevant. Considering RNA localization in the study of DM1 may help improve our understanding of its molecular basis

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Poster #44 **Anthony Villeneuve** - *MSc* - Labo Chaker-Margot

La régulation mécanistique et structurale de Tiam1 dans le cytosquelette

La formation de métastases est définie par la migration de cellules tumorales vers un nouveau site de colonisation, menant à l'émergence de tumeurs secondaires. Ce processus est responsable d'une forte majorité des décès par cancer chez l'humain. À ce jour, aucune thérapie ne peut cibler adéquatement ce processus. Il a été observé que la GTPase Rac1 est suractivée chez des patients souffrant de métastases. Des études ont aussi montré que l'activation de Rac1 est favorisée par Tiam1, une protéine régulatrice de la structure du cytosquelette. Il est cru que Tiam1 peut être activé par Ras. Une voie de signalisation ayant un potentiel thérapeutique devient ainsi claire. Cependant, les mécanismes de la régulation structurale de Tiam1, ainsi que son rôle sur des facteurs en aval, demeurent peu compris. Ici, par photométrie de masse, un complexe Ras-Tiam1 a été observé. Des essais enzymatiques utilisant un analogue fluorescent de GDP indiquent que Ras favoriserait l'activation de Tiam1. Des structures 3D préliminaires obtenues par Cryo-EM suggèrent qu'il y a formation d'un complexe Ras-Tiam1. Ces modèles sont cependant à faible résolution. En somme, les résultats préliminaires suggèrent la présence d'une interaction Ras-Tiam1, et que celle-ci favoriserait l'activation subséquente de Rac1.

Poster #45 **Romain Villot** - *PhD* - Labo Mallette

CH25H drives the senescence-associated secretory phenotype and promotes retinopathy

Cellular senescence is a biological response to stress associated with numerous pathological conditions, including ischemic retinopathies. Clearance of senescent cells or limiting their senescence-associated secretory phenotype (SASP) improved vascular phenotypes in mouse models of retinopathies and vision in human clinical trials for diabetic eye disease. However, the molecular mechanisms underlying the secretory phenotype of senescent cells in ischemic retinopathy remain unclear. Using a mouse model of retinopathy (oxygen-induced retinopathy, OIR), we identify a central role for cholesterol 25-hydroxylase (CH25H)—the enzyme that produces 25-hydroxycholesterol (25-HC)—in driving cellular senescence. The level of CH25H is high in senescent cells and its depletion limits stress-induced senescence. In addition, 25-HC triggers cellular senescence and the SASP through calcineurin-mediated activation of lysosome-associated transcription factors. In a mouse model of retinopathy, CH25H deletion decreases the senescence burden within the retina leading to improved physiological revascularization of the retina. Thus, CH25H and the oxysterol 25-HC are critical mediators of cellular senescence contributing to ischemic retinopathies.

Poster #46 **Yonglin Zhu** - *PhD* - Labo Hussin

Chromatin landscape and enhancer-gene interaction differences between three cardiac cell types

Genome-wide association studies (GWAS) have identified single-nucleotide polymorphisms (SNPs) that are associated with a specific phenotype. One limitation for the identification of disease-relevant genes from GWAS results is that most of the SNPs identified are non-coding. Mapping non-coding SNPs to enhancers is a known approach to relate the non-coding variant to a disease-relevant gene. While previous focusing on cardiac diseases using this approach has been carried out for the contractile and predominant cell type in the heart -cardiomyocytes (CMs), the involvement of other non-CM cell types has not been looked at. We hypothesized that characterizing cell-type-specific enhancer-gene interactions (EGIs) for these non-CMs, namely cardiac fibroblasts (CFs), endothelial cells (ECs), and smooth muscle cells (SMCs), followed by mapping cardiac-disease-associated non-coding SNPs to those enhancers could lead to disease-relevant gene identification and provide insights for future mechanistical research. We have employed the activity-by-Contact (ABC) model, which integrates assay for transposase-accessible chromatin sequencing (ATAC-seq), H3K27ac chromatin immunoprecipitation with sequencing (ChIP-seq), and high-throughput chromosome conformation capture with H3K27ac immunoprecipitation (H3K27ac HiChIP) data for the three non-CMs. We have identified the landscape of cell-type specific EGIs in cardiac cells. Furthermore, a higher similarity of the chromatin accessibility profile (ATAC-seq) between CF and SMC compared to CF and EC, and SMC and EC was observed. Finally, overlapping identified EGIs with cardiac-disease-associated non-coding variants has allowed to identify a QT-interval-associated SNP that has been mapped to the enhancer regions of an EC-specific EGI.

Poster #47 **Mehdi Zemouri** - *MSc* - Labo Pelletier

Accelerated Substrate Screening Guides Evaluation of Regio- and Enantioselectivity in Variants of Cytochrome P450 BM3

Cytochrome P450 BM3 monooxygenase is capable of selective C-H bond functionalization, offering sustainable and selective access to high-value compounds for industrial and pharmaceutical applications. In the past, we generated large libraries of P450 BM3 variants through mutagenesis and combinatorial approaches and screened them against compounds of interest using rapid colorimetric assays, to discover highly active and selective biocatalysts. However, high-throughput screening using colorimetric assays can be limiting, as they provide little or no information on regio- and enantioselectivity, which are essential for biocatalyst development. Here, we developed a rapid HPLC-based method to identify new reactive substrates by screening pooled P450 BM3 variants, enabling accelerated assessment of oxidative activity and early identification of substrate classes suitable for detailed regioselectivity studies. Twenty-five compounds were screened against seven biocatalyst pools, each containing 96 P450 BM3 variants. From those compounds, five alkylbenzenes providing high product formation were selected to characterize asymmetric hydroxylation. Subsequent evaluation of individual variants revealed biocatalysts with enhanced activity compared to wild-type P450 BM3 and high regioselectivity. Guided by these findings, we aim to screen this alkylbenzene panel against a large combinatorial library of P450 BM3 variants using chiral column chromatography (SFC/HPLC) to map variations in regio- and enantioselectivity. This approach will enable systematic analysis of the relationship between sequence identity and catalytic selectivity.

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