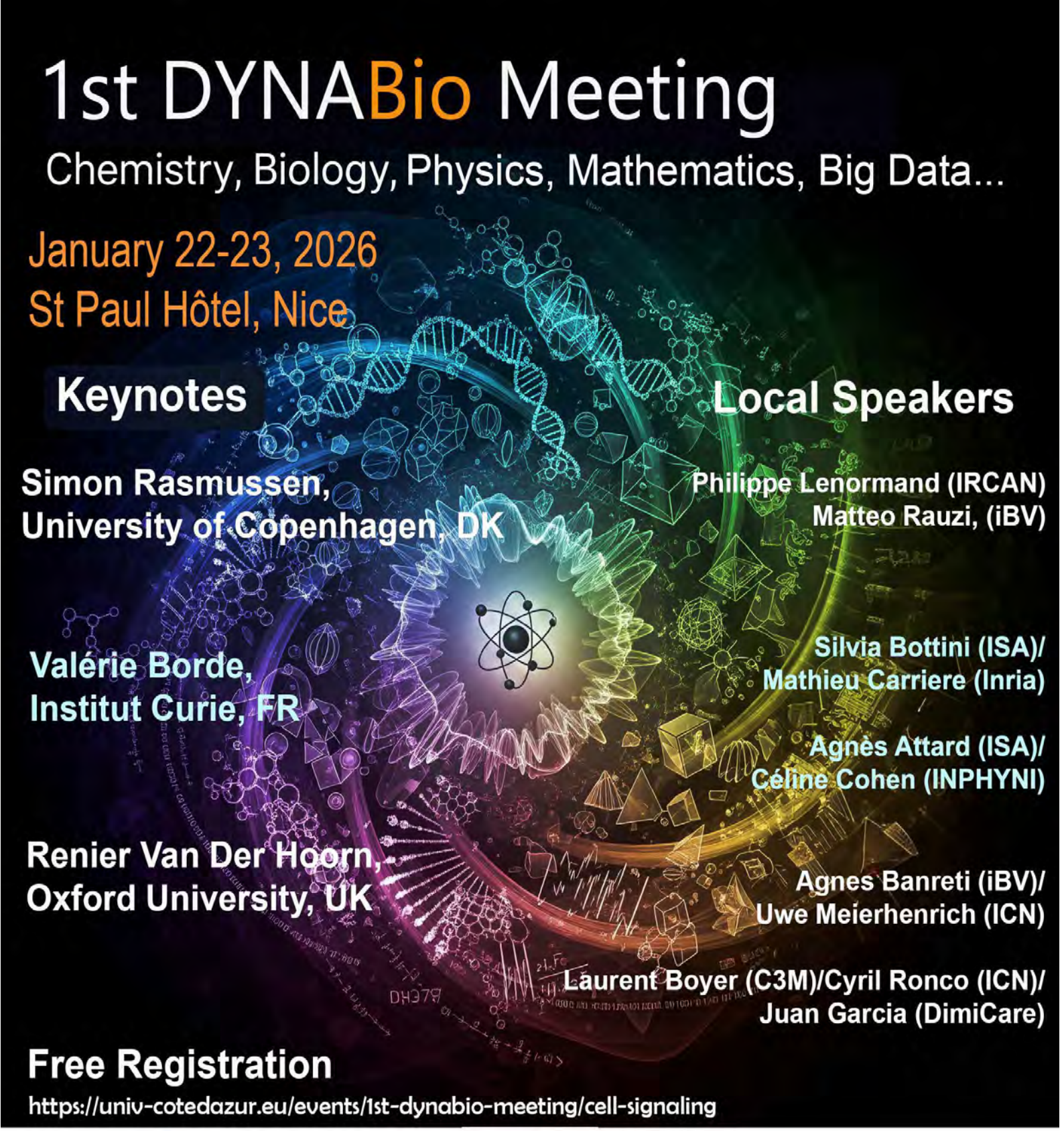
1st DYNABio Meeting

Chemistry, Biology, Physics, Mathematics, Big Data...

January 22-23, 2026
St Paul Hôtel, Nice



Keynotes

Simon Rasmussen,
University of Copenhagen, DK

Valérie Borde,
Institut Curie, FR

Renier Van Der Hoorn,
Oxford University, UK

Local Speakers

Philippe Lenormand (IRCAN)
Matteo Rauzi, (iBV)

Silvia Bottini (ISA)/
Mathieu Carriere (Inria)

Agnès Attard (ISA)/
Céline Cohen (INPHYNI)

Agnes Banreti (iBV)/
Uwe Meierhenrich (ICN)

Laurent Boyer (C3M)/Cyril Ronco (ICN)/
Juan Garcia (DimiCare)

Free Registration

https://univ-cotedazur.eu/events/1st-dynabio-meeting/cell-signaling

DYNABio

UNIVERSITÉ CÔTE D'AZUR

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ORGANIZATION

The 1st PSI DYNABio Meeting is organised by the Scientific Animation Committee (CAS)

- Arkowitz Robert
- Banreti Agnes
- **Barres Romain** (CAS Co-Director)
- Bécavin Christophe
- Bianchini Laurence
- Blancou Philippe
- **Boisson-Dernier Aurélien** *(Task Force)*
- **Bottini Silvia** (CAS Co-Director)
- Braendle Christian
- Brest Patrick
- **Busca Roser** *(Task Force)*
- Cazals Frederic
- Cerezo Michaël
- Chaves Madalena
- Cherfils-Vicini Julien
- **Drin Guillaume** *(Task Force)*
- Favery Bruno
- Fernandez Sebastian
- **Gilleron Jérôme** *(Task Force)*
- Gogl Gergo
- Hilliou Frédérique
- Ivanov Stoyan
- Prod'homme Virginie
- Rauzi Matteo
- Sandoz Guillaume
- Sarti Edoardo
- **Studer Michele** *(Task Force)*
- Trabucchi Michele
- Wakkach Abdelilah
- Zaragosi Laure-Emmanuelle

Logistics

Bliznyuk Anna

PROGRAM

DYNABio

DARE INTERDISCIPLINARITY IN BIOLOGY

Time	Event
	1st DYNABio Meeting, January 22-23, St Paul Hôtel, Nice
	Thursday, Januray 22 (DAY 1)
9:00 - 9:10	Welcome remarks S. Antoniotti (IdEx), F. Besse (Co-director), J-F. Tanti (Co-director)
	Session 1: Biological Data Science
09:10 - 10:00	Simon Rasmussen, University of Copenhagen, DK *Multi-modal data integration using deep learning on biological data*
10:00 - 10:30	Philippe Lenormand (IRCAN) *Expanding the scope of a new molecular mechanism via computational biology: choosing the start codon*
10:30 - 11:00	Coffee Break
11:00 - 11:30	Matteo Rauzi, (iBV) *Composite morphogenesis: how can a tissue fold and extend at the same time*
11:30 - 11:50	Fast Talks
11:50 - 12:30	Poster Session
12:30 - 14:00	Lunch
14:00-15:00	**Free Exchange Session**
	Session 2: Biological Network Modeling
15:00 - 15:50	Valérie Borde, Institut Curie, FR *One molecule at a time: visualizing the hidden face of DNA repair by homologous recombination*
15:50 - 16:20	Silvia Bottini (ISA) / Mathieu Carriere (Inria) *From knowledge graph to topological data analysis: a novel framework to infer and analyse gene regulatory network to improve plant health*
16:20 - 16:50	Coffee Break
16:50 - 17:20	Agnès Attard (ISA) / Céline Cohen (INPHYNI) *Unravelling the spatiotemporal dynamics of the early dialogue between host plants and pathogenic Oomycetes: Biological and Physical approaches*
17:20 - 18:00	Fast Talks
18:00 - 19:30	Poster Session
19:30 - 20:30	Wine, Socca and Cheese
	Friday, Januray 23 (DAY 2)
	Session 3: Chemistry of Biological Systems
09:00 - 09:30	Agnes Banreti (iBV) / Uwe Meierhenrich (ICN) *Homochirality Maintenance and Its Biological Roles*
09:30 - 10:00	Laurent Boyer (C3M) / Cyril Ronco (ICN) / Juan Garcia (DimiCare) *Discovery of a Novel Antibiotic: Bridging Chemistry, Microbiology and Entrepreneurship*
10:00 - 10:20	Fast Talks
10:20 - 10:50	Coffee Break
10:50 - 11:30	Poster Session
11:30 - 12:30	Renier Van Der Hoorn, Oxford University, UK *Molecular manipulations of the plant apoplast by a bacterial model pathogen*
12:30 - 13:00	Concluding Remarks S. Bottini (CAS Co-director), R. Barrès (CAS Co-director)
13:00 - 14:00	Lunch

Keynote Speakers

Session 1 : Biological Data Science

Simon Rasmussen, University of Copenhagen, DK

Multi-modal data integration using deep learning on biological data

Simon Rasmussen

University of Copenhagen

Corresponding author: srasmuss@sund.ku.dk

Keywords: AI, deep learning, multi-modal data, multi-omics, health

Simon Rasmussen is Professor of Multi-Modal Bioinformatics at the Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, and an Affiliate Researcher at the Novo Nordisk Foundation Center for Genomic Mechanisms of Disease at the Broad Institute of MIT and Harvard. Trained as a biochemical engineer, he obtained his PhD in systems biology from the Technical University of Denmark in 2010. Professor Rasmussen's research focuses on developing deep learning methods for integrating large-scale, heterogeneous biological and clinical data. His group combines genomics, proteomics, metabolomics, microbiome profiles, and electronic health records to model complex biological systems and human disease at population scale. A central aim of this work is to move beyond single-modality analyses by training large multi-modal foundation models that learn shared representations across data types while retaining biologically meaningful structure. These models are designed to support transfer learning across diseases, populations, and modalities, and to serve as general-purpose foundations for downstream tasks such as disease risk prediction, patient stratification, and mechanistic inference. In parallel, he actively engages in building scalable AI infrastructure that enables training and deployment of such models on population-scale health data using high-performance computing resources, with the goal of translating advances in deep learning into deployable systems for precision medicine and clinical decision-making. He has played a leading role in advancing AI-driven bioinformatics, contributing foundational methods for large-scale omics analysis, metagenomics, and health data integration. He has authored over 120 peer-reviewed publications, including papers in Nature, Science, Cell, Nature Biotechnology, and Nature Medicine, and has been recognized multiple times as a Highly Cited Researcher by Clarivate Analytics.

Session 2: Biological Network Modeling

Valérie Borde, Institut Curie, FR

One molecule at a time: visualizing the hidden face of DNA repair by homologous recombination

Valerie Borde

Institut Curie

Corresponding author: valerie.borde@curie.fr

Keywords: Long-read sequencing - genome stability - DNA double-strand breaks - Meiosis - Mutagenesis

DNA double-strand breaks (DSBs) are the most hazardous DNA lesions for genome integrity since they interrupt the DNA chain, generating risks of chromosomal rearrangements, mutations or loss-of -heterozygosity frequently seen in cancers. During meiosis, DSBs are programmed and their repair by homologous recombination (HR) is key to the production of normal euploid gametes, by promoting homolog pairing and crossovers. HR requires DNA synthesis to reconstitute the DNA degraded during DSB resection. Despite playing crucial roles in the outcome of DSB repair in both meiotic and somatic cells and being potentially mutagenic, this step is poorly characterized at the protein level but also how the extent of DNA synthesis is regulated and what are the consequences of its deregulation. We are using genome-wide mapping of DNA synthesis at meiotic DSBs to study how excess DNA synthesis is prevented, how the length of repair-associated DNA synthesis is influenced by the extent of end resection and other cis and trans-acting factors. In addition to these population-based studies, we also developed the use of single molecule approaches, allowing us to visualize the distribution of DSB repair synthesis on whole chromosomes, but also at a very fine, nucleotide-resolution, level. This allows us as well to distinguish repair events occuring between sister chromatids or between homologs. I will present our latest progress on these approaches, and what they can tell us about the fine mechanisms of DSB repair by homologous recombination.

Session 3: Chemistry of Biological Systems

Renier Van Der Hoorn, Oxford University, UK

Extracellular molecular antagonisms at the plant-pathogen interface

Nattapong Sanguankiattichai, Pierre Buscaill, Balakumaran Chandrasekar, Gail Preston, Renier van der Hoorn

University of Oxford

Corresponding author: renier.vanderhoorn@biology.ox.ac.uk

Keywords: glycosidase inhibitor, chemical proteomics, subtilase, flagellin

Plants are able to recognise bacterial pathogens through conserved fragments of flagellin (flg22) that bind the cell surface receptor FLS2 in most flowering plants. These immunogenic fragments are hidden in the glycosylated flagellin polymer. We discovered that their release is initiated by glycosidase BGAL1, which acts on the terminal glycan of flagellin. Next, plant-secreted subtilases release of flg22 from the monomeric flagellin precursor. But unexpectedly, we discovered that inactivation of the flg22 epitope by the same subtilases is a dominant, conserved process that might be a logic consequence of bacteria avoiding recognition by taking advantage of host-secreted proteases. I will also discuss the identity of the BGAL1 inhibitor secreted by Pseudomonas syringae, called 'glycosyrin', which is a novel iminosugar. We resolved the glycosyrin biosynthesis, regulation and structure and discovered that it not only suppresses flg22 recognition but also dramatically alters the glycobiology of the host plant.

Local Speakers

Session 1 : Biological Data Science

Philippe Lenormand, IRCAN

Expanding the scope of a new molecular mechanism via computational biology: choosing the start codon.

Monssef Idrissi, Cercina Onesto, Gilles Pagès, Olivier Croce, Roser Busca and Philippe Lenormand

Université Côte d'Azur

Corresponding author: lenorman@unice.fr

Keywords: start-codon; translation; codon optimization; protein databases; ERK

For an entire family of proteins that we have termed NTAR (N-terminal alanine-rich) proteins, we have uncovered a mechanism in which precise start-codon selection is dictated by a stretch of repeated alanine codons immediately downstream of the initiating methionine. We have validated this mechanism in cellulo across multiple, unrelated proteins. Although targeted mutagenesis has offered valuable insights, it cannot fully disentangle the contributions of amino-acid repetition from those of RNA sequence or structure, raising a key question: Is translation initiation controlled by the repeated alanine residues themselves, or by the RNA architecture created by their codons? To address this, we used unbiased computational analyses to define the complete NTAR family and to identify shared features that will guide our experimental testing. Our findings suggest that up to 10% of human proteins may rely on this mechanism for accurate translation initiation. The presence of NTAR sequences across evolutionarily unrelated proteins further suggests convergent evolution and a strong selective pressure for tightly regulated translation. More broadly, our data indicate that codon optimization near the start of open reading frames requires special consideration, and that new design principles may improve the expression of synthetic or engineered proteins.

Session 1: Biological Data Science

Matteo Rauzi, iBV

Composite morphogenesis: how can a tissue fold and extend at the same time

Matteo Rauzi

Université Côte d'Azur

Corresponding author: matteo.rauzi@univ-cotedazur.fr

Keywords: tissue morphogenesis, gene patterning, tensile-stress patterns, embryo development, cell cytoskeleton

During embryo development, epithelia can undergo different shape transformations. While these changes can be sequential, and thus driven by specific sequential cellular mechanisms, this is not always the case. A single tissue can undergo multiple simultaneous shape transformations resulting in a composite process. For instance, in vertebrates, during neurulation, the dorsal tissue folds forming the neural tube while elongating along the anterior-posterior axis separating the future head from the anus (Keller, 2002). This raises an important question: how can a tissue undergo multiple simultaneous shape transformations if each transformation is per se driven by different and functionally specific cellular mechanisms? In addition, which signaling pathways are controlling composite morphogenetic processes? We use the protostome Drosophila and the deuterostome sea urchin P. lividus embryo as model systems and focus on the process of simultaneous tissue folding and extension resulting in the formation of an epithelial tube at the onset of gastrulation. By using advanced multi-view light sheet microscopy coupled to infrared femtosecond laser manipulation, optogenetics and quantitative big data analysis, we aim to shed new light on evolutionary conserved signaling pathways, mechanisms and mechanics controlling and driving composite morphogenesis.

Session 2: Biological Network Modeling

Silvia Bottini, ISA / Mathieu Carriere, Inria

From a comprehensive knowledge graph to topological data analysis: a novel framework to analyze gene regulatory networks to improve plant health

Maxime Multari, Mathieu Carrière, Xavier Amorós-Gabarrón, Alexina Damy, Ludo Andrianirina Mamisoa, Sebastian Lobentanzer, Julio Saez-Rodriguez, Stéphanie Jaubert, Aurélien Dugourd and Silvia Bottini

Institut Sophia Agrobiotech

Corresponding author: silvia.bottini@inrae.fr

Keywords: plant multi-stress response; plant-pathogens interactions; gene regulatory networks; topological data analysis; omics

Plants live in a constantly changing environment, consequently they are exposed to multiple stresses. In particular tomato, (Solanum lycopersicum), despite being among the most important vegetable crops worldwide, yet it remains highly vulnerable to over 200 diseases caused by different pests. Although the molecular response of tomato to individual stresses is well studied, the gene regulatory network (GRN) representing the crosstalk and trade-offs of multi-stress responses remains almost unexplored. To tackle this question, we developed the GENIAL (Gene rEgulatory Network and topologIcal datA anaLysis) framework to refine and analyze complex GRNs. Since to build the GRN we need to retrieve information about known molecular interactions in tomato, first we developed a knowledge graph. TomTom gathers molecular interactions from eleven publicly available databases, including transcription factors (TF)- or microRNAs- targets, protein-protein interactions, and functional annotations in a unique FAIR resource. To test the potentiality of GENIAL to study the molecular multi-stress response, we used transcriptomics data from tomato subjected to six distinct pathogens from the literature. By using only one layer of TomTom molecular interactions, namely the TF-targets, we extracted a fingerprint GRN representing the single and multiple pathogens response. To analyze this complex GRN we complemented our framework with tools from the topological data analysis. Using the Mapper algorithm, we encoded the topological structures within the GRN and using ToMATo, we identified 18 hot spots of TFs sharing targets. By crossing those structural hot spots with the TF activities, we identified four clusters corresponding to different configurations of the core and specific of tomato multi-stress response. Overall, GENIAL yielded the identification of novel and known TFs and pathways coordinating the tomato multiple pathogens response. This study represents a proof of concept of our novel framework and can be easily extended to include other molecular layers and is also scalable to other questions involving tomato and beyond.

Session 2: Biological Network Modeling

Agnès Attard, ISA / Céline Cohen, INPHYNI

Unravelling the spatiotemporal dynamics of the early dialogue between host plants and pathogenic Oomycetes: Biological and Physical approaches

Celine Cohen (1), Agnès Attard (2)

Université Côte d'Azur

Corresponding author: agnes.attard@inrae.fr; celine.cohen@univ-cotedazur.fr

Keywords: Early infection process, Root exudates, Chemotaxis, Zoospore behavior, Microfluidics

Oomycete plant pathogens have evolved a wide range of strategies to infect host tissues. Among these, the ability to sense host-derived signals is crucial for initiating infection. However, the mechanisms underlying pathogen attraction to the host prior to penetration remain poorly understood (Bassani et al., 2020). We developed a multidisciplinary project combining biological and physical approaches to investigate the rhizospheric dialogue between the soilborne oomycete Phytophthora parasitica and the model plant, Arabidopsis (Le Berre et al., 2017). Our aim was to understand how motile spores (zoospores) swim through porous environment of moist soils and which root-derived signals guide them toward host roots. To address these questions, we developed microscale spatiotemporal phenotyping tools (using microsystems, microfluidics, and high speed camera) that allow the imaging of zoospore-specific behaviors such as velocity, swimming direction and flagella beating, under conditions that closely mimic the rhizospheric microenvironment, including the vicinity of living roots (Galiana et al., 2019; Tran et al. 2022; Lupatelli et al, 2023; Cohen et al., 2025; unpublished data). We investigated zoospores chemotaxis (the ability of zoospores to orient in response to a chemical stimulus), and the spatiotemporal dynamics of early stages of infection focusing on the role of root exudates (including proton gradients) in host attractions, the specific swimming mechanisms of zoospores, and the influence of external environment factors on their mobility. Together these insights refine our understanding of early infection dynamics at fine spatiotemporal scales (µm, ms), enabling the exploration of plant-oomycete signaling with unprecedented resolutions. Bassani et al., 2020. Computational and Structural Biotechnology Journal 18:3766–3773. https://doi.org/10.1016/j.csbj. 2020.10.045 Cohen et al., 2025. Physical Review E 111, 024411. DOI: 10.1103/PhysRevE.111.024411 Galiana et al., 2019. J R Soc Interface (2019) 16 (157): 20190367. https://doi.org/10.1098/rsif.2019.0367 Le Berre et al., 2017. PLoS One 12(12):e0190341. doi:10.1371/journal.pone.0190341 Lupatelli et al., 2023. Comput Struct Biotechnol J 21:5640-5649. doi: 10.1016/j.csbj.2023.10.055 Tran et al., 2022. Elife. 2022 Mar 28;11:e71227. https://doi.org/10.7554/eLife.71227.

Session 3: Chemistry of Biological Systems

Agnes Banreti, iBV / Uwe Meierhenrich, ICN

Homochirality Maintenance and Its Biological Roles

Agnes Banreti, Uwe Meierhenrich

Université Côte d'Azur

Corresponding author: agnes.banreti@univ-cotedazur.fr

Keywords: chirality, D-amino acid, homochirality, heterochirality syndrome, chromatography

One of the most fascinating and unexplored questions in life sciences is the origin and significance of biomolecular homochirality, a key feature that distinguishes all living organisms from inorganic and abiotic matter. Proteins employ exclusively L-amino acids in their molecular architecture, the mirror-image D-amino acid counterparts are not used in proteins, molecular symmetry is broken. Our research established a direct link between D-amino acids and protein dysfunction in vivo, leading to a progressive "heterochirality syndrome." This syndrome cascades across biological scales, from the loss of molecular homochirality to increased tumor susceptibility in organs, ultimately resulting in a shortened lifespan in chiral-deficient animals. We deepened our understanding of the molecular, cellular, and developmental mechanisms that connect heterochirality to these biological effects, employing a range of genetic, cellular, and biochemical approaches. We now start to understand how organisms actively maintain the homochirality of their proteins. Specifically, we focus in our experimental research on identifying enzymes and mechanisms that regulate chirality by repairing post-translationally epimerized amino acid residues in peptides and proteins. To date, a single enzyme has been identified and characterized in eukaryotes that ensures the post-translational repair of iso-L- and D-aspartate residues derived from L-aspartate. We combine interdisciplinary chiral-selective detection tools with reverse genetic screening to identify new chirality-regulating genes specialized in repairing non-L-amino acid residues, thereby preserving proteome homochirality. We characterize and quantify chiral compounds and chirality markers such as amino acids in biological samples by multidimensional and enantioselective gas chromatography. Our aim is to better understand the chemical basis of chirality changes under stress. This collaboration, a joint effort between the Institute of Biology Valrose (iBV, Dr. Agnes Banreti) and the Institute of Chemistry Nice (ICN, Prof. Dr. Uwe Meierhenrich) will help uncovering a novel family of genes responsible for maintaining biological homochirality and thereby to understand the link in between chirality and protein dysfunction on the molecular level.

Session 3: Chemistry of Biological Systems

Laurent Boyer, C3M / Cyril Ronco, ICN / Juan Garcia, DimiCare

Discovery of a Novel Antibiotic: Bridging Chemistry, Microbiology and Entrepreneurship

DimiCare: Developing a New Generation of Targeted Antibiotics Less Vulnerable to Resistance

BOYER Laurent, GARCIA-SANCHEZ Juan A., RONCO Cyril

Université Côte d'Azur

Corresponding author: juan.garcia@dimicare-biotech.com

Keywords: AMR, Antibiotics, Medicinal Chemistry, Microbiology, Staphylococcus

Antimicrobial resistance (AMR) represents a major global health issue, with an estimated 4.7 million deaths associated with drug-resistant infections in 2021. Notably, nearly three-quarters of these deaths were linked to a defined group of high-priority pathogens collectively known as the ESKAPE bacteria. This crisis results from both the widespread misuse of antibiotics and the intrinsic capacity of certain bacterial groups to rapidly develop resistance. Historically, pharmaceutical strategies have relied on modifying existing antibiotic families to improve potency against resistance bacteria. However, this approach has repeatedly led to cross-resistance and accelerated loss of efficacy. Consequently, the development of new antibiotic classes is now recognized as an urgent priority by the World Health Organization. Beyond efficacy, next-generation antibiotics must also minimize collateral damage to the microbiota and reduce long-term environmental impact. With these objectives in mind, two research teams from the Centre Méditerranéen de Médecine Moléculaire (C3M) and the Institut de Chimie de Nice (ICN), led by Dr Laurent Boyer and Pr Cyril Ronco, identified by focused screening of newly synthesized chemical entities against ESKAPE pathogens a promising new chemical class: trichloroacetimidamides, showing highly specific activity against Staphylococcus aureus. Following three years of medicinal chemistry and biological optimization, the initial hit compound was refined into a lead molecule demonstrating potent efficacy against all multidrug-resistant S. aureus strains tested and no cross-resistance. The lead showed low cytotoxicity in human cells and no detectable resistance development in standard evolution assays after 30 days. Importantly, its main degradation product exhibited no antibacterial activity. This, together with the high specificity of this compound, suggests a minimal ecological footprint if released into the environment. These findings led to the creation of DimiCare Biotech, a startup dedicated to developing a new generation of targeted antibiotics with reduced propensity for resistance. As a first proof of concept, DimiCare's first development program (DCB001) is focused on developping a topical drug candidate for the treatment of S. aureus-associated skin infections. In a murine acute bacterial skin and skin-structure infection (ABSSSI) model, the compound achieved strong therapeutic efficacy, confirming its preclinical potential. DimiCare Biotech is now advancing toward incorporation and further development as a company aiming to discover and develop new drugs against additional bacterial pathogens. By leveraging new mechanisms of action and designing compounds inherently resilient to resistance, the company seeks to contribute to a new era of antibiotic innovation, from priority infections to opportunistic and neglected diseases.

Posters

Alphabetical order

1 – Amorós-Gabarrón Xavier– Session 2

PIMENTO: a hybrid modelling approach for gene regulatory dynamics of plant response to biotic stresses

Xavier Amorós-Gabarrón, Lorenzo Sala, Régis Duvigneau, Silvia Bottini

Université Côte d'Azur

Corresponding author: xavier.amoros-gabarron@inrae.fr

Keywords: Gene regulatory network, Plant-pathogen interaction, Physics-informed neural networks, Transcriptomics, Time-series

A major question in plant biology is how plant growth, development, and environmental responses are coordinated by the activity of regulatory factors. In particular, infections trigger a dynamic cascade of reciprocal events between host and pathogen, leading to large-scale changes in gene expression as plants recognize the presence of a pathogen and activate complex defense mechanisms, while the pathogens adjust their virulence to circumvent them and establish a successful infection. Timely and rapid plant responses are essential in determining the fate of these interactions, and uncovering how transcription factors regulate their targets across this process is critical to unveil the differing responses in normal and diseased states. Gene regulatory networks (GRNs) provide a powerful representation of these intricate regulatory systems, and although several high-throughput experimental procedures are available, most inference methods measure only static properties of these networks. Additionally, most approaches face a fundamental trade-off between scalability and mechanistic interpretability. Highly descriptive and explicit ODE-based models rapidly become intractable as the number of genes and regulatory interactions grows, while scalable methods often rely on heuristics lacking direct parallels with biological processes. Machine-learning and deep-learning approaches have been proposed recently to analyze high-throughput, high-dimensional data, and despite showing promising performances, their characteristic lack of explainability has motivated the development of frameworks that embed mechanistic structure into data-driven models. The term Scientific Machine Learning encompasses such methods, and physics-informed neural networks (PINNs) in particular enable the estimation of ODE parameters describing dynamics through an inverse-problem formulation. Here, we propose a novel hybrid modela, PIMENTO (Physics and bIology-inforMed Neural neTwOrk), based on the PINN framework to infer fully interpretable GRNs from time-series omics data. This approach exploits the ability of neural-networks to approximate high-dimensional systems in combination with constraints imposed in the form of explicit ODEs describing dynamic regulatory interactions and prior biological knowledge in the form of sequence-based predictions of transcription-factor binding-sites, restricting the solution space to biologically plausible interactions. We have applied PIMENTO on a transcriptomics time-series of tomato plants upon infection by diverse economically important pathogens, illustrating its scalability and robustness to scarce and noisy data. This is the first model to integrate ODEs and neural networks to study plant-pathogen interactions, providing a scalable and interpretable framework to model GRN and gene-expression dynamics and to advance our understanding of molecular reprogramming during biotic stress response.

2 – Barbry Pascal– Session 1

Heterogeneity of the cellular response to cigarette smoke revealed by a high-resolution, multimodal atlas of the airway wall in Chronic Obstructive Pulmonary Disease

McAndrew E, Maasen S, Fierville M, Collin A, Suleimanov S,Gillett TE,Banchero M,Arguel MJ,Dahlenberg J,Pouwels DS,Marquette CH,Lebrigand K, Heijink IH,¨Demaria M, Dormoy V, Waldmann R, Griffonnet J, Leroy S, van den Berge M, Zaragosi LE, Nawijn M, Barbry P

CNRS

Corresponding author: barbry@ipmc.cnrs.fr

Keywords: Human cell atlas, lung, chronic lung disease, exposome

Chronic Obstructive Pulmonary Disease (COPD) is a progressive and heterogeneous disorder associated with altered repair/tissue remodelling and inflammatory response. A largely underexplored area concerns the molecular and cellular mechanisms acting in the lower airway wall of COPD patients at the onset of the disease, after interactions with triggering factors such as cigarette smoke. To analyze these events, we constructed a cellular and molecular atlas of clinically relevant samples from the airways of COPD patients (GOLD-I/II/III/IV) and healthy controls matched for age and smoking status. 396,000 cells were classified into 65 distinct cell types after analysis by single-cell/nuclear short-read RNA-sequencing (sc/snRNA-seq) of 136 biopsy samples from 52 donors, collected at three anatomical sites (nose, trachea, bronchi). Five COPD and five control bronchial samples and four control nasal samples, totalling 64,000 cells, were also further characterized by long-read scRNA-seq to map cell-type-specific expression of mRNA isoforms. Results were aligned with spatial transcriptomics data generated with the Xenium 5K In Situ platform on 13 bronchial biopsy sections from patients with COPD GOLD-I/II (5 active and 8 former smokers). Transcriptional and gene regulatory landscape of airway epithelial cells were analyzed as a function of smoking history and COPD severity, introducing a first description of the cell specificity of expression of the RNA isoforms in the lung. Long-read scRNA-seq revealed differences in mRNA isoform expression of the same gene between cell types and anatomical locations as well as donor-specific mRNA isoform usage likely driven by common variants underlying splicing quantitative trait loci (sQTL), identifying specific changes in mRNA isoform usage along the differentiation trajectory from basal to goblet and multiciliated cells, with extensive mRNA isoform usage exclusive to multiciliated cells. Active smoking, a central trigger in COPD, altered the cellular ecosystem, with a partial reversibility after smoke cessation. A smoke-exposure (SE) score derived from the expression of 16 detoxification-related transcripts was used to quantify smoking-related effects between and within cell-type labels. The highest SE scores were observed in surface epithelial cells, in which subsets of ‘bystander’ cells that remained negative were identified. This atlas enhances our understanding of the differential smoke response across and within airway-wall cell types and identifies early epithelial alterations that distinguish cells directly affected by smoke exposure, and their spatial niche, which may influence the trajectory of COPD from unresponsive bystander cells.

3 – Bersanoukaeva Elza– Session 1

Ultra-Processed Foods and the Human Sperm Epigenome: Evidence from a Monozygotic Twin Intervention Study

V. George1,3*, J. M. Preston1*, MC. Dumargne1,2, Elza Bersanoukaeva2, A. Alintas1, L. Wang1,2, J. Iversen1, A. Hufnagel1, L. Hjort1, J.Taylor1, C. Sanchez2, A. N. Hansen1, L. Ängquist1, S. Hermann4, J. M. Craig3,5,6, S. Torekov7, C. Lindh8, K. S.Hougaard9

Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Copenhagen, Denmark; Université Côte d'Azur,

IMPACT, Institute for Mental and Physical Health and Clinical Translation

Corresponding author: elza.bersanoukaeva@etu.univ-cotedazur.fr

Keywords: Ultra-processed foods; human sperm epigenome; long-read sequencing; metabolic outcomes; germline epigenetics

Ultra-processed foods (UPFs; NOVA Category 4) now contribute more than half of daily energy intake in many Western countries (Monteiro et al., 2018; Marino et al., 2021) and have been repeatedly linked to adverse metabolic and cardiovascular outcomes (Lane et al., 2024). These foods contain industrial additives, contaminants, and packaging-derived chemicals, and higher consumption is associated with increased urinary concentrations of phthalates and bisphenols (Buckley et al., 2019). Over the same period, global sperm counts have fallen by approximately 60% since the 1970s (Levine et al., 2023). Although recent studies report associations between UPF intake and impaired male reproductive parameters (Valle-Hita et al., 2024), causal evidence in humans remains scarce. This project aims to address this gap by investigating how controlled dietary exposures affect metabolic and reproductive outcomes, with a particular focus on sperm epigenetics. Diet is increasingly recognised as a key regulator of male germ-cell epigenomic variation, yet its specific effects—independent of caloric load—are not well characterised in humans. Our study uses monozygotic twin pairs, providing a highly controlled design to isolate environmental effects: twins share nearly identical genomes but are exposed to distinct dietary patterns. This reduces genetic confounding and allows precise identification of diet- related changes in DNA methylation and metabolic physiology. In a three-week controlled crossover trial, five monozygotic twin pairs adhered to either an ultra-processed or unprocessed diet. Total caloric intake was held constant across conditions to disentangle the influence of food processing from energy intake. Twins assigned to the UPF diet exhibited increased body weight, altered LDL:HDL ratios, and a trend toward reduced sperm motility. Across the intervention, we collected detailed health measures and biological samples, including blood, semen, and saliva. The processed diet reflected the typical intake of American men, while the unprocessed diet aligned with Australian Dietary Guidelines. Sperm samples were analysed using Oxford Nanopore Technologies long-read sequencing, enabling comprehensive profiling of DNA methylation (5mC), hydroxymethylation (5hmC), and potential diet-associated genomic variation. Analyses will compare each twin pair, processed versus unprocessed dietary exposures, and also assess any pre-existing differences at baseline. This integrated approach provides an unprecedented opportunity to determine how modern dietary patterns reshape the molecular and functional features of human sperm. Data analysis is currently underway, and full epigenetic and functional results will be presented.

4 – Calaud Calixte– Session 1

Investigation of combinatorial epigenetic therapies to treat lymphoma

C. Calaud, E. Serrano-Lopez, L. A. Cluse, I. Todorovski, T. Mardivirin, M. Teater, A. Maarad, N. Tawfic, S. Rutaquio, P. J. Fraser, K. Guiraud, D. Yoannidis, E. Kerreneur, A. Jacquel, A. M. Melnick, R. W. Johnstone, P. M. Dominguez

Université Côte d'Azur

Corresponding author: calixte.calaud@etu.univ-cotedazur.fr

Keywords: lymphoma - epigenetic - combinatorial treatment - High-throuput assays – Transcriptomic

Diffuse Large B-cell lymphoma (DLBCL), the most frequent type of lymphoma, originates from germinal center (GC) B-cells that acquire malignant characteristics. The standard immunochemotherapy does not work for 40% of DLBCL patients. Since epigenetic deregulation (DNA methylation, histone modifications) disrupts GC formation and contributes to lymphomagenesis, epigenetic drugs have been developed. However, they have low applicability for two main reasons: 1) limited efficacy, due to targeting only one epigenetic mechanism, and 2) high toxicity, due to low specificity. Therefore, we hypothesize that since there are multiple layers of the epigenome, combining two epigenetic therapies will enhance their efficacy while reducing their side effects, since each drug will be used at a lower concentration in combination than as a single agent. We tested the efficacy of a combination consisting of a specific histone deacetylase 3 inhibitor (HDAC3) and the FDA approved, DNA methyltransferase inhibitor, 5-Azacytidine (5-Aza). We treated DLBCL cell lines in vitro to characterize the effect of the combinatorial treatment, measuring cell proliferation and cell death by flow cytometry and western blot; we also did experiments in vivo analyzing the survival after treatment. Then, we analyzed the transcriptomic changes induced by treatment using RNA-seq and confirmed the results by RT-qPCR. We also analyzed epigenetic changes by chromatin immunoprecipitation sequencing (ChIP-seq;histone acetylation) and reduced representation bisulfite sequencing (RRBS; DNA methylation). Finally, we tested the effect of the combinatorial treatment on normal human peripheral blood mononuclear cells (PBMC) by flow cytometry. In vitro, we showed that the 5-Aza+HDAC3i combination had a synergic effect by inhibiting proliferation (CellTrace Violet dye) and increasing apoptosis (Annexin V/Propidium Iodide and caspase-3 cleavage) compared to single compound or vehicle. In vivo, we observed a significant delay in tumor growth for 5-Aza+HDAC3i mice compared to single- or vehicle-treated mice. At the transcriptomic level, we found that the combination treatment induced GC B cell differentiation genes. By ChIP-seq, we observed that HDA3i alone or in combo with 5-Aza, induced changes in histone acetylation. By RRBS, we showed that 5-Aza alone or in combo with HDAC3i induced DNA hypomethylation. Finally, we confirmed that 5-Aza+HDAC3i did not impact T cell survival. My results demonstrate the superior efficacy of the combination of the epigenetic agents 5-Aza and HDAC3i against DLBCL. They suggest that the induction of cell death and inhibition of proliferation mediated by the combination treatment are associated with the re-expression of genes inducing GC-B cell differentiation, which are aberrantly repressed in DLBCL. These promising results support our hypothesis that targeting diverse epigenetic mechanisms could be a novel therapeutic approach for treating DLBCL.

5 – Calia Giulia– Session 1

Deciphering plants molecular cross-talk during multi-factorial stress response with HIVE.

Giulia Calia, Sophia Marguerit, Ana Paula Zotta Mota, Manon Vidal, Hannes Schuler, Ana Cristina Miranda Brasileiro, Patricia Messenberg Guimaraes, Silvia Bottini

Université Côte d'Azur

Corresponding author: giulia.calia@inrae.fr

Keywords: Multi-condition omics integration; variational autoencoders; POWERSHAP; plant responses to stress; biotic and abiotic stress

The characterization of the molecular cross-talk between plants and environmental stressors, either biotic or abiotic, is fundamental, especially in the context of the climate change era. As sessile organisms, plants show incredible molecular plasticity to adapt to these stresses. Omics data are a powerful approach to have a global overview of the different levels of molecular regulation in an organism, but our understanding of convergence points between biotic and abiotic stress-related signatures is still limited by the current set of tools at our disposal for integrating omics information, leading to a prioritization of specific response description over the common one. To bridge this gap, we have developed HIVE (Horizontal Integration analysis using Variational AutoEncoders), a new tool for performing integrative analysis of single omics stress experiments. HIVE couples a variational autoencoder to alleviate batch effects and uses a random forest regression integrating the POWERSHAP method to select relevant genes modulated in response to one or multiple stresses. Our tool outperformed state-of-the-art methods in identifying genes at the core of plant defence response to multiple stresses in multiple phytopathosystems of both scientific and agricultural interest. These core genes represent valuable candidates in describing a general molecular crosstalk in the stressed plant and will help in elaborating more effective and safe approaches to crop protection and environmental preservation.

6 – Camilli Victoria– Session 1

Analysis of gene regulation during plant-nematode interactions.

Victoria CAMILLI, Cyril VAN GHELDER, Emerald Flor FELICITAS, Martine DA ROCHA, Julia TRUCH

Université Côte d'Azur

Corresponding author: julia.truch@inrae.fr

Keywords: Root-knot nematode (Meloidogyne incognita), RNA-seq, ATAC-seq, chromatin accessibility, cisDynet, regulatory networks

Root-knot nematodes (RKN) Meloidogyne spp. are among the most damaging soil-borne threats to crops worldwide. These plant-parasitic microscopic worms are highly polyphagous and current control methods are limited [1]. The only free-living mobile stage in soil, the second-stage juvenile (J2), penetrates host roots and induces the formation of a feeding site, made of hypertrophied and polynucleated giant cells, resulting from developmental reprogramming induced by RKN. A vascular system develops around the RKN and giant cells, providing nutrients essential for nematode's development. This process gives rise to root galls and relies on effector proteins produced mainly by the esophageal glands to achieve parasitic success [1,2]. In roots, parasitic J2 develops into J3, J4 and female, which produces up to a thousand eggs. RKN life cycle and gall ontogeny involve complex regulations of gene expression [2,3] and bring together two multicellular organisms from different kingdoms. RNA-seq analyses from the RKN M. incognita, have showed a strong stage-dependent regulation with approximately 30% of genes differentially expressed across development [2]. The regulatory elements orchestrating this developmental gene regulation remain, despite their key role, poorly understood. A pioneer study identified a motif called Mel-DOG, enriched in promoters of dorsal gland (DG) effector genes. This motif (TGCMCTT) is found in about 60% of known DG effectors, suggesting a shared regulatory mechanism for parasitism genes. ATAC-seq assay is a powerful method to investigate chromatin accessibility and pinpoint regulatory elements by detecting open chromatin regions (OCRs) in a genome-wide manner [4]. OCRs are nucleosome-depleted regions allowing transcription factors to bind regulatory elements and modulate gene expression [3]. This project aims to characterize gene-regulatory dynamics during the RKN life cycle by integrating ATAC-seq and RNA-seq data using M. incognita-Solanum lycopersicum (tomato) interaction as model. Analyses will use cisDynet [5], a pipeline designed for multi-omics integration to link chromatin accessibility with gene expression and infer gene regulatory networks. We will: (1) describe transcriptional and chromatin accessibility dynamics across the parasitic cycle, (2) identify OCRs linked to effector genes, (3) detect enriched cis-regulatory motifs, (4) perform transcription factor footprinting to propose candidate regulators, and (5) build gene regulatory networks combining ATAC-seq and RNA-seq. This work will be the first part of a larger study applying the same approach to the host plant. The integration of the bi-partite datasets from the RKN and its host should shed light on the trans-kingdom co-evolution of regulatory networks between both players. This should reveal the regulatory networks and pathways involved in gall formation and clarify how host defenses are suppressed and root cells are reprogrammed to the benefit of RKN development.

7 – Carrión Hidalgo Pablo– Session 2

MILDEW RESISTANCE LOCUS O (MLO) proteins during oomycete infection: An evolutionary perspective

Pablo Carrión Hidalgo (1), Ornella Robert (1), Naïma Minet (1), Jan W. Huebbers (2), Ralph Panstruga (2), Aurélien Boisson-Dernier (1)

Université Côte d'Azur

Unit of Plant Molecular Cell Biology, Institute for Biology I, RWTH Aachen University, Worringerweg 1, 52056 Aachen, Germany

Corresponding author: aurelien.boisson-dernier@inrae.fr

Keywords: Evolutionary plant–microbe interactions; Oomycete infection; Cell wall integrity; Calcium signaling; Reverse genetics

MLO loci were discovered more than 80 years ago in barley as the first plant susceptibility factors. Since then, they have been successfully used in agriculture to provide broad and robust resistance in different crops to powdery mildew (PM) caused by filamentous fungi. Despite decades of study, the role of the plant-unique MLO proteins in response to filamentous oomycetes remains largely unexplored, even though oomycetes and fungi share similar infection strategies. Recent studies have contributed to a better understanding of the biological functions of MLO family members. Beyond PM susceptibility, MLOs were shown to regulate root thigmotropism, pollen tube growth and perception of ovule signals, or symbiosis with beneficial fungi. Moreover, many MLOs were recently characterized as Ca2+ influx channels, likely triggering downstream cellular responses in multiple plant developmental and defence pathways through Ca2+ signatures. Interestingly, the receptor-like cytoplasmic kinase MARIS (MRI) was recently found to interact with MLOs and activate their ability to mediate Ca2+ influx. In this context, MRI and its upstream receptor-like kinase FERONIA (FER) are key regulators of cell wall integrity mechanisms that protect plant cells from environmental stresses. Notably, recent insights revealed that these mechanisms initially discovered in flowering plants are conserved in the early-diverging bryophyte Marchantia polymorpha, a simplified and powerful genetic model. This conservation suggests that ancient signaling modules may have shaped how susceptibility and defence mechanisms evolved across land plants. Building on this idea, this project focuses on deciphering how MLO proteins regulate plant infection by filamentous oomycetes of the genus Phytophthora and whether this regulation has changed during land plant evolution. Our work will combine diverse approaches such as reverse genetics, plant infection assays, protein subcellular localization, protein-protein interactions, 3D-stucture-guided mutagenesis and calcium channel activity analyses to investigate the evolution and diversification of MLO in land plants. Additionally, we will perform interspecies complementation assays in collaboration with other research groups to test whether some bryophyte Marchantia MLO proteins can rescue angiosperms Arabidopsis MLO-dependent processes including susceptibility to powdery mildew fungi. The dissection of the evolutionary trajectory of MLOs during plant-microbe interactions could decipher whether they constitute an ancient signaling hub exploitable by oomycetes and whether early-diverging MLOs represent untapped resources for engineering resistance to devastating oomycete diseases.

8 – Cayron Christina– Session 1

Characterization and optimization of Novel Ribonucleoprotein-based Vaccines – RNPVAX

Christina CAYRON - Patrick BREST - Guillaume KELLERMANN - Magali BLAUD

Université Côte d'Azur

Unit of Plant Molecular Cell Biology, Institute for Biology I, RWTH Aachen University, Worringerweg 1, 52056 Aachen, Germany

Corresponding author: christina.cayron@univ-cotedazur.fr

Keywords: Telomerase - RNA - Toll-like receptor-induced signaling - Immunogenicity – Cancer

Vaccination has been highly successful in preventing infectious diseases and improving global health; however, therapeutic cancer vaccines have shown limited efficacy, largely due to the challenge of overcoming immune self-tolerance. Ribonucleoprotein complexes (RNPs) are well known in autoimmune diseases for their capacity to break tolerance through the induction of combined B-cell receptor (BCR) and Toll-like receptor (TLR) signaling. We propose RNPs as a novel vaccine platform for cancer immunotherapy when coupled to tumor-associated antigens, such as telomerase reverse transcriptase (TERT), which is overexpressed in approximately 90% of human cancers. TERT naturally associates with RNA to form ribonucleoprotein complexes, making it an attractive candidate both as a direct cancer vaccine antigen and as a potential vector to enhance immunogenicity of other self-antigens. To date, RNP-based vaccines remain poorly explored and insufficiently characterized at the biochemical and immunological levels. Our preliminary data demonstrate that a TERT-RNP vaccine elicits robust and broad $CD4^+$ and $CD8^+$ T-cell responses and induces strong antitumor activity in murine TC-1 tumor models, as well as in spontaneous tumors in dogs, without detectable adverse effects in mice, dogs, or non-human primates. This project aims to elucidate the mechanisms underlying TERT-RNP–mediated antitumor immunity, to define the optimal RNP design, and to optimize both RNA and protein components to maximize immune activation. Ultimately, this work seeks to establish RNPs as a new therapeutic vaccine platform capable of inducing durable antitumor immune responses.

9 – Diken Dilara – Session 2

Deciphering the Role of Genome Maintenance in the Longevity of Nematostella vectensis

Dilara Diken, Eric Röttinger, Pablo Huertas

Université Côte d'Azur

Corresponding author: dilara.diken99@gmail.com

Keywords: Aging, DNA Repair, Genome Maintenance, Radiation Stress, Cnidarians

Aging is a complex and multifactorial process that is typically accompanied by progressive functional decay, including a decline in the efficient response to environmental stresses and diminished regenerative capacities. This age-related functional decline is associated with a variety of changes, termed the “hallmarks of aging,” across the molecular, cellular, and tissular levels. DNA damage and genomic instability is one of hallmarks that can be causally and mechanistically linked to most of the others. Thus, DNA repair, an evolutionarily conserved processes, plays an important role in maintaining genomic stability to prevent aging & related diseases. Nematostella vectensis is a species of sea anemone that possesses exceptional longevity and the virtual absence of age-related diseases. This extreme longevity is associated with an exceptional regenerative capacity and a strong capacity to resist stresses (e.g. irradiation) at levels that would be deleterious to mammalian cells. Its apparent morphological simplicity yet shared similarity with vertebrate genomic features (gene content and synteny) along with the wealth of functional genomics resources, including CRISPR/Cas9 developed within the research community, highlights it as a potent model for aging / longevity research. My research is aimed at gaining insight into the molecular mechanisms underlying the extreme lifespan of the sea anemone N.vectensis. More specifically the role that the genome maintenance machinery in N.vectensis may play in this longevity. This will be done using in silico and functional genomics approaches by first characterizing the genome maintenance genes (GMGs) content in this sea anemone using in silico techniques. Next, we will assess the morphological, physiological, cellular, and molecular effects of varying levels of irradiations. Finally, using KO and OE approaches, the role of some of these genome maintenance genes will be determined not only for irradiation resistance but also to gain a broader insight into the importance of the genome maintenance machinery for the extreme longevity of N.vectensis and its application in mammalian cell lines.

10 – El Hasbany Marc – Session 3

Decipher the molecular basis of activation and inhibition of olfactive receptors

Marc El Hasbany, Hee-Jung Choi, Jeremie Topin

Université Côte d'Azur

Corresponding author: marc.el-hasbany@univ-cotedazur.fr, hjchoi95129@gmail.com , Jeremie.TOPIN@univ-cotedazur.fr

Keywords: Olfactory receptors, Virtual screening, Inverse agonists, Molecular docking, t-distributed stochastic neighbor embedding (t-SNE)

Olfaction relies on a set of receptors dedicated to detecting our volatile chemical environment, enabling the identification of odour molecules present in the air we breathe. Deciphering the molecular mechanisms underlying the activation and inhibition of olfactory receptors (ORs) is a transdisciplinary project aimed at deepening our understanding of odour recognition at the molecular level.
In this study, we focused on the identification of antagonists or inverse agonists targeting a specific olfactory receptor, OR1D2, which is ectopically expressed in diverse tissues and organs, including sperm cells. Identifying compounds that reduce OR activity may enable industrial applications in the flavor and fragrance sector, as well as pharmaceutical applications, given the widespread expression of ORs and their involvement in tumor overexpression and sperm chemotaxis.
A virtual screening approach was developed to identify new agonists as well as inhibitors (inverse agonists) of the OR1D2 receptor. The protocol was benchmarked against a set of 771 known agonists and non-agonists from the M2OR database, which were screened using AutoDock Vina. The chemical properties of the identified compounds were subsequently visualized using t-distributed stochastic neighbor embedding (t-SNE) and clustered to identify candidates most similar to experimentally validated active molecules, which will then be experimentally tested by our collaborator.

11 – Fabbre Alicia – Session 2

Reconstitution and analyses of networks combining lipid transfer proteins and lipid-modifying enzymes

Alicia Fabbre, Amazigh Hamaï, Anna Cardinal, Maud Magdeleine, Julie Milanini and Guillaume Drin

Université Côte d'Azur

Corresponding author: fabbre@ipmc.cnrs.fr

Keywords: Lipids, Proteins, Synthetic biology, Metabolism, Fluorescence

Lipids are the key building blocks of cellular membranes. They are precisely and asymmetrically distributed within eukaryotic cells, giving each organelle and the plasma membrane distinct physical and molecular features. However, the mechanisms that ensure and maintain such a distribution remain quite elusive. It is critical to understand them better, particularly as some are thought to be associated with severe cellular dysfunctions and pathological disorders. To reach this goal, our team studies how several cytosolic proteins, called lipid transfer proteins, precisely and rapidly transport lipids between membranes. Moreover, we examine how these processes are coupled to those that generate and modify lipids. To perform these investigations, we reconstitute in vitro complex networks combining purified lipid transfer proteins and lipid-modifying enzymes with artificial membranes. These reconstitution efforts, similar to synthetic biology, are associated with advanced fluorescence-based assays. This allows us to get in-depth mechanistic insights into how specific lipids are unevenly distributed between the ER and other cellular membranes. Using this strategy, we have recently quantified how PI(4)P metabolism drives sterol transfer by Osh4 and how Osh6 and the scramblase/membrane tether Ist2 work together to transfer phosphatidylserine. We now aim to tackle an even more difficult challenge: reconstituting the so-called phosphatidylinositol cycle, involving the lipid transfer protein Nir2 and multiple enzymes, which plays a central role in maintaining the signaling competence of eukaryotic cells.

12 – Forcioli Didier– Session 1

Identifying the genetic basis of local adaptation to sea surface temperature variation in natural populations of Pocillopora spp. corals

Sebastian Arenas, Keyla Plichon, Thamilla Zamoum, TARA Pacific consortium, Paola Furla1, Didier Forcioli

Université Côte d'Azur

LIA ROPSE, Laboratoire International Associé Université Côte d'Azur - Centre Scientifique de Monaco

TARA Pacific Consortium, DOI 10.5281/zenodo.3777759

Corresponding author: didier.forcioli@univ-cotedazur.fr

Keywords: Coral Reefs, Genome Wide SNPs, Genotype - Environment Associations, Adaptation, Speciation

Coral reefs face severe vulnerabilities to environmental fluctuations and are poised to endure adverse consequences amid escalating climate change impacts. However, current research remains confined to localized contexts, failing to provide a comprehensive understanding of how various coral species respond to these global stressors across macrogeographic scales. This knowledge gap inhibits a nuanced grasp of the broader ecological and evolutionary dynamics at play. During the TARA Pacific expedition from 2016 to 2018, we conducted an extensive study involving the collection of ~300 samples of Pocillopora spp. from 32 Pacific islands. from which we obtained comprehensive genome-wide diversity. This diversity was then confronted to environmental data, in the form of more than ten years of satellite monitored Sea Surface Temperature (SST) variation through Genotype Environment Association analyses (GEA). This allowed, by conducting a stringent selection of outlier loci, for the identification of genes and genetic regions pivotal to the adaptive response of these organisms to SST variations throughout the distribution area. By exploring the allelic diversity at these loci and its responsiveness to environmental cues, we described differentiated adaptive responses among Pocillopora species even if they are often found in sympatry, a finding of crucial importance for the tailoring of conservation strategies Pacific Ocean coral reefs.

13 – Gautier-Isola Marine– Session 1

Molecular and spatial characterization of pulmonary capillary endothelial cells states during the regeneration of the alveolar niche

Marine Gautier-Isola, Marin Truchi, Hugo Cadis, Nihad Boukrout, Paul Hofman, Christelle Cauffiez, Georges Vassaux, Sylvie Leroy, Nicolas Pottier, Pascal Barbry, Kevin Lebrigand, Bernard Mari.

Université Côte d'Azur

Université de Lille

IHU RepirERA

Corresponding author: isola@ipmc.cnrs.fr

Keywords: Spatial transcriptomic, endothelium, lung fibrosis, regeneration, scRNAseq

Aging increases the risk of developing pulmonary fibrosis by hampering tissue regeneration after injury. We recently characterized new subpopulations of capillary endothelial cells (PCECs) during the formation and resolution of pulmonary fibrosis in the bleomycin mouse model (Truchi et al. 2025). These PCECs have a pro-angiogenic phenotype expressing the Lrg1 marker and this state appears to correlate with alveolar niche regeneration in young animals, whereas this process is delayed in older animals. Moreover, part of this set of resolution-associated markers is also detected in PCEC from samples of patients with idiopathic pulmonary fibrosis (IPF). We have now initiated functional experiments in mouse to study the impact of Lrg1 overexpression in PCEC on alveolar niche regeneration. We have also initiated spatial analysis of these subpopulations during fibrogenesis and its resolution, using an optimized Xenium probe set with the aim of better characterizing alveolar niches with different cell types/states based on the presence of different PCEC subpopulations, identifying the cell types and states that interact directly with these cells and generating hypotheses about the ligand-receptor pairs associated with these mechanisms. Overall, our findings shed light on the molecular mechanisms involved in the resolution of alveolar endothelial capillaries and how aging influences specific PCECs to delay this resolution process. The functional importance of these specific PCEC populations in lung repair could lead to new therapeutic strategies promoting alveolar niche regeneration. Reference: Truchi M*, Gautier-Isola M* et al. Aging affects reprogramming of pulmonary capillary endothelial cells after lung injury in male mice. Nat Commun. 2025 Aug 6;16(1):7234.

14 – Goomanee Salvish – Session 2

3D emulation of embryo mechanics using geometric graph neural networks

Salvish Goomanee & Hervé Turlier

Université Côte d'Azur

Collège de France, CNRS

Corresponding author: salvish.GOOMANEE@univ-cotedazur.fr

Keywords: graph neural networks, 3D embryos, deep learning, networks, topologically constrained diffusion

In this work, we develop a framework that emulates computationally expensive 3D simulations of embryo mechanics using graph neural networks (GNNs). We develop a surrogate geometric graph model where nodes represent cells, and edges correspond to interfacial areas between them. To accurately predict topological transitions we implement a 3D rotationally and translationally equivariant topologically constrained diffusive geometric GNN. This enhances our ability to capture the Markovian nature of the simulated processes. We then benchmark our model against a simple 3D equivariant MPNN model.

15 – Grataitong Khwanthana– Session 3

Genetic Code Expansion for Probing Protein Dynamics and Pathological Mechanisms in Living Cells

Khwanthana Grataitong, Krittalak Chakrabandhu

Université Côte d'Azur

Corresponding author: kk.anatomy@gmail.com

Keywords: Genetic code expansion, unnatural amino acids (UAAs), orthogonal tRNA/synthetase pairs, click chemistry, and photo-crosslinking

Genetic code expansion (GCE) provides a versatile platform for introducing unnatural amino acids (UAAs) into proteins with site-specific precision, greatly enhancing the functional and chemical repertoire available for biological research. By utilizing engineered orthogonal tRNA/synthetase pairs that selectively incorporate UAAs in response to reassigned codons, GCE enables the creation of proteins with novel properties beyond those encoded by the standard genetic code. This methodology has broad applications across protein engineering, synthetic biology, and drug discovery. Here, we employ GCE to develop tools for interrogating molecular events underlying pathological conditions in living cells. Our approach integrates UAA incorporation with click chemistry, site-specific fluorescent labeling, and photo-crosslinking to monitor protein interactions, misfolding, aggregation, and other dynamic processes. By optimizing these GCE-based strategies, we aim to establish advanced protein-based sensors and expand the capacity to study real-time cellular events at high resolution. This work highlights the potential of GCE to drive innovation in molecular biology and biomedical research.

16 – Hofmänner Kai– Session 2

Initiating regeneration: from regeneration-specific expression dynamics to ectopic head formation

Kai Hofmänner, Aldine Amiel, Eric Röttinger

Université Côte d'Azur

Corresponding author: kai.hofmaenner@etu.unice.fr

Keywords: pro-regenerative response, Gene-Regulatory-Network, Tissue-engineering, cWNT activation, tissue-permissibility

To what extend regeneration redeploys the molecular mechanisms underlying embryogenesis is a historical question in regeneration biology. Using the sea anemone Nematostella vectensis, a research model well suited to address this question and able to regenerate its entire body after injury, a recent study has performed a comparative transcriptome analysis and revealed a set of genes with a regeneration-specific expression dynamic (https://doi.org/10.1101/658930). To decipher the role these genes may play during the initiation of the regeneration process in Nematstella vectensis the project is articulated around three specific axes: i. Select and characterize spatio-temporally "regeneration-specific" genes of interest (rsGOIs) using existing bibliographic and expression data. ii. Investigate the role (required / sufficient) of rsGOIs using KO/KI approaches. Based on their nature and gene expresssion profile after injury (2hpa) and at the onset of regeneration 14-20hpa, we have determined a list of 20 genes, i) begun to perform in situ hybridization revealing amputation-site specific expression and ii) design sgRNA for CRISPR/Cas9 KO's. In order to test the sufficency of the rsGOI's to induce a regenerative response, we have initiated the development of a conditional overexpression system (TetOn/TetOFF). To develop relevant "sufficiency" assays, we have also begun an in-depth analysis of the capacity of cWnt activation to initiate the formation of an ectopic head following injury. Current work, using an innovative whole-body regeneration model, sets the foundation to assess and understand the roles of "regeneration-specific" genes at the onset of regeneration and their potential sufficiency to induce a regenerative response.

17 – Jezso Balint– Session 2

Redox-driven control of 4-1BB interactome and signaling

Balint Jezso*, Boglarka Zambo*, Salla Keskitalo*, Arnaud Landra Willm, Antti Tuhkele, Carole Belliardo, Bastien Morlet, Luc Negroni, Andras Zeke, Guillaume Sandoz, Markku Varjosalo, Gergo Gogl

Université Cote d'Azur

Corresponding author: gergo.gogl@univ-cotedazur.fr

Keywords: interactome, binding affinities, redox regulation, immunoreceptors, fluorescent native holdup

4-1BB (also known as TNFRSF9 or CD137) is a receptor protein, having important role in T-cell activation, but it is also widely expressed in non-lymphoid tissues. 4-1BB contains an intrinsically disordered cytoplasmic tail that contains multiple evolutionary conserved residues that serve as interaction surface for its canonical interaction partner TRAF2. This disordered tail is incorporated as a co-stimulatory domain in most clinically approved CAR-T construct, thus a better understanding of its interactions and their biochemistry is important. Using state-of-the-art interactomic approaches, we have found that at least two additional partner also binds to the same tail besides TRAF2, and these interactions are all impacted by mutations of conserved cysteine residues of 4-1BB. Our results outline a redox-dependent regulatory mechanism that happens during T-cell activation that could be further exploited for the development of new CAR-T strategies.

18 – Khatir Wassila – Session 1

MCVAE-based anomaly detection in Fragile X Syndrome

Wassila KHATIR, Irene BALELLI, Marco LORENZI, Carole GWIZDEK

Université Cote d'Azur

Corresponding author: wassila.khatir@inria.fr

Keywords: Multi-omic, Variational autoencoders, Tranlatomic, Transcriptomic, Fragile X Syndrome

Fragile X Syndrome (FXS) is a neurodevelopmental disorder caused by mutations in the FMR1 gene, leading to the loss of FMRP, an RNA-binding protein that regulates translation. The Fmr1 knockout (KO) mouse recapitulates this phenotype and has been widely used to access the perturbations in molecular homeostasis in the FXS brain, notably via omics approaches. These studies showed that the absence of FMRP disrupts coordination between transcriptomic and translatomic layers, impairing neurogenesis and resulting in intellectual disability. However, limited sample availability and inter-dataset heterogeneity hinder the detection of coordinated multi-omic disruptions. To address this, we trained a Multi-Channel Variational Autoencoder (MCVAE) exclusively on wild-type (WT) samples, learning a shared latent representation across transcriptomic and translatomic modalities via cross-modal reconstruction. Testing on Fmr1 KO samples identified anomalies through 20-fold cross-validation, revealing disruptions in both modalities, including Fmr1 itself. Translatomic anomalies aligned with curated FXS-related databases and showed regulatory associations with the transcriptomic anomalies, validated by ChIP-seq data. MCVAE outperformed alternative integration methods in biological coherence, demonstrated by enrichment of external CLIP-seq targets, providing a robust framework for uncovering coordinated molecular dysregulation in FXS.

19 – Kraimi Narjis – Session 3

Microbial metabolite p-cresol correlates with constipation in high-functioning adults with autism spectrum disorder and induces constipation-like symptoms in mice

Narjis Kraimi, David Fabregat-Safont, Juliette Canaguier, Claire Sendra, Geoffroy Mallaret, Susana Barbosa, Julie Brouillet, Florian Lejuste, Alexandru Gaman, Jean-Romain Richard, Marion Leboyer, Oscar J. Pozo, Laetitia Davidovic

Université Cote d'Azur

Corresponding author: kraimi@ipmc.cnrs.fr

Keywords: ASD, microbiota, p-cresol, gastro-intestinal symptoms, cohort

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by social interaction deficits, restricted and repetitive behaviors, and atypical sensory processing. Gastrointestinal (GI) symptoms are frequently reported in individuals with ASD, yet their biological correlates remain poorly understood in adults. Growing evidence suggests that alterations in gut microbiota and microbial metabolites may contribute to both GI symptoms and behavioral features of ASD. Among these metabolites, p-cresol has been found elevated in ASD, but its relationship with specific GI symptoms and its metabolism in high-functioning adults remain largely unexplored.We investigated associations between serum p-cresol and its conjugates (p-cresol sulfate and p-cresol glucuronide) and GI symptoms in adults with high-functioning ASD. In parallel, based on previous findings showing that chronic p-cresol exposure induces ASD-like behaviors and microbiota changes in mice, we assessed whether p-cresol also affects GI function in a preclinical model. The human cohort included 272 adults with high-functioning ASD. ASD symptoms were assessed using ADOS and ADI-R scales, while GI symptoms (diarrhea, constipation, abnormal stool aspect, abdominal pain, bloating) were self-reported. Dietary habits were evaluated using a food frequency questionnaire. Serum p-cresol and conjugates were quantified by liquid chromatography–tandem mass spectrometry. Associations with GI symptoms were analyzed using Spearman correlations and multivariable linear regression models adjusted for age, sex, and diet. In mice, chronic p-cresol exposure was assessed through in vivo GI phenotyping, including fecal output and dry matter content, intestinal permeability (paracellular and transcellular tracers), colonic motility, whole-gut transit time, and histological analysis of intestinal architecture. Multivariable analyses showed that serum free p-cresol, but not its conjugates, was significantly associated with constipation frequency (β=0.749, 95% CI [0.221;1.276], $p<0.01$), with a significant interaction with sex (β=1.305, 95% CI [0.273;2.337], $p<0.05$), females exhibiting higher levels. Age and diet had no significant influence. In mice, chronic p-cresol exposure induced constipation-like alterations, including reduced fecal output, increased fecal dry matter, and increased intestinal permeability, while gut transit time, colonic motility, and epithelial architecture were unaffected. These findings demonstrate that elevated circulating free p-cresol is associated with constipation in adults with high-functioning ASD and that sex modulates this association. Preclinical results support a causal role of p-cresol in GI dysfunction, highlighting its potential involvement in the microbiota–gut–brain axis and its relevance as a therapeutic target for GI symptoms in ASD.

20 – Krawczyk Ines – Session 2

A systems biology approach to analyze intercellular coupling between peripheral circadian clocks

Inès Krawczyk, Odile Burckard, Anastasia Maréchal, Benjamin Bobel, Mathieu Mezache, Sophie Guérin, Antoine Fortuné, Aline Gréchez-Cassiau, Michèle Teboul, Laurent Tournier, Madalena Chaves, Franck Delaunay

Université Cote d'Azur

Corresponding author: ines.krawczyk@univ-cotedazur.fr

Keywords: Circadian clock, hepatocyte, spheroids, synchronization, period locking

A large number of molecular, cellular, physiological and behavioral processes such as gene expression, metabolism, immunity, food intake and sleep, oscillate according to a 24-hour rhythm synchronized with the day/night cycle. These oscillations are controlled by the circadian clock, an endogenous mechanism whose disruption has known adverse consequences on health. The molecular oscillator that governs the circadian clock operates autonomously and is present in almost all cells. In addition to being synchronized by light, hypothalamic central clock neurons are coupled to each other via neurotransmitters, a mechanism necessary to maintain coherent, robust, and high-amplitude oscillations at the tissue level. Despite the lack of evidence for a similar mechanism in peripheral organs, recent work has shown that hepatocytes maintain coherent circadian oscillations in vivo in the absence of extrahepatic synchronization. Along the same lines, the TGFb signaling pathway has been proposed to mediate the phase adjustment of peripheral cellular clocks but this role in vivo is not yet known. To explore the hypothesis of intercellular coupling in the liver, we developed a multidisciplinary approach combining mathematical modeling, 3D-cell culture, real-time luminescence and signal processing methods. Using an ODE based reduced model of a network of coupled oscillators, we predict that cells with different period converge towards a common period upon diffusive coupling. Experiments with spheroids mixing hepatocytes with different periods fully validate this prediction, demonstrating that cells communicate to adjust their periods. Although the underlying mechanism remains to be understood, the experimental results also suggest that direct contact between cells is important for observing this intercellular period locking phenomenon and that specific metabolic pathways may be involved. Studying synchronization at the tissue level will help understand, treat and prevent the negative effects of circadian misalignment and disruption.

21 – La Hoang Anh– Session 1

Mechanisms involved in plant cell injury recognition during pathogen attack and regeneration competence

HOANG ANH LA

Université Cote d'Azur

Corresponding author: Janice.de-almeida@inrae.fr

Keywords: Cell cycle, cell damage, tissue regeneration, root-knot nematode, galls

Hyperactivation of the plant cell cycle is crucial for the ontogenesis of root-knot nematode induced galls. These tumors like structures are formed within the root vascular cylinder harboring the competence for cell cycle reactivation. Herein, we questioned if during the process of nematode infection, cell damage occur triggering cellular dedifferentiation and division. It emerges that the Ethylene Response Factor 115 (ERF115 of the ERF family), together with the Phytochrom A Signal Transduction 1 (PAT1 of the GRAS family) transcription factors (TFs) are able to activate a regeneration program in gall-cells. Upon stem cell death, cells that co-express ERF115 and PAT1 were found to engage recovery cell divisions. Moreover, plants lacking a functional ERF115 or PAT1 showed a reduced ability to perform recovery divisions and displayed a lower regeneration frequency. Our studies demonstrate that root tissue injury caused during nematode infection induces ERF115, ERF114 and PAT1 expression in cells immediately adjacent to damaged root cells and hereby potentially activating cell division to replace damaged cells as part of a regeneration program. These functional studies lead us to conclude that both ERF115 and PAT1 are likely involved in gall homeostasis sensing the damage caused upon nematode infection and working in its replenishment. As follows, we aim to further understand the pathways that activate the plant host regeneration ensuing wounding by nematodes, and map the signaling cascades operating downstream of ERF115. Overall, this knowledge might help us to understand their parasitic success and to fight against these plant pests.

22 – Laghrissi Hiba– Session 1

Investigation of Age-related Translational Regulatory Mechanisms

Hiba Laghrissi, Katarzyna Tomasiak, Lauren Blot, Julien Mozziconacci, Arnaud Hubstenberger & Florence BESSE

Université Cote d'Azur

Corresponding author: hiba.laghrissi@univ-cotedazur.fr

Keywords: aging, translation, Drosophila Melanogaster, ribosome profiling, Machine Learning

Aging is a complex process characterized by a progressive decline in physiological and cognitive abilities. Over the year, numerous studies have explored the molecular, cellular and systemic signatures contributing to aging, thus showing that aging disrupts the coupling between mRNA transcription and translation. The molecular mechanisms underlying this decoupling, however, are still unknown. Our objective is to understand how translation is modulated in the context of brain aging. We use Drosophila Melanogaster, a powerful model in aging studies due to its short lifespan and the fact that ~77% of genes associated with age-related diseases in humans are expressed in the equivalent fly tissues. To first characterize age-dependent changes in translation patterns at a transcriptome-wide level, we performed Ribosome Profiling and Bulk RNA-seq at three different timepoints. Our first analysis of the ribo-seq data uncovered the existence of specific populations of transcripts with concordant and discordant patterns upon aging, highlighting potential regulatory mechanisms. To understand the observed regulatory changes, we compared the molecular characteristics at both the cis-acting and trans-acting levels (GC content, uORFs, RNA sequence, binding to RBPs, etc.). We also use Machine Learning algorithms to link molecular signatures we identified at the translational level in order to predict mRNA regulation patterns upon aging. This work will not only deepen our understanding regarding the poorly studied translational regulatory mechanisms but will also open further questions regarding the differences between healthy and pathological aging.

23 – Le Parc Lucie – Session 1

Role of a small Rab GTPase in metabolic dysfunction-associated steatotic liver disease.

Lucie Le Parc, Nathalie Boulet, Iman Mamjoud, Philippe Gual, Hervé Guillou, Jean-François Tanti, Mireille Cormont, Jérôme Gilleron

Université Côte d'Azur

Corresponding author: lucie.le-parc@etu.univ-cotedazur.fr

Keywords: Rab protein, PPARa, MASLD, Transcription, B-oxidation

Although metabolic dysfunction-associated steatotic liver diseases (MASLD) is a major public health issue, approved pharmacological treatment remain limited. Identifying new molecular mechanisms involved in MASLD has become a therapeutic priority. The transcription factor peroxisome proliferator-activated receptor α (PPARα), which plays a central role in regulating lipid metabolism, exerts a protective effect on MASLD. Indeed, PPARα favors lipid oxidation and enhance mitochondrial biogenesis. However, these beneficial effects are limited in strength and duration. Hence improving our understanding of PPARα targets may have important therapeutic applications. During the last decades, endocytic trafficking, governed by proteins from the Rab family, has been implicated in obesity-related liver metabolic dysfunction. Recently, we identified a Rab protein as a target gene of PPARα, whose expression is increased in the livers of mice developing MASLD. Using siRNA knockdown approaches, we sought to understand the physiological impact of this Rab protein and its involvement in the development of MASLD. We knocked down this Rab protein in vitro in primary mouse hepatocytes and in vivo in the liver of mice. In a model of primary mouse hepatocytes mimicking steatosis through fatty acids exposure, the silencing of this Rab protein led to a reduction in lipid droplet accumulation. Through the integration of several RNA-sequencing from PPARα knockout mouse livers and primary mouse hepatocytes cultured in fasting conditions, we identified the selective set of PPARα target genes induced in vitro by the PPARα agonist, pemafibrate. Strikingly, we discovered that the silencing of the Rab protein in vitro led to the induction of more than half of the PPARα target genes, especially those involved in fatty acid oxidation and peroxisomal biogenesis. These results suggest that this Rab protein is involved in a negative feedback loop on PPARα-dependent transcription. Consistently, the silencing of this Rab protein in vivo in the liver of lean mice resulted in decreased hepatic triglycerides levels, and a dramatic reduction in adipose tissue mass and adipocyte size. Altogether, these results evidenced that this Rab protein tunes hepatic lipid homeostasis through the control of PPARα-dependent transcription.

24 – Lima Fernandes Vânia Filipa – Session 1

Unravelling the Minimum Requirements for Cell Migration in Lung Adenocarcinoma

Nesrine Rachedi, Vânia Fernandes, Mathilde Dupart and Patrick Brest

Université Côte d'Azur

Corresponding author: vania.lima-fernandes@univ-cotedazur.fr

Keywords: LUAD, Migration, p-bodies, Metastasis

Lung adenocarcinoma (LUAD) is one of the leading causes of cancer-related mortality worldwide, with a five-year survival rate of approximately 15%. This poor prognosis is primarily driven by metastatic disease, which remains the major cause of death in LUAD patients. Metastasis is frequently observed due to late-stage diagnosis and the emergence of intrinsic or acquired resistance to current therapies. Most existing therapeutic strategies are developed based on specific genetic alterations and predominantly target proteins or enzymatic activities involved in tumor cell proliferation. While these treatments can effectively limit tumor growth, they mainly reduce the number of proliferative events and do not directly address the probability of metastatic dissemination, as they are not designed to target the cellular processes governing migration, invasion, and colonization of distant organs. As a result, disease progression through metastasis often persists despite initial control of primary tumor growth. In addition, therapeutic approaches are largely guided by transcriptomic profiles, although mRNA abundance poorly correlates with protein levels. Importantly, untranslated mRNAs can be selectively degraded or sequestered within membrane-less ribonucleoprotein condensates (biocondensates), where they may exert regulatory functions independently of active translation. The contribution of these stored mRNAs and associated biocondensates to tumor adaptation, therapy resistance, and metastatic competence remains largely unexplored. The objective of this project is to elucidate the role of untranslated mRNA pools and ribonucleoprotein biocondensates in LUAD progression, with a particular focus on their involvement in metastatic potential and resistance to therapy. By shifting the focus from tumor growth to the molecular mechanisms underlying dissemination, this work aims to identify novel vulnerabilities that could lead to more effective anti-metastatic therapeutic strategies.

25 – Loures Da Silva Mirielson– Session 1

Silencing maize AIP10 gene expression with CRISPR-Cas9 drives shifts in the rhizosphere microbiome, enhances diazotrophic bacterial associations, and increases CO2 sequestration

Mirielson Loures da Silva, Patrícia Montessoro, Maria C. O. Urquiaga, Helkin Ballesteros, Pan Gong, Wallace P. Bernardo, Jelmir C. de Andrade, Segundo Urquiaga, Eliemar Campostrini, Carlos A. Conte-Junior, Hilde Nelissen, Dirk Inzé, Adriana S. Hemerly.

ISA - Instituto Sophia Agrobiotech (INRAe), France

Federal University of Rio de Janeiro (UFRJ), Brazil

Corresponding author: mirielsonlouress@gmail.com

Keywords: AIP10 mutation; maize development; cell cycle; carbon fixation; bioeconomy

Maize (Zea mays) is a globally important crop, serving as a major food source and bioenergy feedstock. Its high productivity depends on chemical inputs, management practices and genetic improvement, making maize a valuable model for investigating complex physiological and ecological interactions. As a C4 plant, maize efficiently fixes CO_2, supporting rapid growth and high yield. Beyond primary metabolism, root-associated microbiota-particularly plant growth-promoting bacteria (PGPB)-enhance nutrient uptake and stress tolerance, although the effectiveness of these interactions is strongly shaped by plant genotype, bacterial identity and environmental conditions. AIP10 (ABAP1 Interacting Protein 10) was identified as a key regulator integrating cell division and primary metabolism. In Arabidopsis thaliana, AIP10 controls the G1/S transition and metabolic reprogramming through interactions with ABAP1 and KIN10, a catalytic subunit of the SnRK1 kinase complex. AIP10 silencing enhances carbon fixation, biomass accumulation, nutritional value and association with PGPB. To assess conservation of these functions in maize, CRISPR–Cas9 was used to generate knockout lines aip10-1, aip10-2 and aip10-4. Loss of AIP10 reduced ABAP1 abundance, extended cell-cycle progression and increased cell division rates. Edited plants exhibited higher chlorophyll content (ChlorofiLOG®), enhanced CO_2 assimilation and carbon fixation, and improved water-use efficiency (IRGA Licor 6400 XT), resulting in increased biomass accumulation and elevated lignin and cellulose deposition in root cell walls. Leaf nutritional content was also increased, as determined by ATR-FTIR. These phenotypes were supported by molecular validation of marker genes associated with the cell cycle (CyclinB1;1, ABAP1 and CDT1a), photosynthesis (LHCB1, PSAD2, RBCS2 and DJC22) and metabolism (SEN1, TPS11 and PPDK/SnRK1). Notably, the aip10-1 line displayed enhanced colonization by diazotrophic bacteria and commercial bioinoculants, accompanied by gains in growth and root architecture. AIP10 silencing also promoted enrichment of beneficial rhizosphere microbiota and increased expression of the nifH gene associated with biological nitrogen fixation. Metabarcoding analyses revealed a richer and more diverse microbial community in aip10-1, dominated by putative plant growth-promoting taxa, likely contributing to improved nutrient assimilation, carbon sequestration and water-use efficiency. Collectively, these findings demonstrate that AIP10 silencing in maize mirrors key physiological and metabolic outcomes previously observed in Arabidopsis, enhancing photosynthetic performance, metabolic regulation and beneficial plant–microbe interactions. This strategy highlights AIP10 as a promising target for developing maize cultivars with improved productivity, resilience and compatibility with sustainable and regenerative agricultural systems.

26 – Mercier Julien – Session 1

Immune cells metabolism of lifelong athletes in perspective with their vitality capacity

Julien MERCIER, Serge S. COLSON, Anne-Sophie ROUSSEAU

Université Côte d'Azur

Corresponding author: julien.mercier@univ-cotedazur.fr

Keywords: ageing, metabolism, physical activity, T cells

If you change T-cell metabolism in a mouse using a gene knockout, depending on the gene, you can either precipitate ageing or make the mouse more athletic. Therefore, we decided to recruit humans aged over 55 years who are (or are not) lifelong athletes.We first evaluated healthy ageing in each individual using a combination of immune, metabolic, and neuromuscular measures. This gave us a global picture of the physiological health of our participants. We then used single-cell RNA sequencing to explore their immune landscape and to make correlations between their immune transcriptome and healthy ageing.Based on these results, we plan to further investigate immune cell metabolism using SCENITH, a new method that allows the measurement of cell metabolism by flow cytometry using metabolic blockers. This research aims to open the field of immunometabolism in human ageing and translational research.

27 – Multari Maxime – Session 2

TomTom: a tomato (Solanum lycopersicum) knowledge graph gathering molecular interactions from public databases in a unique resource allowing network-based analysis of omics data

Maxime Multari, Mathieu Carrière, Xavier Amorós-Gabarrón, Alexina Damy, Ludo Andrianirina Mamisoa, Sebastian Lobentanzer, Julio Saez-Rodriguez, Stéphanie Jaubert, Aurélien Dugourd and Silvia Bottini

Université Côte d'Azur

Corresponding author: silvia.bottini@inrae.fr

Keywords: Bioinformatics ,Solanum lycopersicum, Knowledge graph, Network analysis, Meta-database

The tomato, Solanum lycopersicum, is a model organism of great agro-economic interest. Like other plants, tomato is susceptible to many biotic and abiotic stresses and must defend itself despite its immobility. Many processes are involved in the plant's response to such stresses, including specific molecular interactions and pathways. Omics technologies have become widely used to study plant responses. These technologies allow the study of diverse biological processes at different molecular levels, such as transcriptomics, which analyzes expressed mRNAs under specific conditions, and proteomics, which investigates the proteins produced in an organism. Furthermore, understanding the relationships among and between different omics layers enhances our comprehension of these biological processes. However, studying these interactions can be challenging because the information is scattered across multiple databases, often using different identifiers for the same molecules. Therefore, unifying the information to reduce time-consuming and error-prone searches is essential for improving the efficiency and accuracy of such studies. To address this, we developed TomTom, a knowledge graph for S. lycopersicum, built with the BioCypher framework. TomTom compiles molecular interactions from multiple databases, including transcription factor and microRNA targets, protein-protein interactions, and pathways, organizing them under strict construction rules to improve reliability. The resulting graph includes over 100,000 objects connected by nearly 600,000 relationships, offering a unified resource that facilitates hypothesis generation and network-based analyses. We further demonstrate TomTom's usefulness by analyzing integrated transcriptomic data from tomato plants exposed to six different pathogens, retrieving a gene regulatory network (GRN) and pathways describing this integrated data. The constructed GRN with TomTom, comprising 71 transcription factors (TFs) and 1,715 target genes, was analyzed using a topological data analysis approach combined with transcription factor activity inference. This led to the identification of four distinct TF cluster configurations, each representing a different response strategy of the regulatory response to pathogens. Although originally designed for S. lycopersicum, the knowledge graph can be adapted for any species supported by the integrated databases, facilitating studies for other organisms.

28 – Nasr Lara– Session 3

Glutaminase self-regulation via mechanosensitive glutamylation

L.Nasr, I.Sanchez-Burgos, C.Jardin, ATejedor, C.Colson, L.Barban, N.Glise, J.Te, C.Sbai, A.Gay, S.Abélanet, V.Henriot, H.Carr, L.Camoin, J.Topin, S.Clavel, R.Collepardo-Guevara, C.Janke, S.Audebert, J.Topin, J.Espinosa, I.Ben-Sahra, T.Bertero, S.Torrino

Université Côte d'Azur

Corresponding author: nasr@ipmc.cnrs.fr

Keywords: glutamylation, cell mechanics, metabolism, GLS

Interplay between tissue stiffness and metabolism promotes cancer cell aggressiveness1. Beyond glycolysis, glutamine catabolism has emerged as a central mechano-adaptive pathway that sustains biosynthesis, energy production, and cell mechanics during tumor progression. Yet, the molecular mechanisms linking mechanical forces to cancer cell addiction to glutamine remain undefined. Glutaminase (GLS) catalyses the first step of this pathway, producing glutamate, which fuels anabolic processes and serves as a substrate for protein glutamylation. Although discovered in the 1990s, glutamylation has mainly been reported as a posttranslational modification of tubulin. Yet, glutamylation is not restricted to tubulin, and whether mechano-induced glutamine catabolism drives protein glutamylation to promote cancer cell aggressiveness remains unknown. Here, we report that matrix stiffening controls the glutamylation of hundreds of proteins. Specifically, we show that matrix stiffening induces the glutamylation of several metabolic enzymes, such as GLS. Mechanistically, GLS glutamylation promotes its phase separation via electrostatic interactions, modulating its activity. Mutations preventing GLS glutamylation impair its function, reduce glutamine catabolism, and blunt cancer cells' aggressiveness. Thus, glutamate produced by glutaminase serves as a substrate for its own modification, revealing a self-regulating loop connecting mechanical stress to metabolic flux with implication in breast cancer—a mechano-dependent disease.

29 – Porracciolo Paola – Session 2

Identification of cellular circuit alterations in the airways at different stages of chronic obstructive pulmonary disease (COPD)

Paola Porracciolo, Christophe Becavin, Simon Girel, Pascal Barbry, Laure-Emmanuelle Zaragosi

Université Côte d'Azur

Corresponding author: zaragosi@ipmc.cnrs.fr

Keywords: Chronic obstructive pulmonary disease (COPD), respiratory epithelium, gene regulatory networks, systems biology, mitochondrial heteroplasmy

Chronic obstructive pulmonary disease (COPD) is the third leading global cause of death (WHO), and significantly raises lung cancer risk (Shin, S. H., et al., 2024). A feature of COPD is a dysregulation of cell type equilibrium of the epithelium that lines the airways, leading to defective mucociliary clearance, a crucial lung defense mechanism. Mucociliary clearance is the result of the combined function of goblet cells, secreting mucus, and multiciliated cells, evacuating mucus form the airways. Both these cell types are differentiated from resident basal cells. While the various airway cell types are well-documented, the kinetics of their differentiation are only partially understood, and there is a notable lack of descriptive mathematical models for airway cell differentiation, especially under pathological conditions. To understand early COPD determinants, my group has analyzed 119 airways biopsies from healthy and COPD patients by single-cell RNA sequencing, with the pneumology unit of Nice University Hospital. This resulted in a human airway single-cell atlas at early-stages of COPD, which I am analyzing in my Ph.D. project. My aim is to predict consequences of any disease-related modification from our atlas on cell differentiation. My first objective is to model the gene regulatory networks that control cell differentiation, and to infer the determinants that control transition from a cell type to another. My second objective is to further explore the impact of smoking in COPD patients, as cigarette smoke represents the first cause of the disease. I am currently analyzing the genetic signatures of the cells susceptible to cancerous transformation, defined by their high level of mitochondrial DNA mutations. I am developping a pipeline to assess quantitatively nucleic acid modifications at initial steps of the pathology.

30 – Prieur Léa – Session 1

Molecules Improving the Motility Of Sperm for Assisted reproduction

Romain BARRES, Jérémie TOPIN

Université Côte d'Azur

Corresponding author: romain.barres@univ-cotedazur.fr

Keywords: Sperm, Motility, Olfactory receptors, Fertility, ART

The world is experiencing a dramatic decline in fertility, partly driven by a massive decrease in sperm quality. This trend has led to a steady increase in the use of assisted reproductive technology (ART), which now accounts for approximately 4% of births in France. However, the success rate of ART remains relatively low, highlighting the urgent need for innovative approaches to enhance in vitro fertilization outcomes. Olfactory receptors, initially discovered in the olfactory epithelium, are expressed in various tissues and, quite surprisingly, spermatozoa. Beyond their role in the perception of smell, olfactory receptors on sperm cells receptors are thought to play critical roles in sperm function. Some olfactory receptors located on the surface of spermatozoa have been shown to modulate motility, suggesting their involvement in chemotaxis as sperm navigate the female reproductive tract. Our studies have identified genetic polymorphisms in olfactory receptor genes among individuals at risk of infertility. Coupled with the documented association between anosmia (the inability to perceive certain smells) and infertility, these findings support the hypothesis that olfactory receptors expressed in sperm contribute to fertility. Our overarching objective is to identify compounds improving olfactory receptors on human sperm cells to improve assisted reproduction techniques and improve fertility outcomes. For this specific project, we aim to screen compounds that target the 40 olfactory receptors expressed on human spermatozoa and improve motility. To achieve this, we will develop a mid-throughput assay using a compound library to stimulate human spermatozoa in tissue culture, monitoring motility changes via video microscopy and specialized sperm-tracking software. This project represents a multidisciplinary and synergistic collaboration between experts in reproductive biology and olfactory receptor pharmacology. Additionally, we will build on established partnerships with clinicians at CECOS in Nice Hospital Archet 2 and physicists at INPHYNI to ensure the success of this initiative. We expect that results from this study will form the basis for the development of innovative microfluidic devices for fertility clinics.

31 – Roubeaud Vanessa – Session 1

A functional genomic approach to identify factors controlling the benefits of exercise training on brain health

Vanessa Roubeaud, Romain Barrès

Université Côte d'Azur

Corresponding author: vanessa.roubeaud@etu.univ-cotedazur.fr

Keywords: Genomics, Brain Function, Muscle-Brain signaling, Physical exercise, Cognition

Physical activity represents one of the most powerful lifestyle interventions to prevent and treat numerous diseases, including disorders of the central nervous system. Genome-wide association studies (GWAS) have identified thousands of genetic variants that associate with traits of brain function but, as most identified genetic variants locate in non-coding DNA regions, their biological function is vastly unknown. GWAS variants are enriched within gene-regulatory regions called enhancers, which regulate gene expression in a tissue- specific manner. We discovered that GWAS variants linked to cognition are enriched within exercise training-regulated enhancers [1]. We hypothesized that extracellular factors regulated by exercise enhancers mediate the positive effects of physical exercise on brain function. We aim to identify these factors by performing integrated genomic analyses of allele-specific enhancer activity in skeletal muscle at sites of genetic variants that associate with cognitive traits. We have used a CRISPR-based, perturb-seq approach to screen for factors secreted by the skeletal muscle cells upon activation or inhibition of a selection exercise-regulated enhancers. We will test how these factors affect neuronal differentiation. This project will improve our understanding of muscle-brain signalling and the molecular mechanisms by which exercise improves the function of the central nervous system.

32 – Ruffino Lou– Session 1

CCL5: A Key Regulator of Neuroinflammation and Type 2 Diabetes Associated with Nutritional Obesity

Clara Sanchez1, Katharina Stobbe1, Selma Ben Fradj1, Fayrouz Khiar2, Ophélia Le Thuc1, Lou Ruffino1, Ahmed Negm1, Céline Cansell1, Maxime Villet1, Nadine Gautier3, Ez-Zoubir Amri3, Jacques Noel1, Nicolas Chartrel2, Carole Rovère1

Université Côte d'Azur

Université Rouen Normandie, NorDiC UMR 1239, Inserm, Rouen, France

Corresponding author: ruffino@ipmc.cnrs.fr

Keywords: Obesity, Nutrition, Neuroinflammation, Hypothalamus, Chemokine CCL5

Despite its high prevalence and societal impact, obesity treatment remains largely ineffective, mainly due to limited understanding of its pathophysiology. A better comprehension of central mechanisms regulating eating behavior is crucial to develop novel treatment approaches. A hallmark of obesity is the accumulation of pro-inflammatory molecules, but the role of inflammatory cytokines and chemokines in regulating feeding and body weight remains unclear. This project aims to investigate, under normal and obese/T2D conditions, the role of the inflammatory chemokine pathway CCL5/CCR5 within the hypothalamic neuropeptide network involved in the regulation of eating behavior and glucose homeostasis. We propose that CCL5 signaling is a key modulator in obesity and T2D, influencing orexigenic peptides such as MCH and ORX/26RFa, and that its dysregulation contributes to metabolic disorders. The study has two objectives: Investigate the development of nutritional obesity and its metabolic consequences in a CCL5 knockout mouse model. Mice will be fed a high-fat diet to induce obesity, and parameters such as body weight, circulating leptin, fat/lean mass composition and inflammatory factors will be monitored. Glucose tolerance will also be evaluated to assess the development of a diabetes-like phenotype.Investigate the effects of acuate peripheral and central injection of CCL5. We will monitor the evolution over time of weight, food intake and the expression of orexigenic peptides. This work aims to clarify the link between neuroinflammation,hypothalamic regulation, and metabolism, offering potential new therapeutic targets for obesity and type 2 diabetes.

33 – Sandjak Asma– Session 2

Dissecting natural variation in genotype–environment interactions modulating the C. elegans germ stem cell niche

Asma Sandjak, Sarah R Fausett & Christian Braendle

Université Côte d'Azur

Corresponding author: asandjak@unice.fr

Keywords: Genetic variation; Environmental stress; Stem cell niche; Genotype-by-environment (G×E) interaction; PZ plasticity

A major challenge in biology is understanding how genetic variation interacts with environmental factors to influence development. We previously showed that natural variation in germ stem cell niche activity-as reflected by differences in progenitor zone (PZ) size-is partially driven by a regulatory polymorphism in the promoter of the Delta/Notch ligand lag-2. Using this system, we now investigate how genetic variation influences the environmentally regulated plasticity of germline proliferation. Our previous work shows that C. elegans do not only display extensive natural variation in PZ size and corresponding mitotic activity under standard conditions, but also variation in response to different environmental stimulus. We have started to quantify how wild isolates differ in PZ plasticity in response to different key stressors (temperature shift, oxidative stress and dietary restriction). Preliminary data reveal strong genotype-by-environment (GxE) effects: a low-dose of paraquat (oxidative stress) induces large, strain-specific changes in PZ size suggesting that the environmental sensitivity of niche activity significantly differs between C. elegans wild isolates. We are now mapping such strain differences in (GxE) interactions using F2 recombinant inbred lines (RILS). Ultimately, this will allow us to identify the molecular mechanisms of such (GxE) interactions. Our work will yield fundamental insights into how natural genetic variation modulates environmental influences affecting stem cell niche activity and involved molecular processes.

34 – Te Julie – Session 3

Structural Characterization of a Rab Protein and Discovery of Inhibitors to Enhance MASLD Therapy

Julie TE, Jérôme GILLERON, Jérémie TOPIN

Université Côte d'Azur

Corresponding author: jerome.gilleron@univ-cotedazur.fr, jeremie.topin@univ-cotedazur.fr

Keywords: Structural Modelling, Bioinformatics, Molecular Biology, MASLD, Obesity

Obesity promotes hepatic lipid accumulation, leading to the development of Metabolic Associated Steatotic Liver Disease (MASLD). Unfortunately, treatment options for MASLD remain limited. Rab proteins, key regulators of intracellular trafficking, represent promising targets for combating hepatic metabolic diseases. Recently, our laboratory identified a Rab protein whose inactivation reduces hepatic steatosis by enhancing the expression of lipid catabolism genes. However, no inhibitors for this Rab protein are currently known. Our aim is to characterize the structural determinants guiding its organization and regulation to identify targetable sites for selective inhibition. Using structural biology approaches, combining sequence conservation analysis and residue network analysis, we identified several amino acids essential and specific to our Rab protein of interest. Through molecular and cellular biology approaches, including site-directed mutagenesis of these residues and overexpression of the resulting mutants in hepatocytes, we found mutations that alter the subcellular localization of the Rab protein. Interestingly, overexpression of these mutants is sufficient to reduce intracellular lipid droplet levels, confirming that loss of Rab protein function decreases steatosis. Surprisingly, we also identified a mutant that drastically reduces lipid droplets without affecting subcellular localization, suggesting that this mutation disrupts the Rab protein's interaction with its effector involved in repressing lipid catabolism. These results reveal an allosteric architecture specific to our Rab protein and highlight critical residues required for repression of lipid catabolism. This work opens the door to developing selective inhibitors targeting these residues to reduce hepatic steatosis.

35 – Topin Jérémie – Session 3

Exploring Odorant-Receptor Interactions in the frame of Human Fertility

Jérémie Topin, Marc El Hasbany, Marie-Charlotte Dumargne, Romain Barrès

Université Côte d'Azur

Corresponding author: jeremie.topin@univ-cotedazur.fr

Keywords: GPCR, Inhibition, Odorants, Fertility

Global fertility is declining, partly due to a marked decrease in sperm quality, leading to increased use of assisted reproductive technologies (ART), which now account for around 4% of births in France. Despite this growth, ART success rates remain limited, highlighting the need for innovative strategies to improve in vitro fertilisation outcomes. Olfactory receptors, initially identified in the nasal epithelium, are unexpectedly expressed in spermatozoa, where they appear to play functional roles beyond odour perception. At the molecular level, the activation or inhibition of certain ORs located on the surface of spermatozoa modulates motility and may therefore be involved in chemotaxis within the female reproductive tract. At the individual level, genetic polymorphisms in OR genes have been identified in individuals at risk of infertility, suggesting an association between anosmia and infertility. These observations highlight a functional link between these receptors and reproductive capacity. The aim of our consortium is to improve sperm quality or fertilisation potential by activating ORs expressed on human spermatozoa. We are developing a medium-throughput screening assay to test compounds targeting the 40 ORs present on spermatozoa. Sperm motility responses to odour stimulation are quantified using video microscopy and advanced cell tracking methods. The results are expected to pave the way for new diagnostic tools and microfluidic devices for fertility clinics.

36 – Tournière Océane– Session 1

X chromosome dosage in respiratory stem cells controls post-embryonic development and survival

Océane Tournière 1, Lucie Goy 1, Irene Miguel-Aliaga 2, and Bruno Hudry 1*

Université Côte d'Azur

The Francis Crick Institute, London, United Kingdom

Corresponding author: Bruno.HUDRY@univ-cotedazur.fr

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Sex chromosome pairs, while carrying sex-determining genes, often exhibit marked structural heteromorphism, due to extensive gene loss on the sex-specific chromosome. This heteromorphism generates a fundamental dosage imbalance in sex-linked gene expression, with one sex having one copy and the other two. To address this imbalance and equalise gene expression between the sexes, many species have evolved epigenetic-based, chromosome-wide dosage compensation mechanisms. While the molecular machinery governing such processes is well-characterized in model organisms, the core question remains: why is the lack of X-chromosome compensation lethal? Here, we innovated Drosophila melanogaster genetic tools to investigate X chromosome dosage compensation in somatic organs. By implementing ~150 cell-type specific perturbations across developmental stages, we generated spatiotemporal maps of cell populations requiring X chromosome dosage compensation for sex-specific survival. Unexpectedly, dosage compensation is largely dispensable across most tissues and developmental stages, with the exception of the respiratory system during metamorphosis, where X chromosome dosage compensation determines adult stem cell viability. Furthermore, we demonstrate that cellular polyploidy confers insensitivity to X dosage perturbations, providing a mechanistic explanation for cell type-specific dispensability of dosage compensation. These findings reveal how X monosomy impairs development and highlight the initial cellular events leading to organismal death.

37 – Tziouvelis Marinos– Session 1

Identification of cellular circuits in the airways in the early stage of chronic obstructive pulmonary disease (COPD)

Marinos Tziouvelis, Florent Foisset, Malte D. Luecken, Laure-Emmanuelle Zaragosi, Pascal Barbry

Université Côte d'Azur

Corresponding author: tziouvelis@ipmc.cnrs.fr

Keywords: Cell Biology, Molecular signaling, Bioinformatics, Single-cell transcriptomics, Machine learning

Identification of cellular circuits in the airways in the early stage of chronic obstructive pulmonary disease (COPD) Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease with high morbidity and mortality. Disease onset is driven by complex and heterogeneous cellular mechanisms that are poorly understood, particularly in the early stages, limiting the potential for early diagnosis and targeted interventions. My PhD project aims to: (1) characterize disease-associated cellular states in the initial stages of COPD, using complementary in vitro and ex vivo airway models, as well as (2) compare these findings with patient-derived tissue data. To answer the first question, I will generate Air–liquid interface (ALI) cultures from primary airway epithelial cells of COPD patients and healthy donors. Then, I will expose the ALI cultures to cigarette smoke using the ExpoCube® exposure system to investigate cell-type-specific smoke responses. In parallel, I will use precision-cut lung slice (PCLS) models as an ex vivo model to preserve tissue architecture and cell–cell interactions under cigarette smoke exposure. In addition, I will infect primary airway cells from patients with rhinovirus to investigate differential antiviral responses and to distinguish between persistent and intrinsic disease-associated phenotypes. Cellular states will be primarily characterized using single-cell RNA sequencing and immunofluorescence analyses across these models. To achieve the second goal, the generated multi-scale dataset will be integrated with single-cell and spatial transcriptomic profiles from airway biopsies and with longitudinal cohort data. By using computational and bioinformatics analyses during a secondment in Malte Luecken's laboratory at the Helmholtz Center Munich, the aim is to link cellular mechanisms to patient trajectories in COPD and pre-COPD. By combining experimental and clinical data, as well as state-of-the-art computational biology, this project seeks to uncover early cellular circuits in COPD and identify potential markers and therapeutic targets for this chronic condition.

38 – Zambo Boglarka– Session 2

The non-catalytic epsilon DNA polymerase subunit POLE2 is an NPF-motif recognition protein

Salla Keskitalo*, Boglarka Zambo*, Dicle Malaymar Pinar, Antti Tuhkala, Kari Salokas, Tanja Turunen, Norbert Deutsch, Norman Davey, Zsuzsanna Dosztányi, Markku Varjosalo, Gergo Gogl

Université Côte d'Azur

Corresponding author: gergo.gogl@univ-cotedazur.fr

Keywords: Short linear motifs (SLiMs), NPF, POLE2, protein-protein interactions (PPIs), native holdup (nHU)

Short linear motifs (SLiMs) are short sequence elements in disordered protein regions that mediate most transient protein-protein interactions. Although computational tools can predict conserved, putative motifs, they cannot identify their binding partners. As a result, most motifs remain “orphan”, and determining their partners experimentally is challenging because SLiM interactions are weak and standard interactomics are often blind to them. Consensus motifs can sometimes suggest candidate binders, but motif patterns are highly degenerate, can be recognized by multiple unrelated proteins, and we rarely aware of affinity differences. Moreover, only a small fraction of motif-recognizing proteins has been cataloged, leaving much of the SLiM interactome unexplored. The NPF (Asn-Pro-Phe) motif illustrates these challenges. First identified as a ligand of EPS15 homology (EH) domains, NPF motifs engage all human EH proteins through a conserved Asx-turn conformation and often act in multivalent interactions during vesicle formation. However, many other unrelated proteins also bind NPF motifs, including components of the COPII coat, the Pygo2–SSBP2/LDB1 complex, Aurora A kinase regulators, fungal internalization proteins, and even viral proteins such as HIV-1 gp41. Recent studies further reported NPF-mediated interactions between the non-catalytic DNA polymerase ε subunit POLE2 and the nuclear proteins DONSON and TTF2. Together, these findings show that NPF motifs can potentially bind a large and diverse set of partners, yet the determinants of specificity - and the extent of each NPF-binding interactome - remain unknown. Here, we developed an unbiased experimental workflow to systematically identify partners of NPF motifs based on the so-called native holdup affinity interactomics method. Using this approach, we discovered that POLE2 functions as a general NPF-motif recognition protein. We mapped its proteome-wide NPF-dependent interaction network, characterized its binding mechanism, and compared the specificity determinants of POLE2 with those of an EH-domain protein, EPS15. Our results reveal that POLE2 engages a broad set of NPF-containing proteins and expand the functional landscape of DNA polymerase ε within the replisome. More broadly, this study highlights the fundamental specificity problem inherent to motif-mediated interactions and provides an experimental framework to address it at scale.