THE HUMAN FRONTIER SCIENCE PROGRAM
ANNOUNCES ITS

2025 Fellowship Awardees





International
Human Frontier
Science Program
Organization

The Human Frontier Science Program (HFSP) is unique in supporting international collaboration to undertake innovative, risky, basic research at the frontiers of the life sciences. Special emphasis is given to the support and training of independent young investigators, beginning at the postdoctoral level.

The Program is implemented by the International Human Frontier Science Program Organization (HFSPO), supported financially by Australia, Canada, the European Commission, France, Germany, India, Israel, Italy, Japan, New Zealand, Norway, the Republic of Korea, Singapore, South Africa, Switzerland, the United Kingdom of Great Britian and Northern Ireland, and the United States of America.

Since 1990, more than 8,500 researchers from more than 70 countries have been supported. Of these, 31 HFSO awardees have gone on to receive the Nobel Prize.

International
Human Frontier
Science Program
Organization

Human Frontier Science Program New Awards Booklet – 2025 Fellowships
Published in 2025 in Strasbourg, France

Photo credits:
page 3: Nitiphol from AdobeStock
page 13: Chansom Pantip from AdobeStock
page 22: Meo from Pexels
page 34: Vegefox.com from AdobeStock
page 44: Ezume Images from AdobeStock
page 51: Igud Supian from Pexels

About HFSP's 2025 fellowships
Message from the Director of Fellowships

Barbara Pauly,
Director HFSP
Fellowship Program

HFSP Postdoctoral Fellowships support early career researchers in carrying out research projects in the world's best laboratories to broaden their research skills by moving into new areas of study and working in a new country.

HFSP just passed an important milestone: supporting more than 3500 young talents during the last 35 years, and it is gratifying to see how HFSP fellows develop from postdoctoral researchers into established faculty members recognized for their seminal contribution and expertise in their field of research. In many ways, the HFSP fellowship program has gone full circle as is evident by the fact that we have former HFSP fellows now as members of the HFSP Review Committees—evaluating the next generation of scientific movers and shakers.

And again in 2025, we welcome 50 new postdoctoral researchers in the HFSP family, representing 28 nations. We are grateful to the host supervisors for welcoming the new HFSP Fellows to their labs and allowing them a generous margin of flexibility to carry out independent, often risky research on frontier topics. Their projects span a wide range of research area from cellular interactions to the complex projects in neuroscience, or seeking to understand the interactions of organisms in changing environments.

In the 2025 HFSP Fellowship Awards Booklet, you will find the abstracts of those proposals that our review committee members found truly outstanding and exciting. They felt these projects offered the promise for being truly frontier, potentially transformative, and have an impact beyond their immediate fields.

HFSP offers Long-Term Fellowships and Cross-Disciplinary Fellowships.

Long-Term Fellowships are for applicants with a PhD in a biological topic who want to embark on a novel frontier project focusing on the life sciences.

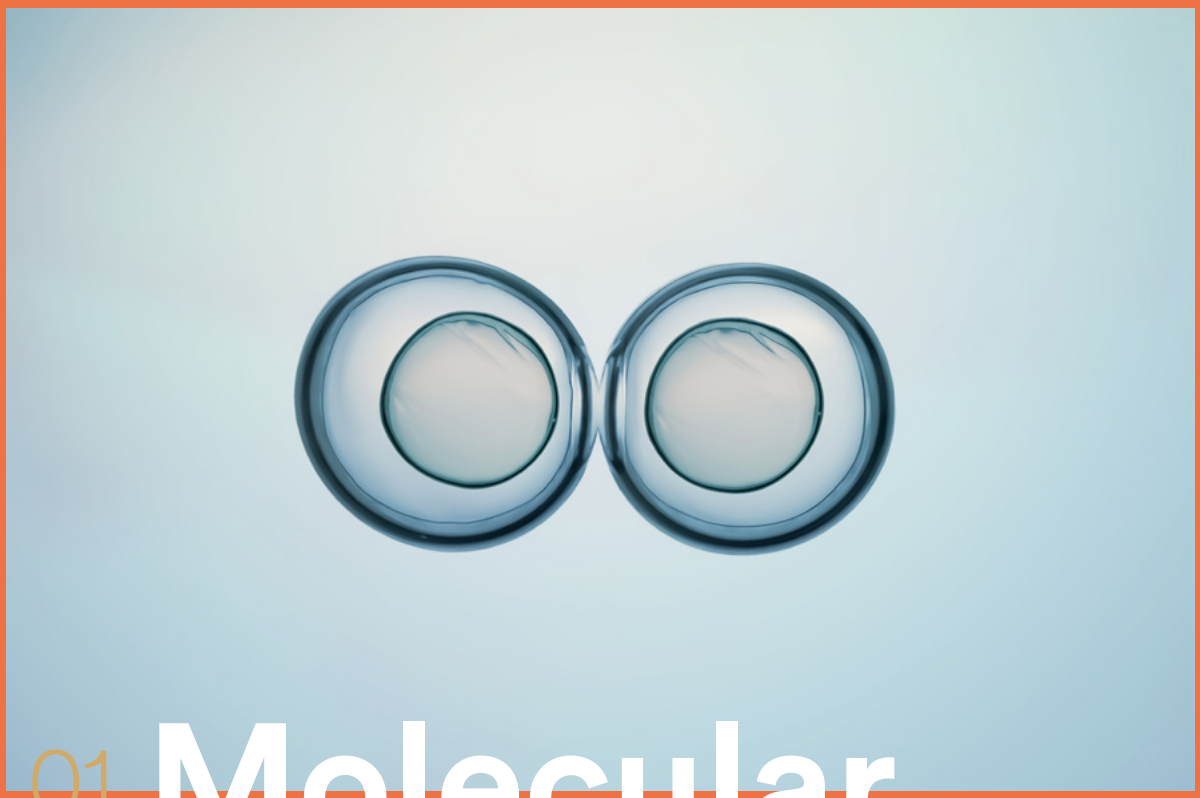
Cross-Disciplinary Fellowships are for applicants who hold a doctoral degree in a non-biological discipline (e.g., physics, chemistry, mathematics, engineering, or computer sciences) and who have no prior training or research experience in the life sciences, but want to work on a novel frontier project in biology.

All HFSP Postdoctoral Fellowships enable their recipients to bridge disciplines – allowing them to integrate perspectives from different fields in a way that would have been difficult under traditional funding schemes.

All HFSP Postdoctoral Fellowships offer support for three years and provide an annual living allowance as well as a research and travel allowance. In addition, child, parental leave, and relocation allowances are provided where appropriate. All HFSP Fellowships must be taken up in a laboratory in a different country to the one where the PhD degree was conferred. They are very flexible and allow interruptions and offer the option of repatriation for the final year of the fellowship. Applicants from a country that is not a member of HFSPO must hold their fellowship in a HFSPO Member country. To take a look at the Fellowships we have funded in the past, please visit our website at www.hfsp.org.

Congratulations to all new awardees and best of luck with your work as you embark on a truly exciting scientific journey!

Table of Contents



01 Molecular and cell biology

Nuclear glycosylation as a new post-translational modification regulating RNA-binding proteins

Kuerbannisha Amahong (China)
PhD Institute: Zhejiang University, China
HFSP Long-Term Fellowship at the University of Gothenburg, Sweden
Host Supervisors: Aishe Sarshad and Daniel Bojar

In the world of molecular biology, post-translational modifications play a crucial role in how proteins function within our cells. Among these, glycosylation, the addition of sugar chains to proteins has long been viewed as a process confined to the secretory pathway, specifically within the endoplasmic reticulum and Golgi apparatus. However, emerging evidence suggests that glycosylation may also occur in other places, particularly in the nucleus.

This research project aims to investigate the fascinating yet largely unexplored role of glycosylation within the nucleus of cells, a process that may hold significant implications for our understanding of gene regulation and cellular functions. First, I will catalog the nuclear glycome—essentially, the complete collection of glycosylated proteins within the nucleus. I will extract nuclei from different mammalian cell lines and tissues. By employing mass spectrometry and glycan-binding assays, I will investigate the diversity and distribution of nuclear glycans, shedding light on their potential roles in cellular functions. Second, I will focus on understanding how these nuclear glycans are synthesized and transported. Despite the primary localization of glycosylation machinery in the secretory pathway, we will utilize innovative genetic techniques, including CRISPR/Cas9, to identify and validate the genes responsible for nuclear glycosylation. This exploration will reveal the mechanisms that allow these modifications to take place in an environment where they were previously thought to be absent. Finally, I will investigate the functional implications of nuclear glycosylation, particularly its impact on RNA-binding proteins (RBPs). Focusing on specific RBPs that play significant roles in gene regulation, I will identify exact sites where sugars attach and create mutant versions that cannot be glycosylated using gene editing techniques. By comparing glycosylated and unglycosylated forms, I will examine changes in protein interactions and cellular localization. This could reveal how glycosylation influences the movement of RBPs between the nucleus and the rest of the cell and their functional roles. In the second part, I will develop an innovative method called “modification-CLIP” to understand how glycosylation affects RBPs’ ability to bind RNA. This allows us to selectively isolate these proteins along with their bound RNAs, enabling a detailed comparison of RNA partners between glycosylated and non-glycosylated RBPs. The anticipated outcomes of this research include a comprehensive characterization of the nuclear glycome, insights into the biosynthesis of nuclear glycans, and a better understanding of how these modifications influence RBP functions, thus opening new avenues for research into disease mechanisms, particularly in cancers where glycosylation patterns are often altered.

The impact of this project extends beyond the immediate field of glycobiology. Through combining cutting-edge proteomics, bioinformatics, and AI-driven machine learning with cell and RNA biology, we will provide the first systematic study of nuclear glycosylation. I will characterize and map the biosynthesis of nuclear glycosylation on RBPs and uncover how these modifications effect their function.

Decoding the evolution of anticipation and decision making in uncertain environments

Lena Boegeholz (Germany)
PhD Institute: Georg August University, Goettingen, Germany
HFSP Long-Term Fellowship at California Institute of Technology, USA
Host Supervisors: Rebecca Voorhees and Douglas Ree

Proteins are molecular machines that are necessary for our cells to survive as they are involved in nearly every process in life. For example, they enable uptake and digestion of nutrients, movement or perception thereof, and communication with the environment. For many of these processes, proteins have to work together in large protein complexes to achieve a certain goal. This is comparable to how a car is assembled from multiple parts that all function together. During its lifetime, the protein complex—similar to a car—experiences wear and tear that will eventually cause individual parts to break. If the car owner wants to continue driving, either the broken part in the car has to be replaced or a new car must be purchased. In cells, the damaged piece has to be discarded correctly as a cluttered environment impairs cellular processes, comparable to how it is difficult to work in a messy garage. Like the manufacturing of a car, production of proteins is a complicated process that costs a lot of energy and resources. Therefore, the cell aims to maintain a balance between production and degradation of proteins to ensure that there are enough functioning protein complexes to survive without cluttering the cell or tying up too many resources.

In this project, I will study whether individual subunits of a protein complex can be replaced or whether the whole complex has to be exchanged. I will also determine whether damaging different proteins in the same complex can lead to different outcomes. As with a car, some parts (such as a broken bulb) may be easily replaced, whereas other parts (such as the engine or car frame) might not be worth exchanging. In the latter case, it might be more cost and time efficient to buy a new car. Individual proteins that will lead to degradation of the whole complex are most likely found in its core and are essential for stability. Next, I will analyze whether specific proteins are needed for the replacement process. While there are specific proteins responsible for the degradation of damaged proteins, sometimes specialized factors are necessary for more difficult tasks. After determining the identity of the necessary, specialized protein tools, I will analyze how they exert their function to improve understanding of why specialized repair proteins are required. Overall, the proposed study will increase knowledge of how damaged proteins in protein complexes are replaced. I will show whether the cell is able to perform cost effective repairs and which other proteins are necessary for the process.

Probing the evolutionary structural biology of the centriole using a unique deep-branching protist

Yana Eglit (Canada)
PhD Institute: Dalhousie University, Halifax, Canada
HFSP Long-Term Fellowship at University of Geneva, Switzerland
Host Supervisors: Paul Guichard and Virginie Hamel

Cells, the basic units of life, come in many shapes and sizes. Whether they are part of larger organisms like plants and animals or exist independently as single-celled organisms, their structure is essential to how they function. A cell's shape and organisation is largely determined by its cytoskeleton. In many cells, one of the key components of this internal framework, the microtubules, form the backbone of extensions called flagella and cilia. Flagella are whip-like structures that enable cell movement, as for instance in sperm cells. Cilia contribute to sensing the environment and communication between cells. Both flagella and cilia are assembled from a structure called the centriole, which also plays a role during cell division, helping ensure that genetic material (DNA) is properly separated and distributed to new cells. While typical animal cells have centrioles and flagella/cilia, many organisms have lost these structures during evolution. Instead, their cytoskeletons are organized around alternative structures, for instance in cellular slime moulds or yeasts, or through dynamic self-organisation, as in plants and many amoebae. The evolutionary origins of these alternative organising centres remain poorly understood. As the last common ancestor of all modern eukaryotes almost certainly was capable of forming flagella and centrioles, organisms with non-centriolar organising centres must have evolved from ancestors with fully functional centrioles. This raises two questions: Did these organisms simplify their centrioles over time, or did they develop entirely new ways to organise their cells? Answering these questions will deepen our understanding of how life's complexity emerged and evolved.

I will address this by studying *Meteora sporadica*, a recently cultivated single-celled protist with an unusual cellular structure. *Meteora* moves using long protrusions and features several arm-like extensions that swing back and forth, supported by bundles of microtubules. These microtubules converge at seven small organising centres that closely resemble parts of centrioles. I hypothesize that these organising centres may be remnants of centrioles that have evolved over time. *Meteora* is closely related to other protists with flagella, which supports the idea that these organising centres are related to centrioles. To explore this question, I will use cutting-edge imaging techniques to develop detailed models of *Meteora*'s organising centres. As *Meteora* is extremely small, I will use the highly resolved cryo-electron tomography to create a model of the organising centres. Moreover, I will search its genome to identify proteins of plausible centriolar origin, and generate antibodies to label these proteins with fluorescent tags. I will then use expansion microscopy to pinpoint the location of these proteins in the cell. By using these state-of-the-art techniques, we aim to unlock the mysteries of *Meteora*'s organizing centers and illuminate the ancient pathways of evolution that shaped the complexity of life.

Ancestral reconstruction and biochemical resurrection of hydrogenases

Leonard Ernst (Germany)
PhD Institute: MPI for Terrestrial Microbiology, Marburg, Germany
HFSP Long-Term Fellowship at Monash Biomedicine Discovery Institute, Melbourne, Australia
Host Supervisors: Chris Greening and Rhys Grinter

How did hydrogenase enzymes emerge, driving the first metabolic electron flow in early life? How did evolution bridge the transition from slow and unspecific geochemistry to the fast and specific biochemistry we know today? How were redox-active minerals first integrated into a protein shell? And what is the evolutionary rationale of the diverse hydrogenases we know today in more than 100,000 organisms?

These and more questions will be explored in my project, focusing on the phylogenetic reconstruction, *in vivo* resurrection and biochemical characterization of ancestral hydrogenases. I will (i) create a hydrogenase family-tree, (ii) infer the likely protein sequences of ancient hydrogenase enzymes, the predecessors of all extant hydrogenases, from the tree, (iii) produce them in model organisms, and (iv) investigate their properties. Hydrogenases are the key drivers of hydrogen-based metabolism, catalyzing either the uptake of hydrogen, resulting in protons and electrons, or the reverse reaction, the production of hydrogen from protons and electrons. Hydrogenases are metalloproteins, consisting of an apoprotein built from amino acids, which incorporates metal clusters required for their enzymatic function.

It is proposed that during the origin of life, hydrogen served as the first electron donor. Thus, in evolution, hydrogenase gain-of-function represents a critical step due to the rise of the first metabolic electron transport chain from hydrogen to CO_2, resembling the electron flow between deep sea vents and their environment. Supposedly having originated in the transition from geochemistry to biochemistry, hydrogenases did not only exist in the last universal common ancestor, but evolved in all three kingdoms of life. The occurrence of oxygen-tolerant hydrogenases illustrates that hydrogenase activity is not limited to anaerobic environmental niches, but plays an important role in many aerobic microorganisms. These enzymes therefore also gain industrial attention for their ability to consume and produce hydrogen under biotechnologically feasible conditions.

However, many questions regarding these enzymes remain: the catalytic bias of hydrogenases, facilitating either hydrogen uptake or production, still lacks a mechanistic explanation. As hydrogenase enzymes are evolutionarily isolated from other enzyme classes, and as these enzymes facilitated the first electron uptake in evolution, their gain-of-function remains to be unsolved. With more hydrogenase sequences available, old phylogenetic trees are outdated, and no efforts have been undertaken to resurrect, produce, or characterize these enzymes. My project on hydrogenases will address these questions. I aim to propose an evolutionary rationale how hydrogenase classes emerged, model the transition from geo- to biochemistry, identify key requirements for hydrogenase activity that can pave the way for potential industrial applications.

The regulation of mitochondrial dynamics by local protein translation in neurons

Raluca Groza (Romania)
PhD Institute: Freie Universität Berlin, Germany
HFSP Long-Term Fellowship at Swiss Federal Institute of Technology, Zürich, Switzerland
Host Supervisor: Tatjana Kleele

Mitochondria perform numerous cellular functions and form a highly dynamic network which rapidly modulates its structure through fission and fusion to meet cellular needs. Disturbances in mitochondrial dynamics have severe bioenergetic consequences in all cells but primarily manifest in neurological disorders. In neurons, mitochondria face particular challenges: thousands of mitochondria have to be distributed throughout the neuronal arbores to account for the high energetic demand of neurons. At the same time, neurons are not renewed over a humans' lifetime, meaning that oxidative damage and mitochondrial DNA mutations escaping quality control accumulate over decades. However, little is known about how mitochondrial dynamics ensure lifelong adaptation and rejuvenation of the mitochondrial network. Given that local protein synthesis is an important process that enables the polarized functions of neurons, we hypothesize that it also plays a role in mediating mitochondrial dynamics. However, barriers in spatial and temporal imaging resolution have made it difficult so far to study local protein synthesis in neurons.

In this project I will investigate whether local protein synthesis is responsible for the local regulation of fission, fusion and mitophagy and how it supports the maintenance of mitochondrial homeostasis in human neurons derived from induced pluripotent stem cells. I will develop a novel live-cell super-resolution imaging pipeline to characterize the dynamics of local mRNA translation in different neuronal compartments based on the SunTag reporter system. Concomitantly, I will image the mitochondrial dynamics events that are mediated by local protein translation in real-time in live neurons. Lastly, I aim to compare local protein translation and mitochondrial dynamics between healthy and aged neurons to identify possible mitochondrial dysfunctions that lead to aging or neurodegenerative diseases. The chosen methodology will not only allow me to address so far unresolved questions in the mitochondrial field, it can also be expanded towards other fundamental cellular processes, potentially opening new research directions.

Mechanistic insight into cell fate decision and memory driving drug resistance

Nitu Kumari (India)
PhD Institute: Indian Institute of Science (IISc), India
HFSP Long-Term Fellowship at Northwestern University Feinberg School of Medicine, Chicago, USA
Host Supervisor: Yogesh Goyal

Cell fate determination is crucial for development, tissue maintenance, and disease progression. It is the process by which cells commit to specific roles while excluding other potential fates. This ability of cells to choose different paths, despite containing identical genetic material, has long fascinated scientists. Our DNA, which carries genetic information, is too large to fit inside a cell's nucleus without folding. Recent discoveries reveal that the 3D organization of the genome plays a pivotal role in this process, adding complexity to our understanding of cellular decision-making. 3D genome organization refers to how DNA is folded within the cell nucleus. This arrangement is highly structured, with specific genome regions in close contact. Their interactions influence gene activity and affect cell fate decisions. It is like complex origami of genetic material, where folding patterns expose or hide genetic instructions.

My project explores cell fate decisions, focusing on DNA organization within the nucleus. While scientists have long assumed DNA folding did not affect cell function, new technologies have revealed the importance of the 3D organization of DNA. Research now explores how 3D arrangement affects cellular processes, particularly gene activity. Examining DNA folding and gene activity separately or in large cell groups, misses crucial details. My project uses cancer cells for studying cell fate choice, which can adapt to and resist treatment despite having the same genetic material as normal cells. To study this, I have developed "FateWatch," an innovative tool combining DNA barcoding with advanced sequencing techniques, which allows me to track thousands of cells simultaneously, observing their lineages, gene activity, and 3D genome organization in unprecedented detail. FateWatch uses DNA barcoding, introducing unique genetic tags into each cell, enabling us to trace cellular lineages and track the fate of their descendants. By combining this barcoding technique with single-cell RNA sequencing and Hi-C, we create a powerful system for observing cellular behavior.

My approach captures the interplay between genome structure, gene expression, and cell fate. I will investigate how treating cancer cells with drugs affects their DNA arrangement and gene activity. Comparing "twin" cell populations will help me to understand whether certain cells are predisposed to resistance. I also aim to identify key proteins that help cells maintain their identity during division and examine whether cells are more likely to become resistant at specific stages of the cell cycle. This could reveal critical windows of vulnerability or resilience in cell cycle phases for cell fate determination.

Ultimately, the insights from this research could revolutionize our understanding of cell fate determination, with far-reaching implications for cancer biology, developmental biology, and stem cell research.

Deciphering the molecular mechanisms of intercellular mitochondrial transfer

Karishma Patel (New Zealand (Aotearoa))
PhD Institute: University of Sydney, Australia
HFSP Long-Term Fellowship at The Francis Crick Institute Ltd, UK
Host Supervisor: Michael Devine

Mitochondria, the energy producing powerhouses of cells, play a crucial role in maintaining brain health and function. When mitochondria malfunction in the central nervous system, it can contribute to the development of devastating neurological disorders. Mitochondria are highly mobile and can move around cells to fuel biochemical processes where they are needed the most. A fascinating process called intercellular mitochondrial transfer (IMT) has been discovered that allows mitochondria to be transferred between distinct cell types. IMT is guided by tunnelling nanotubes which are membranous channels that connect cells for the exchange of various cellular signals and cargo. The transfer of mitochondria to stressed neurons appears to have striking protective effects and holds the potential to be exploited to aid recovery from brain disease or injury. Understanding IMT is therefore essential for developing new treatments. While IMT has been documented in diverse tissues and biological contexts, the exact molecular mechanisms underlying the process remain a mystery.

This project aims to shed light on the mechanisms guiding IMT using state-of-the-art methods investigating how mitochondria are transferred between neurons and affect brain function by developing an innovative and precise platform for detecting IMT between neurons. We will use this platform to to uncover the genes and pathways that are responsible for IMT and investigate the protein-protein interactions that mediate transfer. Cutting-edge electron microscopy techniques will be applied to track IMT at the single molecule level and to three-dimensionally reconstruct tunnelling nanotubes transporting mitochondria in cells at high resolution. The findings from this research could lead to the development of novel therapeutic approaches for conditions like Alzheimer's, Parkinson's, and ischemic diseases and introduce new paradigms to the field of IMT.

Decoding structural dynamics of charge transfer in cryptochromes by time-resolved crystallography

Yalin Zhou (China)
PhD Institute: Shanghai Jiao Tong University, China
HFSP Long-Term Fellowship at Uppsala University, Sweden
Host Supervisor: Sebastian Westenhoff

Cryptochrome proteins play crucial roles in plant growth and circadian rhythms; and they are believed to help migratory animals (e.g., birds, turtles, fish) navigate using Earth's magnetic fields. They are activated by transferring charges across a series of aromatic residues, a critical process also fundamental to broader biological systems including photosynthesis and respiration.

This project aims at uncovering how avian cryptochromes—nature's tiny internal compasses—operate at the atomic level. Utilizing cutting-edge techniques in time-resolved serial crystallography at X-ray free-electron laser facilities, I intend to capture the hidden three-dimensional structural transformations from femtoseconds to milliseconds after energy input by a short light pulse. I will observe how "protein quakes" (i.e., structural changes) emerge, propagate, and eventually subside with the cryptochrome proteins, shedding light on how they manage electron flow—a crucial process for their activation and downstream biological capabilities. I will then interpret the observed structural changes with respect to charge transfer theory. I anticipate that the results may challenge conventional knowledge in electron transfer, which neglect the intricate motions of proteins/solvents in biological environments. A particularly intriguing aspect of this study is the exploration of how these proteins may enable birds to detect geomagnetic fields. By contrasting cryptochromes from migratory and non-migratory species, I hope to reveal the structural basis that could underpin this fascinating magnetosensing ability.

This project is poised to bridge gaps in our understanding of molecular dynamics and charge transfer within biological systems. This could impact a range of scientific fields, from revising existing theoretical mechanisms to deepen our comprehension of how birds utilize quantum mechanics to navigate over vast distances.

Investigating CD1a-driven T-cell responses to UVB light exposure

Laura Ciacchi (Australia)
PhD Institute: Monash University, Melbourne, Australia
HFSP Long-Term Fellowship at the University of Oxford, UK
Host Supervisor: Graham Ogg

Ultraviolet light (UV) from direct sun exposure can induce skin inflammation, sunburn and skin cancers in humans. Skin lipids (fats or oils) play an essential role in maintaining skin integrity and barrier function in protecting the body from foreign microbes and from the harmful effects of UV.

I hypothesize that natural skin lipids are altered by UV exposure and accumulate in the skin subsequently promoting inflammatory responses via a skin-specific novel ('CD1') pathway. Specifically, I will study the role of immune cells ('T-cells') which are usually involved in the defence against infections, but in some cases can cause excess skin inflammation in chronic conditions such as psoriasis and other diseases. Despite research over many decades, we still know relatively little about why the T-cells are active in inflamed skin.

I propose to test the central hypothesis that human skin sebum lipid neo-antigens generated by exposure to UV light can promote CD1a-driven inflammatory T-cell responses. This new functional work will build on and complement my structural biology expertise. I have three aims; first, to detect human CD1a-reactive T-cells that recognise skin sebum lipid peroxides using tetramer staining, flow cytometry, and single-cell sequencing techniques. Second, I will define spatial distribution of skin lipid peroxides following skin UVB (wavelengths of 280–315 nm) exposure using spatial lipidomics. In parallel, I will undertake spatial transcriptomics to define enzymatic changes, and third, perform T-cell functional assays on UV oxidised skin lipid reactive T-cells using primary T-cell clones and CRISPR-mediated TCR transfer. The key risk is that lipids altered by UVB may not be relevant antigens involved in driving psoriasis pathology. The general view is that UVB treatment of skin has an immunosuppressive effect in psoriasis. However, I propose that UVB may lead to the accumulation of neo-lipids with relevance to chronic relapse and pathology.

The data collected in this project will be the first to define UV-altered neo-lipids and responsive T-cells that are induced following UV radiation. This study will allow us to uncover associated mechanisms underlying UV-induced skin inflammation. The insights gained would challenge current perspectives on the role of UV exposure and skin disease and has broader implications for pathogenesis of photosensitive skin disorders. Overall, these studies have the potential to challenge existing ideas of how T-cells function and will assess the effect of environmental UV on skin inflammation and disease.

02 Microbiology

Deciphering how microbial interactions drive horizontal gene transfer of antibiotic resistance

Matteo Sireci (Italy)
PhD Institute: University of Granada, Spain
HFSP Long-Term Fellowship at CNRS - Délégation Paris-Centre, Paris, France
Host Supervisors: Daniel Amor and Martin Polz

The evolution of antibiotic resistance in bacterial communities presents a formidable scientific challenge with profound implications for human health, which led the WHO to include it in the top 10 global health threats. Antibiotic treatments have favored the evolution of antibiotic resistance in many bacteria including deadly pathogens that developed multi-drug resistance. The antibiotic resistance mechanisms identified since the discovery of the penicillin are alarmingly diverse. A major threat in the fight against pathogens relies on an evolutionary mechanism that makes such mechanisms potentially available to all pathogens: Horizontal Gene Transfer. Antibiotic resistant genes often occur in small, mobile DNA molecules called plasmids, which can be transferred via a process known as conjugation, even between unrelated species. This constant genetic sharing happens in natural environments, including the human gut, where bacteria frequently exchange resistance genes. Bacterial communities are complex ecosystems where species interact in multiple ways. Some bacteria cooperate by sharing nutrients, others compete for resources or release antibiotics to suppress rivals. These interactions create a dense network of relationships, which are not well understood. A key question is how these interactions influence the spread of antibiotic resistance through horizontal genetic transfer.

My project aims to answer this question with an interdisciplinary approach combining microbial community ecology experiments with theory and concepts from statistical physics. I will cultivate bacterial communities that include multiple species and various environmental conditions, such as different types of nutrients and antibiotics. I will then observe how different interactions between species affect the transfer of resistance genes between species. I will examine how the frequency of horizontal transfer changes with the intensity of species interactions and the concentration of antibiotics. In highly interactive ecosystems, bacteria can exhibit complex and emergent behaviors, such as strong fluctuations of species abundances or dramatic shifts in composition in response to different initial states. Statistical physics will provide powerful tools to model these complex bacterial dynamics. Just as water can shift between liquid, solid, and gas states, bacterial communities display distinct “ecological phases” that can affect gene transfer. I will also investigate how bacterial immune systems, like the well-known CRISPR/Cas, affect the exchange of plasmids. By exploring the interplay between these immune defenses and the surrounding ecological environment, I aim to understand how plasmids, and the resistance genes they carry, can persist and spread among bacteria. Ultimately, the project aims to develop a predictive framework that explains how antibiotic resistance spreads through ecological interactions and gene transfer in bacterial communities. This research will help lay the groundwork for new therapies based on microbial ecology to combat antibiotic resistance, offering new strategies in the fight against this growing threat.

Dissecting bacterial defense to antibiotics

Divya Choudhary (India)
PhD Institute: University of Oxford, UK
HFSP Long-Term Fellowship at Havard University, USA
Host Supervisors: Ethan Garner and Johan Paulsson

Antibiotic resistance is a growing global health crisis, leading to millions of deaths annually and threatening the success of routine medical procedures. The rise of resistant bacteria outpaces the development of new antibiotics, making development of improved treatment strategies urgent. One serious problem is that genetically identical bacteria often react differently to the same antibiotic. Antibiotics typically target essential bacterial components like the cell membrane, DNA replication, or protein synthesis, which are present in every cell. While these drugs affect all cells in a population, not all cells are killed, a few tolerant cells regrow, resulting in persistent infections. Understanding why certain bacteria survive antibiotic treatment, while others do not, is crucial for addressing antibiotic resistance. The cellular antibiotic response can either allow bacteria to survive or, paradoxically, contribute to cell death. While genetic resistance—which is passed down to subsequent generations—is well-studied, phenotypic resistance—where individual cells temporarily tolerate antibiotics due to environmental factors—is less well understood and more challenging to study without advanced techniques.

I will fill this knowledge gap by examining global gene expression fingerprints at the single cell level to identify key genes that can predict cell survival under antibiotics. Each bacterial genome acts as a codebook for producing thousands of proteins. It is the timing, levels, and lifetime of these proteins that dictate how individual bacteria behave under stress. I will probe the transcription of all protein coding genes in the bacterial cell to identify the key genes that enable bacterial survival under antibiotics. The three essential methods include time-lapse imaging to track lineage information, single cell resolution assay to visualize individual bacteria, and high throughput scaling using custom built microscopes in combination with genetic barcoding to assay the whole library in each experiment. This systematic approach is possible due to technological advancement in my host labs at Harvard University and their collaborators. I will use a microfluidic based system with quantitative time-lapse imaging, enabling the analysis of over one million bacterial lineages over time independently. This will allow me to capture an entire library of transcriptional reporter strains in an optical-pooled-screen approach, with each growth trench serving as a distinct experiment. By analysing individual lineages using machine learning, I aim to identify candidate genes whose expression differentiates live cells from dead ones under antibiotic treatment. Modulating the levels of protein products of the key genes associated with dead cells will aid in developing strategies to enhance bacterial susceptibility to antibiotics.

The findings will be applied to multidrug-resistant bacteria. This project has the potential to make a significant impact beyond antibiotic resistance by offering insights into other fields such as cancer research, immunology, and developmental biology, where understanding variability in cellular responses is vital.

Towards programmable multicellular logic networks

Christopher Jonkergouw (Netherlands)
PhD Institute: Aalto University, Helsinki, Finland
HFSP Long-Term Fellowship at MIT, Cambridge, USA
Host Supervisor: Christopher Voigt

Cooperation among cells is a key evolutionary innovation, allowing specialization and distinct roles within a community. For example, bacterial biofilms show how cooperation enhances survival through shared metabolites and resistance to environmental stresses. Specialization enables spatial segregation of functions, with one species focusing on adhesion and another producing energy-intensive compounds. Such systems have long intrigued microbiologists. In contrast, synthetic biology often prioritizes the creation of new, non-natural functions and constraints within living cells. Drawing inspiration from fields like engineering and photonics where increasing the number of logic circuits on chips results in greater computational power, synthetic biology aims to impose more rules and programmable controls on biological systems. As the complexity and quantity of these synthetic functions grow, they impose a significant burden on the cells, diverting critical resources away from essential processes required for survival. With the increase in complexity, the challenges in engineering such systems escalate dramatically.

This project aims to overcome these challenges by drawing inspiration from natural microbial communities and engineering cooperative behavior among microbes. Instead of burdening a single cell with all synthetic functions, the overall logic circuit is divided into smaller, manageable pieces and distributed across different cells. These cells communicate and work together to execute the full function of the circuit. By engineering cooperation among cells, the workload is distributed, reducing the burden on individual cells and allowing them to specialize in specific tasks, much like the division of labor seen in natural systems. This strategy has the potential to significantly enhance the complexity of engineered biological systems, opening up new possibilities for medical, industrial and agricultural applications.

In medicine, particularly cancer diagnostics and/or treatment, cells can be programmed to detect specific biomarkers or disease states, triggering coordinated therapeutic responses. Multiple cell types work together to detect a wide array of cancer-specific miRNAs. Once the biomarkers are identified, one set of cells can produce a targeted therapeutic protein, while another set enhances the body's immune response. In industrial settings, engineered multicellular systems could enhance the production of biofuels, bioplastics, and other valuable compounds. By dividing complex metabolic pathways across different microbial strains or species, each strain can specialize in producing key intermediates, improving overall efficiency and yield. In agriculture technology, engineered microbial consortia could simultaneously improve soil health, enhance nutrient availability, and protect plants from pests or pathogens. These cooperative systems would promote sustainable agriculture by reducing the need for chemical fertilizers and pesticides while improving crop yields. To summarize, this project explores a revolutionary new strategy towards increasing the capacity and complexity of genetic circuit design, with the potential to generate numerous applications accross multiple biological disciplines.

Unfolding the mechanisms of Tiamat, a unique prokaryotic defense system

Balwina Koopal (Netherlands)
PhD Institute: Wageningen University & Research, Netherlands
HFSP Long-Term Fellowship at Institute of Science and Technology Austria, Klosterneuburg, Austria
Host Supervisor: Jack Bravo

Like other living beings, bacteria are under constant threat of being attacked by viruses. To defend themselves against these invaders, bacteria have evolved a variety of immune systems that can recognize the infection. Upon detection, the immune system then either neutralizes the virus directly, or kills the infected host cell to prevent spread of the virus to neighbouring cells. Due to their ability to detect viruses with great specificity, several bacterial immune systems have been applied in various biotechnological applications with great success. However, new bacterial immune systems are being discovered at a rapid pace, and the mechanisms that underly many of these systems remain to be investigated. One of these systems is the recently discovered Tiamat system. Tiamat is unique among bacterial immune systems because (i) whereas other bacterial immune systems consist of multiple small proteins, Tiamat consists of only one large protein that must be responsible for both sensing the virus and executing the immune function, and (ii) this protein has a unique domain that is known from entirely different cellular processes, which has not been described as part of a bacterial defence system before. It was demonstrated that Tiamat confers moderate immunity against two viruses, but it is unknown how the infection is recognized, and how immunity is secured.

In this project, I aim to resolve these knowledge gaps. To do so, I will first identify viruses that are more strongly affected by Tiamat-based immunity. I will then use these viruses to discover the trigger of activation by identifying proteins that bind to Tiamat. Next, I will assess what happens after Tiamat gets activated. Our preliminary analysis of the Tiamat system has indicated that upon activation it may degrade DNA and/or RNA, presumably from the infecting virus. I will first confirm whether this is the case. Then I will elucidate the underlying mechanism of Tiamat by using the identified trigger for Tiamat activation, as well as a suitable DNA/RNA target, to recapitulate the enzymatic activity of Tiamat outside of the bacterial cell. Subsequently, I will use the outcome of these experiments as a guide to visualize the activation of Tiamat using cryo-EM. The resulting structural models of Tiamat will provide a molecular basis for its function. Lastly, I will explore divergent Tiamat systems to increase our mechanistic understanding of Tiamat in a broader sense, and provide guidance for engineering these systems for their application in biotechnology.

Together, the findings of this project will provide critical insights into a unique, uncharacterized bacterial immune system, both on a cellular and on a molecular level. This will not only broaden our understanding of bacterial immune systems in general, but will also help us understand how a domain that is typically associated with entirely different biological processes could be adapted to function as an immune system.

Assembly and function of surface (S)-layers in Bacillus anthracis

Chen Zhang (China)
PhD Institute: Swiss Federal Institute of Technology, Lausanne, Switzerland
HFSP Long-Term Fellowship at Harvard Medical School, Boston, USA
Host Supervisor: David Rudner

Bacteria are surrounded by a cell envelope that is essential for growth, integrity, and pathogenesis. The envelope and the synthesis pathways that build it are the target of our most effective antibiotics and vaccines. In most bacteria, the envelope is composed of sugar polymers crosslinked into a dense meshwork called the cell wall. The growing cell must constantly expand this meshwork. A subset of bacteria including the human pathogens *Bacillus anthracis* and *Clostridiodes difficile*, assemble a crystalline shell on top of the cell wall. This shell, called the surface layer ("S-layer"), is a crystalline monolayer made of about half a million copies of a single protein. The therapeutic potential of disrupting this layer motivates a more holistic and mechanistic understanding of how the S-layer is assembled and a detailed picture of its function.

In this project, I will investigate the assembly and function of the surface layer in the bacterium *Bacillus anthracis*. In *B. anthracis*, the individual S-layer proteins are connected to the underlying cell wall. During growth, the rod-shaped *B. anthracis* inserts its cell wall material uniformly along the cell cylinder. There is evidence suggesting that growth of the S-layer occurs in gaps or fissures in the crystalline array but it is unknown how these gaps are generated and what dictates where they occur. This project seeks to explain how the S-layer expands during growth. The S-layer is also important for envelope integrity but this function is also poorly understood. My second aim is to determine the function of this protein array.

To study how the *Bacillus anthracis* S-layer is assembled and remodeled, newly synthesized S-layer proteins and the cell wall will be fluorescently labeled and imaged by high-resolution fluorescence microscopy. This will establish the size and position of the gaps in the surface layer that allow its expansion. We assume that surface layer assembly is mediated by crack propagation, in which cracks or fissures are generated by imperfections in the two-dimensional crystalline layer. Some of the surface-layer-associated proteins in *Bacillus anthracis* may generate inhomogeneities in the crystal layer that nucleate the cracks. To explore S-layer function and the interplay between the synthesis of the surface layer and the underlying cell wall, I will perform genetic screens and identify factors critical for cell viability when the surface layer is absent. I will identify genes involved in cell wall synthesis or modification and genes that coordinate cell wall and surface layer synthesis. An unbiased genetic screen holds the promise of elucidating critical roles for this protein monolayer. I will characterize the identified factors using the fluorescence imaging tools he develops to study S-layer assembly.

This project will provide a deeper understanding of surface layer assembly and function in *Bacillus anthracis* and reveal fundamental and biomedical insights with implications for how to combat this important human pathogen.

Microbes also need their space: A bioprinting approach to unravel host-microbe interactions in inflammatory bowel disease

Inez Roegiers (Belgium)
PhD Institute: Ghent University, Belgium
HFSP Long-Term Fellowship at Imperial College London, UK
Host Supervisor: Tamas Korcsmaros and Ravinash Krishna Kumar

Our bodies host trillions of microorganisms, collectively known as the microbiome, which play a crucial role in maintaining our health by aiding digestion and supporting our immune system. Recent studies have revealed that not only the types of microbes, but also how they are spatially arranged in our gut, can significantly impact their interactions with human cells. These interactions are linked to conditions such as colorectal cancer, obesity, and inflammatory bowel disease (IBD), a chronic gut disorder affecting nearly 1 in 100 people in the Western world, for which there is currently no cure. Gaining a better understanding of how microbes are arranged in both healthy and diseased guts could provide new insights into their role in human health and open up novel treatment options for currently incurable diseases.

In this project, I will explore how the 3D arrangement of gut microorganisms influences their interactions with the cells lining the gut wall, in both healthy and IBD-affected individuals. To investigate this, I will employ advanced 3D printing technology to recreate the human gut environment in the lab, printing gut bacteria alongside the slimy mucus layer they live in, arranged in precise 3D patterns. To model the gut wall, I will grow human “mini guts” in a petri dish using a cutting-edge, non-animal experimental approach. By carefully positioning bacteria that play a key role in IBD into different patterns within the mucus layer and combining them with lab-grown “mini guts,” I will, for the first time, study how these different 3D arrangements affect gut wall function. I will examine whether changes in microbial patterns influence the leakiness of the gut barrier and its ability to trigger immune responses, both critical factors in preventing inflammatory conditions like IBD. This project aims to establish a new method to study bacterial communities in the lab, enhancing our ability to understand and manipulate these complex systems. This method has the potential to serve as an alternative to using mice in biomedical research, which has significant limitations. In the future, this approach could replace many current uses of mice in research and provide a more accurate model that resembles the human gut environment.

This bold, high-risk, high-reward project sits at the intersection of microbiology, cell biology, bioengineering, and computational biology. The expected benefits of developing 3D bioprinting techniques to study microbial arrangement are enormous, potentially uncovering key disease mechanisms and leading to groundbreaking new treatments that could benefit people globally. Beyond understanding gut health, this project will highlight the broader importance of 3D microbial arrangement in other areas of the body, such as the skin and respiratory tract, where microbes play vital roles.

Predicting phage dynamics in microbial communities

Rachel Szabo (USA)
PhD Institute: Massachusetts Institute of Technology, USA
HFSP Long-Term Fellowship at the Swiss Federal Institute of Technology, Zürich, Switzerland
Host Supervisors: Martin Ackermann and Olga Schubert

Wherever there is life, viruses will inevitably be found. The bacterial communities that drive metabolic transformations across our planet are no exception. Viruses infecting bacteria—known as bacteriophages or phages—vastly outnumber their hosts in nearly every environment and re-wire the membership and functions of bacterial communities in stunningly diverse ways. Because the health of our ecosystems depends on these phage-bacteria communities (or "microbiomes"), we need to understand how these collectives respond to environmental change. While scientists have long studied how bacterial communities respond to environmental changes, our understanding of the impacts of phages is still limited, especially regarding how their roles might change with the environment. This knowledge gap remains in large part because of the tremendous diversity of phages. Our current framework for interpreting this laregely unexplored diversity is based on phage taxonomy. However, taxonomy is a poor indicator of which hosts pages are infecting and how quickly they spread through a population. This leaves us unable to predict how phages function and shape microbiomes.

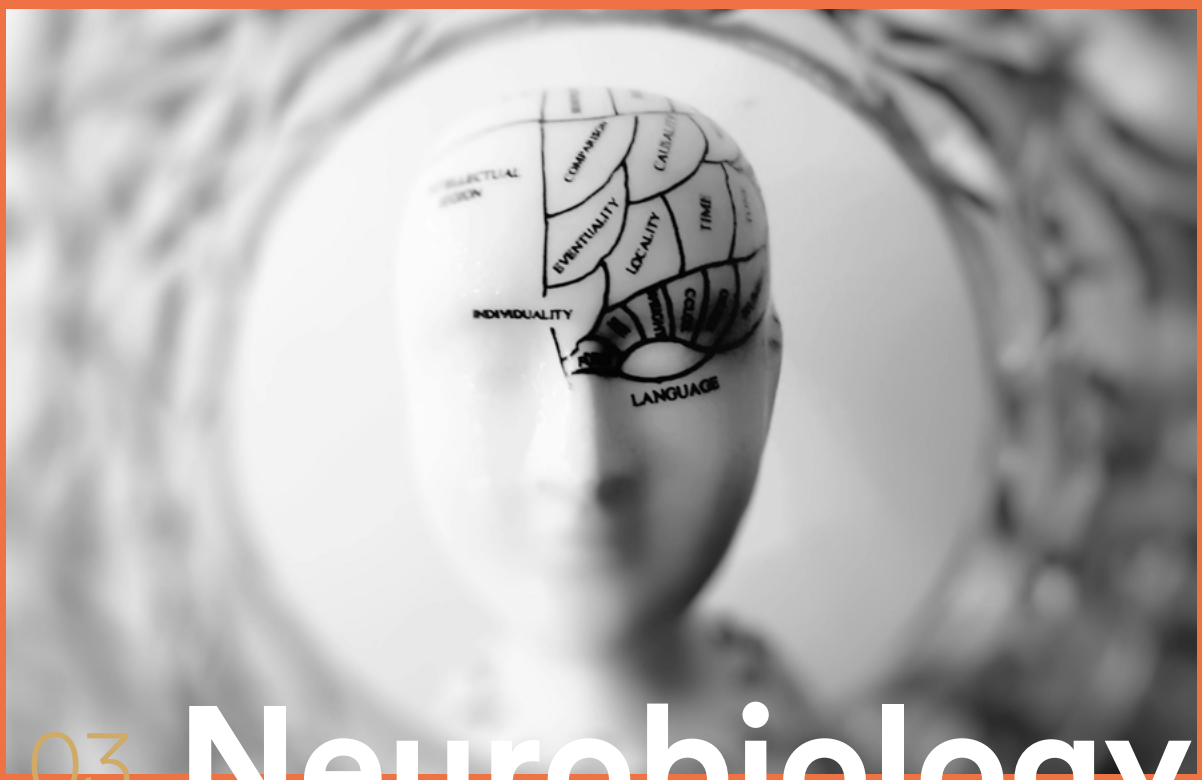
My project aims to fill this gap by developing a novel framework for studying phages and their impacts on microbial communities. I will categorize phages based on their functional traits —their specific characteristics that determine how they reproduce and survive. To develop this trait-based framework for phages, I will systematically quantify how environmental conditions tune phage traits and their interactions within microbiomes, thereby driving the assembly of phage-bacteria communities. I will focus on phage communities in soil microbiomes as an experimental system because these ecosystems are a reservoir for largely untapped phage diversity and hold vast potential as biotechnological interventions (e.g., in agriculture, carbon capture, and bioremediation). I will use a systems biology approach to identify the environmental drivers of phage community assembly, combining the enrichment of soil microbiomes along resource gradients in the laboratory with high-throughput phage-host trait quantification to systematically map how environmental conditions select for phages through their traits. This is possible only now because newly devised approaches have brought phage functional characterization into the high-throughput era. To integrate the resulting datasets, I will build and parameterize mathematical models of phage community assembly using measured phage trait values and test these models with synthetic phage-host communities. This quantitative, large-scale, and integrative approach is key to discovering predictive principles for phage ecology that can bridge observations between nature and the lab. My project will enable us to integrate omnipresent yet often-overlooked phage interactions into predictive models of microbiome assembly and function. Ultimately, these models will empower us to leverage phage communities within a microbiome engineering toolkit for the health of our planet and ourselves.

Systematic discovery of evolutionary origins and functional diversity of methyltransferases

Luis Enrique Valentin-Alvarado (USA)
PhD Institute: University of California Berkeley, USA
HFSP Long-Term Fellowship at Monash University, Melbourne, Australia
Host Supervisor: Gavin Knott

One of the most profound questions in biology is how simple single-celled organisms evolved into the complex eukaryotic cells that make up plants, animals, and humans. This transformation, which occurred billions of years ago, set the stage for the diversity of life we see today. My research project aims to shed light on this pivotal moment in the history of life by exploring a group of enigmatic microbes known as Asgard archaea. Asgard archaea possess features that are remarkably similar to those of eukaryotic cells, making them the closest living relatives to our earliest ancestors. Despite their significance, we know very little about their gene regulation and how this might have influenced the evolution of complex life. Central to this project is the study of epigenetics—the mechanisms that turn genes on or off without changing the DNA sequence. In eukaryotes, epigenetics plays a crucial role in development, allowing cells to differentiate into various types despite having the same genetic code. However, the origins of these complex regulatory systems remain largely unknown.

This research project focuses on enzymes called methyltransferases (MTases), which are essential players in epigenetic regulation. They add chemical “tags” to DNA, RNA, or proteins, influencing how genes are turned on or off. By investigating MTases in Asgard archaea, I aim to discover whether these enigmatic microbes possess complex epigenetic systems similar to those found in eukaryotes. If they do, it could mean that the roots of epigenetic regulation—and thus the foundation of cellular complexity—are much older than previously thought. To achieve this, I will use cutting-edge computational tools and laboratory techniques. First, I will employ advanced artificial intelligence models to scan the genomes of Asgard archaea for genes encoding MTases. This approach allows us to identify potential enzymes even in organisms that cannot be easily grown in the lab. Next, I will develop high throughput methods to produce and study these enzymes. By analyzing the structure and function of archaeal MTases, I hope to reveal similarities and differences with their eukaryotic counterparts. Mapping the patterns of chemical modifications introduced by these enzymes will help us understand their roles in the cell. The methodologies developed in this project—combining advanced computational tools with innovative laboratory techniques—will enable us to study proteins from uncultivated microorganisms efficiently. This approach can be extended to investigate other elusive proteins from a wide array of organisms, enhancing our ability to explore the vast diversity of life.



03 Neurobiology and behavior

Dissecting brainstem neural circuits orchestrating intra-oral tongue movements

Mohamed El Tabbal (Egypt)
PhD Institute: Okinawa Institute of Science and Technology, Japan
HFSP Long-Term Fellowship at The Salk Institute for Biological Studies, La Jolla, USA
Host Supervisors: Eiman Azim and Elizabeth Brainerd

When we chew, speak, or drink our tongue moves precisely inside our mouth. How are these immaculate tongue movements controlled by our brain? Sometimes you bite your tongue or you choke—these unfortunate mishaps are caused by the uncoordinated action of breathing, tongue, and jaw movements. How do breathing and chewing movements coordinate with those of the tongue? To answer these questions, we need to monitor tongue movements with high temporal and spatial precision in animals that provide experimental access to the neural circuits that control these behaviors. Monitoring tongue movements inside the mouth and their precise millisecond coordination with other concomitant motor actions (e.g., breathing and chewing) is challenging.

I propose to integrate micro-X-ray reconstruction of moving morphology (micro-XROMM) with genetic and physiological approaches in mice to dissect, manipulate, and record brainstem neural circuits that control 3D intra-oral tongue movement during natural behaviors like chewing and drinking. Micro-XROMM offers access to detailed intra-oral 3D dynamics and kinematics of the tongue at millisecond temporal and submillimeter spatial resolutions. Moreover, mice offer unparalleled molecular-genetic selectivity for accessing and manipulating specific mammalian neural circuits. By combining these approaches, I aim to characterize the complex motor space of intra-oral tongue movements and how it is coordinated with chewing and breathing at the behavioral level. I will follow this precise behavioral characterization with anatomical and functional dissection of a putative brainstem neural circuit responsible for this coordination. Our work will lay the foundation for exploring the tongue as a unique sensory-motor system. I will introduce a new framework, based on biological insights, to model the circuit-level control of fine-scale complex dynamics of flexible elastic bodies using the tongue as a model, with implications that extend well beyond neuroscience and clinical medicine to soft robotics and continuum mechanics.

Molecular mechanisms underlying the evolution of central neural circuits and behavior

Christoph Giez (Germany)
PhD Institute: Christian-Albrecht University, Kiel, Germany
HFSP Long-Term Fellowship at The Francis Crick Institute, London, UK
Host Supervisor: Laura Lucia Prieto Godino

The brain is one of the most complex structures in the universe and controls behavior. Thus, the immense variety of behaviors displayed by animals—including ourselves—arose through the evolution of the complex neuronal networks in brains. However, we still do not know how central neuronal circuits change over time, integrating modifications in the brain's highly interconnected networks. Evolution acts on genes but behavior arises through the activity of neuronal networks—how are these two levels integrated? How do evolutionary changes in genes lead to changes in neuronal circuits that then lead to behavioral divergences across animals? Understanding the connection between genes, neuronal network function, and behavior will have far-reaching implications beyond the field of circuit evolution. The larval olfactory system of the fruit fly *Drosophila* offers a powerful model to explore this question, because it has been charactized in detail.

I will use this system to pinpoint key areas of central neuronal circuit evolution, both in terms of function and genetics, by comparing two *Drosophila* species. I will use comparative connectomics and create maps of all of the neuronal connections within a brain circuit for two different species to identify differences between these two species. I will then use genetic approaches to investigate how these connectivity changes alter the function of the brain circuits. Introducing genetic tools, I will visualize and manipulate the neuronal activity of networks in the brains of the two species. This will help us to understand whether the observed changes in neuronal connections have functional consequences, and lead to differences in behavior between the two species. I will use mathematical modelling to understand the function of the complex brain networks, because it allows to simplify complex interactions, and to make testable predictions for mechanisms. Next, since evolution acts on genes, I will investigate how the activation of specific genes in the neurons of one species but not the other lead to the observed connectivity differences. I will leverage these insights to re-engineer neuronal circuits across *Drosophila* species by taking the genes from *D. erecta* and transfer them into *D. melanogaster* which will eventually lead to a change in neuronal circuitry and behavior. One prediction is that neurons responsible for processing and filtering inputs are hotspots of change and are responsible for the emergence of new behaviors. One indicator is that these neurons are likely to exhibit variations within a species, a crucial element for evolutionary changes to happen.

Uncovering the genetic basis of these changes will enhance our understanding of the intricate interactions between genes, neuronal circuits, and behavior in the context of evolution. This will uncover fundamental principles of sensory processing in the brain and shed light on the most exciting question: how do brains evolve?

Noninvasive magnetomechanical modulation of microglia

Ananth Kamath (India)
PhD Institute: University of Chicago, USA
HFSP Cross-Disciplinary Fellowship at Katholieke Universiteit Leuven, Belgium
Host Supervisor: Adrian Ranga

Imagine a world where we have the technology to communicate with others directly through our thoughts. It will enable communication between people who speak different languages. It can allow you to visualize the creative imagination of your friend. It can enable communication with the deaf. It can possibly allow the erasing of traumatic memories. The invention of telepathy can enable things that currently seem impossible.

There remain two technological challenges in the way of telepathy. First, the ability to noninvasively interface with the brain. Recently, human brain implants can enable a person to control a computer directly through thoughts, but this requires brain surgery. To communicate with the brain noninvasively, we need to send signals to the brain without attenuation. The only current forms of energy that can penetrate the human brain noninvasively are ultrasound and magnetic fields. Recent advances have allowed control of single cells deep within the brain through ultrasound and magnetic technology. The second technological challenge is the ability to edit information in the brain. Current brain-machine interfaces can record human thoughts, but there is presently no way to write or erase memory in the brain. This can be achieved through engineering glial cells, the non-neuronal cells in the brain. Traditionally believed to be 'supporting cells', glial cells are now increasingly recognized for their ability to modify synaptic information in the brain during learning. Control of glial cells therefore provides a path towards directly editing information in the brain.

In this project, I will build on advances in these two technological frontiers to move towards the goal of memory editing. I will develop magnetic nanoparticles for controlling glial cell behavior in the brain. These nanoparticles will exert local mechanical forces in the brain when a magnetic field is applied. They will be able to exert forces at specific locations in the brain in a noninvasive manner. I will develop a system for testing the effect of mechanical forces on microglia in 3D brain organoids. I will build a system for embedding magnetic nanoparticles in organoids, and test whether it affects microglial migration and neuron-microglia interaction. We will use animal models to test whether mechanical forces can influence the ability of microglia to silence epileptic seizures and improve their ability to clear tumors.

This high-risk project will combine my expertise in nanomaterial chemistry with the expertise of the Ranga lab in organoid engineering. It comes with the potential to provide a completely new way of controlling brain activity. On the long term, my project can serve as a route for noninvasive editing of information in the brain. This will help reach a day when a person can wear a device like a hat and use it to talk to others through telepathy.

Reading and writing stem cell memories for central nervous system repair

Simon Perrin (France)
PhD Institute: Paris Cité University, France
HFSP Long-Term Fellowship at Karolinska Institutet, Stockholm, Sweden
Host Supervisor: Enric Llorens-Bobadilla

Adult resident stem cells mediate tissue repair after injury by differentiating into the specific cell types needed to restore tissue integrity. Recent studies demonstrated that resident stem cells can acquire a memory from previous triggers, encoded in their epigenome, that enhance their responsiveness during subsequent injuries. Thus, modulating stem cell memory could be a promising way to boost stem cell potential and tissue repair, especially in tissue with limited regenerative capacity. The central nervous system (CNS) fails to heal following injury, representing a major challenge in regenerative medicine. While the CNS contains resident stem cells, their contribution is limited, raising the need for new approaches enhancing neural stem cell function *in vivo*.

In this project, I aim to record the formation of chromatin memories in neural stem cells and characterize their functional impact, with the goal of engineering priming memories enhancing their contribution to injury repair. I will use the mouse spinal cord as a model system given that the resident stem cell population, ependymal cells (EpCs), have been well characterized. First, I will investigate the acquisition of inflammatory memory in neural stem cells after injury. The response to injury and fate of EpCs that were never triggered by injury (naive EpCs) and EpCs that were previously exposed to injury (primed EpCs) will be compared using genetic fate mapping, conditional transcriptional factor perturbations, and *in vivo* injury models. Then, I will characterize how memories are encoded in the chromatin of neural stem cells. The chromatin landscape of naive and primed neural stem cells will be compared to identify chromatin regions that remain accessible after EpCs recover their original identity. Spatial genomics analyses of the injury response of naive and primed cells will identify the most promising candidates that modulate the response and plasticity of neural stem cells after injury. Finally, I will engineer chromatin memories in EpCs to enhance their regenerative potential. Using CRISPR-based epigenome editing, I will implant the memory-associated chromatin modifications identified into naive EpCs and assess the impact of this artificial memory on neural stem cell fate and potential.

Overall, this project brings an innovative perspective to unlock the regenerative potential of neural stem cells using targeted molecular engineering and may inspire new strategies to promote CNS repair. Editing epigenetic cell memories could open new therapeutic perspectives for numerous conditions by manipulating the *in vivo* behavior of resident stem cells from many tissues.

Unfolding the genetic and cellular complexities of cerebral cortex folding

Sulov Saha (Bangladesh)
PhD Institute: University of Toulouse, France
HFSP Long-Term Fellowship at Instituto de Neurociencias, Alicante, Spain
Host Supervisor: Victor Borrell

The mammalian cerebral cortex, made up of neurons and glial cells, is crucial for functions like thought, memory, and sensory processing. As the brain grows, the cortex expands more than the rest of the forebrain, forming characteristic folds known as gyri (outward ridges) and sulci (inward grooves between gyri). While it was once believed that these folds formed simply because the cortex grew too large to fit within the skull, research over the last decades has revealed that cortex folding is an intrinsic and highly regulated process, not just a byproduct of growth. The folds play a key role in brain organization, with primary folds aligning with critical functional areas, such as those involved in movement or sensation. Folding patterns are equal across individuals within a species and even among different species, dictated by genetic and cellular processes. Researchers have identified a genetic 'map' that predicts where gyri and sulci will form during brain development. In the developing brain of species with folded cortices, like humans, primates, and some carnivores, these maps are divided into modules, each playing a role in the emergence of the folds. Particular types of progenitor cells—cells that give rise to neurons—are especially active in the regions where folds form, indicating that their behavior may be closely linked to the development of cortical folds. Despite these discoveries, many questions remain about how the genetic, cellular, and metabolic processes work together to guide the organization of cells and the formation of folds in the cortex.

This project aims to shed light on these open questions by exploring how multiple biological processes interact to shape cortical folding. I will use the ferret as an animal model, as the ferret brain has simple but consistent folds across individuals. Mice and chicks, whose brains do not fold naturally, will be used to help manipulate or induce folding patterns, providing insights into how these processes may be triggered in species that don't typically exhibit folds. The goal of my project is to understand how early molecular signals, metabolic activity and cellular processes come together to promote the formation of gyri and sulci. This involves studying the activity of genes, the behavior of progenitor cells and the migration of neurons into regions where folds will form.

By creating a detailed, publicly accessible atlas of cortex folding across a variety of species—from non-mammals to mammals—I hope to offer valuable insights into the evolutionary principles behind brain development. The research may also uncover links between gene mutations, cell behavior, and neurodevelopmental disorders tied to abnormal cortical folding in humans, offering new pathways for diagnosis and treatment.

Polarized trafficking mechanisms of voltage-gated Ca^{2+} channels in neurons

Ke Yang (China)
PhD Institute: Tsinghua University, China
HFSP Long-Term Fellowship at Harvard Medical School, Boston, USA
Host Supervisor: Pascal Kaeser

Neurons are highly polarized cells with distinct protein distribution on its axons and dendrites. This research investigates how neurons organize and transport vital proteins to specific locations to function properly. A disruption in this process is linked to a variety of neurodegenerative and developmental disorders.

This project focuses on calcium channels, ion channels essential for neurons to send signals to each other and to regulate brain activity. I will examine two key types of calcium channels in this project: CaV2 and CaV1. These channel proteins play distinct roles in different parts of the neuron. CaV2 channels are essential for releasing chemical signals at the presynapsic active zone. CaV1 channels are found in somatodendritic parts of the neuron and help control its electrical activity. Both types of channels are made in the soma of the neuron and exhibit limited sequence differences, but they need to be transported to their different locations. Understanding how neurons sort and transport these proteins to their correct locations has been a long-standing question, and this project seeks to uncover the mechanisms involved. Our hypothesis is that specific sequences in the calcium channels that act like address labels help determine where they need to go.

My first goal is to investigate how CaV2 channels are transported: CaV2 channels are made in the neuron's soma and must be moved to the active presynaptic zone. This process likely involves packaging the channels into small transport units, which are then carried along pathways inside the neuron. The study will explore the molecular machinery responsible for this transport, including the proteins that help to direct CaV2 to the correct location. I will also study whether other active zone proteins are traveling together with CaV2 channels, helping to guide them to their final destination.

The second goal is to understand how CaV1 channels are sorted and transported. I will investigate how specific sequences within CaV1 help to guide it to the dendrites. I will test whether switching these sequences between CaV1 and CaV2 channels can redirect them to different parts of the neuron, further illuminating how neurons control the movement and placement of these important proteins. By studying how these calcium channels are sorted, transported, and anchored within neurons, this project aims to better understand the establishment of polarization that keeps neurons functioning correctly. The findings of this project will contribute to a broader understanding of how the brain maintains its complex communication networks and how disruptions in these processes may lead to neurological disorders. The insights could help identify new strategies for treating brain diseases, offering potential pathways for intervention where protein transport goes awry.

Re-engineering memory engrams in mice with brain machine interfaces

Kadjita Asumbisa (Ghana)
PhD Institute: McGill University, Canada
HFSP Long-Term Fellowship at the Biozentrum, University of Basel, Switzerland
Host Supervisor: Flavio Donato

Memory is one of the brain's most essential functions, enabling us to recall past episodes and learn from experience. At the core of this process are memory engrams—groups of neurons believed to store or "bookmark" memories in the brain. These engram neurons work together through coordinated activity, but how these memory networks are formed and which mechanisms govern them remains poorly understood. In the 1940s, Donald Hebb proposed a theory to explain engram formation, suggesting that "cells that fire together, wire together". He posited that repeated co-activity strengthens the connections between neurons, allowing the activation of a subset of the network to reinstate an entire memory through pattern completion—where the network is driven into a state that recalls the full memory. In such systems, memory is distributed across many neurons, meaning the loss of some neurons does not erase the memory. This theory raises intriguing possibilities: if repeated co-activity is sufficient to bind neurons into a memory network, could non-engram neurons be artificially recruited into an existing engram and share the memory? If the original engram neurons were then removed, would the memory persist in the newly incorporated neurons?

My project aims to test this hypothesis by using cutting-edge brain-machine interfaces (BMIs) to integrate non-engram neurons into existing memory traces, potentially transferring memories between neuron groups. BMIs allow real-time control of neuronal activity. While their traditional use leveraged electrophysiological recordings to decode activity patterns for motor rehabilitation, recent advancements in calcium-based BMIs—which combine BMIs with *in-vivo* calcium imaging—allow to monitor and control genetically defined neurons, such as engrams, with unprecedented precision. I will use a calcium-based BMI to synchronize the activity of engram neurons representing a contextual fear memory with non-engram neurons—binding them into a unified memory network. Then I will use genetic tools to selectively ablate the original engram neurons and assess memory retention by evaluating memory-driven behavioral responses and monitoring neuronal coactivation during memory recall.

This project holds the potential to reveal critical insights into the plasticity rules that govern memory networks. By demonstrating that memories can be transferred or expanded to include new neurons, this project could establish a biologically feasible technique using BMIs to restructure memory networks. Such advancements could lead to therapies for memory disorders, providing ways to restore lost memories or alter maladaptive ones.

Neuromodulation of representational stability during learning under uncertainty

Yoshiki Hatashita (Japan)
PhD Institute: Waseda University, Tokyo, Japan
HFSP Long-Term Fellowship at University Hospital Bonn, Germany
Host Supervisor: Tobias Rose

Recent advances in chronic and large-scale neuronal recording in behaving mice have shown that neuronal responses to the same inputs can gradually change over time—even in the primary sensory area of olfaction and the visual cortex. Such "representational drift" poses the critical question of how the brain achieves reliable memory, perception, and action with unstable neuronal processing. Computational studies suggest that representational drift may serve to avoid local minima, reduce overfitting, provide flexibility for continuous learning, or connect temporally separated memories. However, little is known about the cause and function of representational drift. Systematic clarification of the behavioral state-dependence of representational drift, its modulation by task variables, and its relation to the cell-autonomous molecular makeup of neurons is needed.

In this project, I address these questions using a visually guided foraging task with certain and uncertain reward outcome probabilities and explore how continuous learning under uncertain conditions affects the stability of neuronal representation in the visual cortex. In this task, mice need to adapt to uncertain circumstances by continuously updating the behavioral outcome history and internal model based on the experience of reward probability. As the cholinergic signaling encodes behavioral outcome uncertainty and re-balance feed-forward and top-down integration, I hypothesize that higher outcome uncertainty accelerates overall representational drift while shaping neural activity differently in neuronal subtypes under neuromodulatory control. To test this, I will establish the behavioral task built on a head-fixed virtual reality system and perform a combination of chronic two-photon calcium imaging and correlated three-dimensional spatial transcriptomics. Moreover, I propose to monitor and control cholinergic axonal activity during the task to dissect the involved neuromodulatory circuits. The goal is to identify key genetic profiles associated with individual or population neuronal stability and state-dependent modulation. This could be a specific neuronal subtype or sub-network defined by molecular markers such as neuropeptides, adhesion molecules, or heterogeneous combinations of neuromodulator receptors and distinct downstream signaling pathways of immediate early genes.

This study will advance the experimental characterization of representational drift by shedding light on its behavioral state dependence, neuromodulatory circuits, and molecular specificity, likely providing new genetic access and theoretical frameworks to address the biological significance of representational drift in future studies.

Visual and acoustic integration in mating swarms of malaria mosquitoes

Takuro Ohashi (Japan)
PhD Institute: Nagoya University, Japan
HFSP Long-Term Fellowship at University of Washington, Seattle, USA
Host Supervisor: Jeff Riffell

Swarming is among nature's most complex and poorly understood collective behaviors. It occurs in diverse animals, from birds and fish to insects. Although prior work on bird flocking and fish schooling has suggested that the collective behavior follows relatively simple algorithms, research in mosquito swarms has not yet identified the principles of their swarming behavior. Mosquitoes are the world's deadliest creatures and impact a billion people per year with pathogens. Swarms are critical for mosquito reproduction and, hence, the spread of disease. At dusk, thousands of mosquitoes are thought to be attracted to visual markers to form a swarm. In the complex 3D swarm, mosquitoes mate in-flight, and individuals must approach mates while avoiding competitors. Little is known about the sensory mechanisms of swarm formation and the processes that enable these intricate within-swarm behaviors. In malaria-mosquitoes *Anopheles gambiae* these questions can be tackled and the sensory mechanisms can be determined at different scales: long-distance attraction to swarm markers (>10 m) and close-range attraction to mates (<0.1 m).

Male mosquitoes are attracted to, and form a swarm above a visually contrasting object on the ground just before dusk for mating, but it remains unclear which visual features attract the mosquitoes to cause the swarm formation. Once in the swarm, males distinguish males and females based on sex-specific flight tones and avoid collision with other males based on visual and acoustic cues. However, the exact visual features that mediate mating interactions and male-male avoidance are unknown. The sensory and neural bases of swarming behaviors and visual-acoustic processing are poorly understood.

I propose to study the behavioral and neural mechanisms of visual-acoustic-based mating behaviors in the swarm by using an innovative experimental pipeline across organizational scales. This pipeline and computational analyses will allow me to test the visual markers for swarm formation and to analyse mosquito trajectories using a 3D tracking system to investigate stereotypic behaviors during swarm formation and within-swarm interactions. A cutting-edge virtual reality setup with tethered mosquitoes will enable me to recapitulate the visual-acoustic features of the swarm, with time-series observations of behavioral and physiological changes during localization behavior. Last, I will study the neural basis of visual-acoustic integration by recording neural activity from male mosquitoes exposed to these features.

This project will provide a new understanding of the functional neuro-mechanics of mating swarms, and provide crucial knowledge about the mechanisms that underlie the fecundity of malaria vectors that cause >400,000 human deaths each year. My project will directly support the development of malaria-vector control strategies such as acoustic and visual lures. Finally, swarming is an important topic in aerial robotics research; my study may provide bio-inspiration for novel algorithms in swarming robots.

Unravelling the role of proboscis neuronal populations in *Aedes aegypti* blood feeding behavior

Irene Arnoldi (Italy)
PhD Institute: Istituto Universitario di Studi Superiori di Pavia, IUSS, Italy
HFSP Long-Term Fellowship at Radboud University Medical Center, Netherlands
Host Supervisor: Felix Hol

Mosquitoes are often depicted as the deadliest animals of the world, which is partially true: mosquitoes feeding on human blood are a huge burden for our society, mainly because they transmit pathogens causing potentially deadly diseases, including plasmodium, which causes malaria, and mosquito-borne viruses, such as dengue, Chikungunya and Zika. Among blood feeding species, only female mosquitoes feed on vertebrate hosts to acquire blood, which is required to complete egg development. Immature females and males are innocuous, as they feed on nectar. Mosquitoes find a human host by exploiting visual, thermal, and olfactory cues; next, they land on the human skin and move their proboscis around until identifying, based on unknown mechanisms, an area to insert their mouthparts. The mosquito proboscis comprises the labium, which is retracted during blood feeding, and the needle-like labrum, which forms the alimentary canal and is inserted in the skin. The labium and the labrum harbour sensory neurons which are thought to perceive chemical and physical stimuli during feeding. The labium is committed to nectar perception but could have a role in identifying a good area to pierce before biting, whereas the labrum is involved in blood perception. While probing the skin, mosquitoes salivate and move their stylets to find a blood vessel. Then, they start engorging with blood and, finally, remove their mouthparts and fly away for digestion.

Despite the importance of mosquito blood feeding for human health, we know very little about this process and about how chemical stimuli, such as blood-related compounds, or physical stimuli, including temperature or blood flow, are sensed and integrated by sensory neurons within the proboscis. This lack of knowledge prevents us from identifying what makes mosquitoes such efficient feeders, impeding countermeasures. To fill this knowledge gap, I aim to understand the role of neurons in the labrum and the labium for the perception of chemical, thermal and mechanical stimuli during blood feeding, by studying the yellow fever mosquito *Aedes aegypti*, an invasive species transmitting several arboviruses. I will identify and select populations of neurons involved in chemosensation, thermosensation, and mechanosensation during blood feeding. By genetic engineering, I will identify the chemical, thermal and mechanical stimuli which activate each selected population of neurons. Finally, I will use a behavioral assay to quantitatively evaluate biting and feeding behaviors of mosquitoes and investigate effects of elimination of populations of proboscis neurons on blood feeding.

The results of this research project will provide new insights into neuronal control of mosquito. The pathways which I will characterize through this project can be targeted in the future to inhibit the blood feeding process in mosquitoes, leading to the development of novel strategies for mosquito management and control of vector-borne diseases.

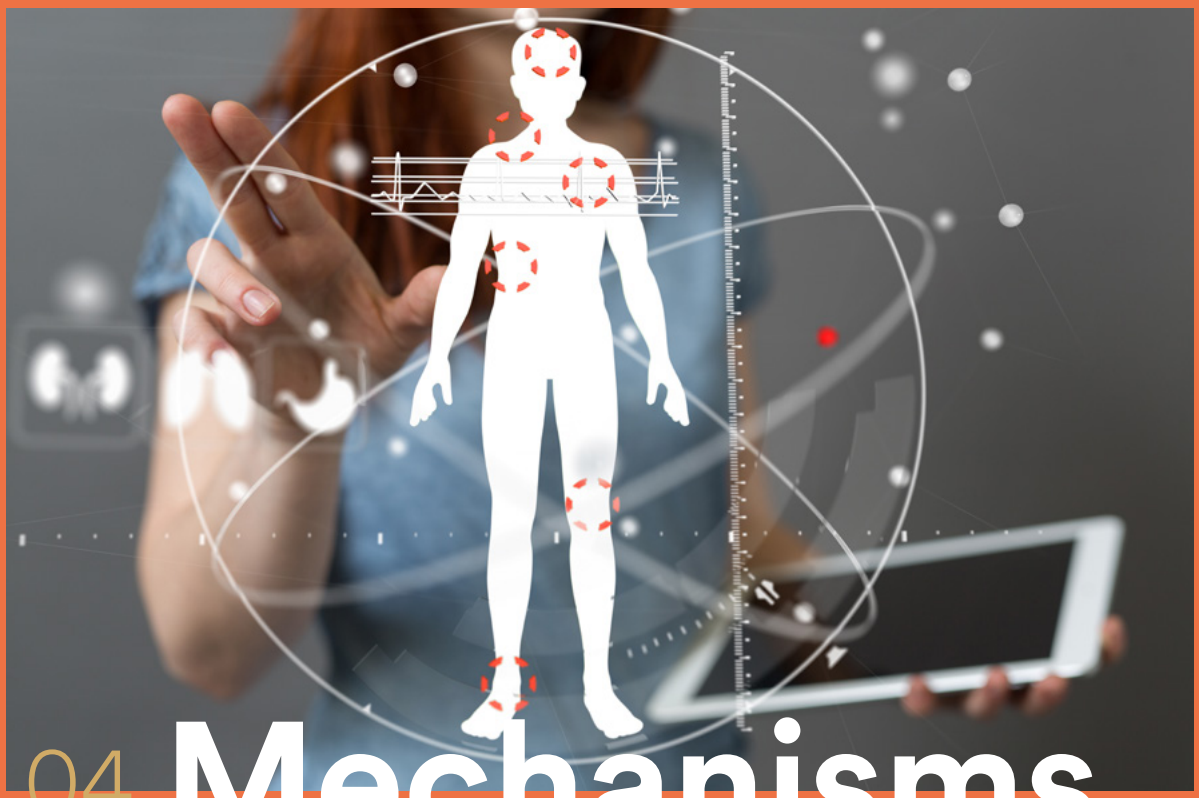
Determining the role of fine-scale structural complexity in animal behaviour in a changing ocean

Catherine Sheppard (UK)
PhD Institute: Lancaster University, UK
HFSP Long-Term Fellowship at Hawai'i Institute of Marine Biology, Kaneohe, USA
Host Supervisors: Elizabeth Madin and Jose Ricardo Paula

Structural complexity mediates species richness and diversity across ecosystems. Yet how fine-scale structural complexity shapes animal populations and communities is unknown. Structural complexity is typically measured on broad spatial scales, leaving a fundamental knowledge gap, as fine-scale variation in complexity may mediate fine-scale variation in animal distribution, behaviour and interspecific interactions. Two such interspecific interactions are those between predator and prey species and cleaning mutualisms, both of which have been shown to be affected by structural complexity. However, how fine-scale structural complexity mediates these relationships, and how these effects cascade throughout the wider interaction network, remains less understood.

This project will employ highly novel and cutting-edge techniques to challenge our current understanding of how changing habitats mediate animal behaviour across ecological and spatial scales. Using coral reefs as a study system, we will test the central hypothesis that fine-scale structural complexity drives significant variation in animal space use, interspecific interactions and cognition. First we will use cognitive tests to determine the extent to which fine-scale structural complexity drives spatial cognition in individuals. Then we will explore how fine-scale structural complexity and cleaning mutualisms mediate predator-prey interactions in a natural, but controlled, environmental setting. Third we aim to incorporate predicted changes to structural complexity, based on climate-derived predictions of reef change, into regional species distribution models. Understanding how fine-scale structural complexity shapes animal behaviour under human-induced environmental change is necessary to accurately predict and manage our impacts. This project will address this fundamental knowledge gap.

As an integrated whole, this project will draw links across ecological scales, from individual-level behaviour to regional species distributions, offering insight into how fine-scale structural complexity mediates behavioural cascades in changing habitats.



04 Mechanisms of health and disease

Understanding the role of tertiary lymphoid structures in chronic hepatitis C infection

Costanza Borrelli (Italy)
PhD Institute: ETH Zürich, Switzerland
HFSP Long-Term Fellowship at The Rockefeller University, USA
Host Supervisor: Gabriel Victora

Tertiary lymphoid structures (TLS) are immune cell aggregates resembling lymph nodes that form in conditions of chronic inflammation or cancer. Such tertiary lymphoid structures are widely observed in the clinics and correlate with detrimental prognosis in autoimmune diseases, COVID infections and transplant patients, but with favorable therapeutic outcomes in several cancer types. While their prognostic value in patients is widely recognized, the molecular mechanisms underlying these clinical associations remain elusive. Little is known about where, why, and how TLS form. Most importantly, their immune function and contribution to disease course remain elusive.

I will study TLS formation and functions in the context of infection with hepatitis C virus (HCV), a virus that affects 1–3% of the human population causing liver damage and hepatocellular carcinoma. TLS are a diagnostic feature of chronic HCV infection, but their role in promoting viral persistence and disease progression is unknown. My aims are to (1) map cellular interactions in TLS arising upon HCV infection, (2) perturb TLS formation in order to functionally evaluate their contribution to disease progression to cirrhosis and hepatocellular carcinoma and (3) track the dynamics of TLS formation and the lymphocyte trafficking to and from these structures. To interrogate the cellular interactions that lead to TLS formation and maturation, I will combine a mouse model of chronic hepatitis C infection with the LIPSTIC technology, recently conceived in the Victora laboratory. LIPSTIC (Labeling of Immune Partnerships by SorTagging Intercellular Contacts) is a method to study cell-cell interactions in the mouse based on enzymatic transfer of a labeled substrate between cells. Like actual lipstick, this system allows tracking of cellular kiss-and-run events and can be applied to contact-trace immune and non-immune cells. Once identified, the cellular interactions occurring in the liver during hepatitis C infection will be tested to uncover which ones are promoting or suppressing formation of TLS. We will further track the trafficking of cells to and from TLS using photoconversion that allows to color cells at specific locations by illumination with light and then follow them as they travel through the body. Finally, we will generate a mouse model in which TLS formation and location can be visualized in living mice, allowing for monitoring of these structures over time and greatly reducing the number of animals used for this study.

This project, which leverages my expertise in *in vivo* screening in the liver and the Victora lab's expertise in recording lymphocyte interactions and dynamics, will yield insights into the cellular events leading to TLS formation and maturation upon hepatitis C virus infection, with unprecedented resolution. It will further our knowledge of TLS function and uncover their role in regulating disease progression and tumorigenesis. It will also generate tools to study TLS biology in other pathological settings such as infections by respiratory viruses, autoimmune diseases and cancer.

Epitranscriptome profiling in the DepMap: An engine for target and biomarker discovery in cancer

Chi Kong Chan (Hong Kong, China)
PhD Institute: The Hong Kong University of Science and Technology, Hong Kong, China
HFSP Cross-Disciplinary Fellowship at MIT, Cambridge, USA
Host Supervisor: Peter Dedon

Cancer is one of the top threats to human health and a leading cause of death worldwide, taking away ~10 million lives each year. Despite significant progress, our understanding of how cancer arises, progresses, and interacts with the body remains inconclusive. Emerging evidence has now linked cancer development with defects in the process that makes proteins, translation, and the levels of key cancer-driving proteins. However, little is known about the precise mechanisms causing these defects. The Dedon Lab discovered a fundamental mechanism in which 50 modifications on 250 expressed human tRNAs—the epitranscriptome—are reprogrammed to cause codon-biased translation of stress response proteins. Growing evidence points to corruption of dozens of tRNA-modifying enzymes as core molecular drivers in many cancers.

In this project, I propose to expand my analytical chemistry background to explore defects in the translation process using a platform of genomic, bioanalytical, and RNA sequencing technologies, including high-throughput small RNA isolation, LC-MS/MS analysis of modified ribonucleosides, and absolute quantification RNA-sequencing library preparation. I will systematically and quantitatively explore corruption of tRNA reprogramming and codon-biased translation across 50 Cancer Dependency Map cell lines from 5 tumor types (lung, glioblastoma, kidney, colon, and breast cancers; 10 cell lines each). The goal is to generate new insights into the mechanisms that drive cancer development and progression, thus revealing novel diagnostic biomarkers for cancer types and potential targets for anticancer drug development. This research has the potential to transform cancer biology by allowing systematic determination of the degree of dysfunction in the translation process in human cancers. This approach could be useful for the study of over 100 other human diseases that have been connected with translation defects. Using data processing, data mining, programming, and machine learning I aim to comprehend the findings and identify patterns and signatures in the data. These signatures could be unique to each cancer type and useful for further development as diagnostic tools and therapeutic targets. I will collaborate with leading medical institutions to extend the studies to dozens of human sarcoma samples to assess whether similar mechanisms and signatures can also be applied to clinical samples.

Not only will this project add new and original knowledge about a frontier area of cancer biology, with creation of a database of translational defects in cancer, but the results will reveal novel potential targets for therapeutic discovery and development.

Epigenetic homeostasis as oncogenic barrier during cell differentiation

Cristina Fracassi (Italy)
PhD Institute: San Raffaele Vita - Salute University, Italy
HFSP Long-Term Fellowship at Institute of Human Genetics, CNRS, Montpellier, France
Host Supervisor: Giacomo Cavalli

Epigenetics refers to the biological processes that alter gene activity in a heritable manner without altering the DNA sequence. These mechanisms modulate cell differentiation, during which a single cell divides, grows, and transforms into various specialized cells, such as neurons. Together, these processes guide the body's development, shaping all the organs and tissues of a living organism. Proper cell differentiation is essential for the development and health of any organism, but when this process goes awry, it can lead to pathologies like cancer. While adults cancers often are characterized by mutations that compromise gene integrity and function, pediatric cancers show few or no mutations but the extensive deregulation of epigenetic process. Pediatric cancers seem to result from an aberrant differentiation process suggesting that disruption of epigenetics processes could lead to an aberrant progression of cell differentiation. Yet, whether this is sufficient to induce cancer still remains elusive.

In this project, I aim to disrupt these processes during cell differentiation in order to test whether cells transform into a tumoral fate and to characterize the epigenetic profiles during and after these epigenetic perturbations. I will employ advanced techniques to manipulate the expression of epigenetic components in laboratory models of cell differentiation. I will deplete or overexpress proteins of the Polycomb group, epigenetic components whose deregulation was shown to be associated with progression of many types of cancer. I will test whether these manipulations are sufficient to transform cells into tumoral fates. In order to understand the molecular effects of the different perturbations, I will apply cutting-edge tools such as genome sequencing, epigenome profiling, 3D genome conformation mapping and super resolution imaging analysis. These techniques will provide a detailed view of the epigenetic changes occurring in individual cells and across various biological processes. Epigenetic mechanisms allow cells to acquire a "memory" of their previous states but, since epigenetic processes are inherently reversible, restoring epigenetic balance offers the potential to reverse their effects. In this context, I will apply transient perturbations of Polycomb protein levels in order to elucidate to what extent the induced alterations are reversible. In this last case, I will co-express a known activated oncogene in addition to applying a transient epigenetic perturbation and test whether and how this additional insult aggravates cell transformation.

By understanding the effect of Polycomb perturbations during cell differentiation and whether they are reversible upon restoration of the initial level of these components, we could gain insights into how cells maintain their identity and whether cancer might be reversed by manipulating epigenetics. This project aims to define cancer as a disease rooted in developmental cell differentiation processes and to deepen our understanding of cell differentiation and development.

Directed evolution of LaccID and discovery of tumor-immune interactions driving cancer progression

Chang Lin (China)
PhD Institute: Peking University, China
HFSP Long-Term Fellowship at Stanford University, USA
Host Supervisor: Alice Ting

Surface proteins, such as checkpoint receptors and co-stimulatory receptors, within the tumor microenvironment (TME) play important roles in regulating tumor growth and immunosuppression. Profiling the dynamic of the surface proteome of cancer cells and tumor-infiltrating T cells, including chimera antigen receptor T (CAR-T) cells, within the TME in animal cancer models can provide a comprehensive understanding of the molecular mechanisms by which tumor cells grow, metastasize, and evade immune detection. Proximity labeling (PL) has emerged as one of the most promising approaches for such studies due to its rapid labeling kinetics (<10 minutes) and high spatial resolution (<10 nm). PL employs engineered promiscuous enzymes fused to specific protein baits to generate reactive species, resulting in the covalent tagging of proximal proteins for proteomic analysis. However, existing PL enzymes have significant limitations in profiling cell surface proteomes *in vivo*. For instance, peroxidases require cytotoxic H_2O_2 as a co-oxidant, while biotin ligases strictly need ATP, which is present in low amounts at the cell surface.

To overcome these technological barriers and gain a deeper understanding of surface proteomes related to tumor-immune interaction, I aim to develop a novel PL enzyme with surface-selective, non-toxic activity. The Ting lab has recently engineered a multicopper oxidase, LaccID, which leverages non-toxic oxygen as a co-oxidant to generate phenoxyl radicals for PL on the cell surface. While potentially compatible with *in vivo* applications, this enzyme requires 1–2 hours to achieve sufficient labeling and is susceptible to endogenous substances such as thiols and halides. Additional engineering is needed to make it a truly useful tool for *in vivo* surface proteome mapping. By implementing protein engineering methods such as directed evolution, I will enhance LaccID for improved activity and resistance to endogenous inhibitors. By expressing the next-generation LaccID on the surface of cancer cells, T cells, or CAR-T cells in mouse cancer models, I will use proximity labeling and mass spectrometry to map surface proteome changes during tumor progression/evasion and immune cell activation/exhaustion. This approach aims to uncover novel protein-mediated signaling axes between cancer and immune cells in mouse models, offering avenues for therapeutic intervention.

This project will provide (i) a transformative technology for profiling the surface proteomes of specific cell types in complex, *in vivo* environments, with high temporal resolution (minutes) and minimal toxicity, and (ii) proteome insight into the mechanisms by which tumor-immune interactions reshape the cell surface landscape, influencing functions related to tumor killing or immune evasion.

Enhancing cell plasticity in models of the human pancreas towards functional beta cell regeneration

Silke Lochs (Netherlands)
PhD Institute: Hubrecht Institute, Utrecht University, Netherlands
HFSP Long-Term Fellowship at Max Delbrück Center for Molecular Medicine, Berlin, Germany
Host Supervisor: Jan Philipp Junker

Diabetes affects over 500 million patients worldwide, significantly impacting their quality of life and posing a substantial burden on healthcare systems. This disease is caused by the gradual destruction of insulin-producing ß-cells, which reside within the islets of the pancreas. Without these cells, the body struggles to regulate blood sugar levels, leading to serious health problems and diabetes symptoms.

This project explores the possibility of restoring or regenerating these insulin-producing cells by studying the concept of cell plasticity in the human pancreas. Cell plasticity refers to a cell's ability to change its function or identity, potentially taking over the role of other cells. In animals like mice and zebrafish, certain pancreatic cells can switch to producing insulin when ß-cells are lost, helping to maintain normal blood sugar levels and preventing diabetes symptoms. It is still unclear whether human pancreatic cells have a similar ability, and if this can be enhanced to recover lost ß-cells in diabetes patients. To investigate this, the project uses lab-grown human pancreatic islet organoids. These organoids resemble the pancreas during fetal development, a stage of life that is known for greater plasticity and ability to regenerate. The organoids provide an ideal model to study whether human pancreatic cells can indeed undergo plasticity and regenerate insulin-producing cells, as well as to identify genetic or epigenetic factors that might block this process.

First, the project will focus on zebrafish, known for its regenerative abilities. By using advanced single-cell sequencing technologies, I will identify which genes and molecular mechanisms are activated when zebrafish ß-cells are lost and how other pancreatic cells can switch states to take over insulin production. I will investigate whether epigenetic factors are involved in this process, as these might block cell plasticity in the human pancreatic islet. Next, I will investigate whether similar mechanisms exist in the human islet organoids, by artificially causing ß-cell loss in this model and analyzing the response with single-cell sequencing technologies. This will reveal whether the organoids, which mimic the fetal stage, indeed have a higher regenerative potential. Alternatively, if the organoids don't show the same plasticity as the zebrafish, this project will reveal the barriers that prevent this, such as absence of specific genes, epigenetic factors, or other causes. Building on this, the project will use innovative gene-editing technologies like CRISPR to modify specific genes in the human organoids, aiming to enhance their cell plasticity. By testing different factors discovered by the zebrafish and organoid studies, I intend to further boost the ability of these organoids to regenerate insulin-producing cells. This could be a key step toward developing helping diabetes patients to naturally recover their insulin production. This project could transform diabetes care by offering a regenerative therapy that allows patients to regain insulin production, potentially reducing or eliminating the need for insulin injections. It will also create a new model for studying tissue regeneration in humans, with insights that could extend beyond diabetes to other diseases and organs.

Exploring the hidden roles of the Y chromosome in Alzheimer's disease: A cutting-edge organoid study

Kotaro Oiwa (Japan)
PhD Institute: Nagoya University, Japan
HFSP Long-Term Fellowship at the Salk Institute for Biological Studies, San Diego, USA
Host Supervisor: Fred Gage

Occurrence of dementia continues to increase as the global population ages. Alzheimer's disease, the most common form of dementia, is characterized by neuroinflammation induced by brain immune cells called microglia. These cells are essential for maintaining brain homeostasis by removing pathogens and dead cells, but once activated, they induce neuroinflammation and exacerbate neurodegeneration. While the importance of neuroinflammation has been pointed out, no treatment for Alzheimer's disease targeting neuroinflammation exists to date. One reason for this is that the microglia of rodent models widely used differ significantly from human microglia, as they do not have orthologs of the risk genes for Alzheimer's disease. Therefore, a model of human microglia is urgently needed for neurodegenerative disease research. In this study, "neuroimmune organoids" will be applied for the first time to investigate microglia in Alzheimer's disease. Organoid technology is a technique for culturing three-dimensional tissue from stem cells on a dish. The neuroimmune organoids are the latest technology ideal for studying neurodegeneration because, in this technique, human brain tissue with microglia is xenotransplanted into mouse brains, allowing human microglia to be cultured for long periods. They can recapitulate the physiological conditions in the human brain and overcome the limitations of earlier rodent models. Meanwhile, the Y chromosome has been considered a "genetic wasteland" because it has lower gene density than the X and autosomal chromosomes. Blood cells lose their Y chromosome with aging, and recent studies suggested that loss of the Y chromosome exacerbates heart failure and cancer and is prevalent in the microglia in patients with Alzheimer's disease. However, it is unclear whether microglia which have lost the Y chromosome worsen Alzheimer's disease. This study primarily aims to elucidate the effect of the loss of the Y chromosome in microglia on Alzheimer's disease. Why do microglia lose their Y chromosomes as they age? The fundamental mechanism of neurodegeneration may be related to the answer to this question. It is believed that there are distinct upstream mechanisms in cancer and neurodegenerative diseases. Cancer characteristically is uncontrolled growth induced by genomic instability, which causes DNA damage and mutations. Although abnormal protein aggregation is essential for neurodegeneration, recent studies have also detected genomic instability in neurodegenerative disease lesions. Furthermore, the loss of the Y chromosome in blood cells has been linked to abnormalities in cancer-driver genes. This project will investigate how genomic instability induces Y chromosome loss in microglia and identify common upstream mechanisms in cancer and neurodegeneration. In summary, this study will use cutting-edge brain organoids to define a new role for the Y chromosome in the human brain. We also propose genomic instability as a common cause of cancer and neurodegeneration. This study has the potential to accelerate Alzheimer's disease research by applying the extensive knowledge and tools developed in cancer research to date, leading to benefiting millions of patients.

Unraveling the role of HSC diversity in aging using intersectional genetics and clonal tracing

Victoria Parreno (France)
PhD Institute: Institute of Human Genetics - UMR 9002 CNRS - Université de Montpellier, France
HFSP Long-Term Fellowship at the Institute for Research in Biomedicine, Barcelona, Spain
Host Supervisor: Alejo Rodriguez-Fraticelli

As the global population ages, the negative effects on health, such as increased vulnerability to infections and diseases, are becoming increasingly apparent. One major factor in this decline is the diminished efficiency of the immune system, which is closely linked to hematopoietic stem cells (HSCs). These cells are crucial for producing all types of blood cells, including those essential for immune responses. HSCs have a remarkable ability to either differentiate into various types of blood cells or self-renew to maintain their own population. Researchers historically thought of HSCs as a uniform group of cells, but advances in single-cell technologies have revealed their high diversity. This means different HSCs may have distinct roles, with some producing a balanced mix of immune cells, i.e. lymphoid and myeloid cells, and others biased towards producing more myeloid cells, which are involved in fighting infections and responding to inflammation. Unlike lymphoid cells, that are crucial for long-term immune responses, myeloid cells do not contribute to immune memory. As we age, this balance shifts towards these myeloid-biased HSCs (my-HSCs), which might contribute to the decline in immune function seen in older individuals. Recent studies have shown that partially removing these my-HSCs in mice can rejuvenate the immune system, restoring it to a more youthful state. However, the exact role of my-HSCs in aging, their origins, and their dependence on epigenetic factors—mechanisms that regulate gene activity without changing the DNA sequence—remain unclear.

This project aims to address these gaps. First, we will use a specialized mouse model to deplete selectively cells that typically give rise to lymphoid cells, allowing us to observe whether my-HSCs alone drive aging. This will help determine if these cells are central to the aging process. Next, we will investigate the development and origins of my-HSCs over time to understand why they become more prevalent with age. This knowledge could reveal new targets for interventions to slow down aging. Finally, we will test whether specific interventions can either reprogram or eliminate my-HSCs to rejuvenate the immune system. Success here could open new pathways for therapies aimed at extending healthy lifespan. In an increasingly aging world, understanding and reversing the decline in immune function is more important than ever. By uncovering the role of my-HSCs in aging, this project could lead to new therapies that enhance healthy lifespan and improve the quality of life for millions of older individuals.

Stem cell memories of inflammation: consequences to tissue fitness and tumor susceptibility

Felipe Rodrigues (Brazil)
PhD Institute: The Francis Crick Institute, UK
HFSP Long-Term Fellowship at The Rockefeller University, New York City, USA
Host Supervisor: Elaine Fuchs

We are living on a fast-changing planet with an unprecedented climate crisis and the growing emergence of pathogens, pollutants, and inflammatory irritants that we have never encountered before. Additionally, our ozone layer is thinning, increasing our exposure to the sun's harmful rays. Not surprisingly, chronic inflammatory disorders and skin cancers are on the rise, because our skin epidermis is at the interface between our body and the outside world. To keep us well protected from scratches, microbes, and the sun's ultraviolet light, barrier tissues such as the skin epithelium exhibit a remarkable ability to regenerate and adapt to these external challenges. This is only possible through the function of specialized cells called epithelial stem cells (EpSCs), which are long-lived and able to self-renew and regenerate the skin's barrier. EpSCs work in coordination with our immune system to repair damage and prevent infections. However, when mutations in EpSCs cause this communication to go awry, the susceptibility to chronic inflammatory skin disorders and cancer emerge, posing ever-increasing global health problems. Recently, we have learned that stem cells in our skin can remember previous experiences of scratches or infections that happened months, even years ago. Physiologically, this memory can result in a swift and enhanced response to subsequent attacks, enabling our skin to heal faster. While a fast response to tissue injury is beneficial, these memories can be maladaptive, leading to chronic inflammatory disorders and cancers. Patients with chronic inflammatory disorders, such as psoriasis, atopic dermatitis (eczema), and inflammatory bowel disease are at increased risk of cancer, but why this is the case remains largely a mystery.

My project seeks to shed light on these clinically relevant observations. More than 200 cases per hour of squamous cell carcinoma (SCC) of the skin are diagnosed in the United States alone, and this has increased by more than 200 percent in the past 30 years. I plan to use suitable mouse models to explore how epithelial stem cells in our skin respond to different types of inflammation, such as those observed in psoriasis and eczema, and how these inflammatory challenges could then impact organismal fitness. I plan to investigate how localized skin inflammation may impact other organs, such as the lungs. This question is important because babies suffering from eczema in the skin later in life develop inflammatory syndromes in the airway (i.e. asthma), a phenomenon called 'Atopic March'. In addition, patients with eczema are at increased risk of cancer, but again why this happens remains unexplored. My project could have enormous implications for the long-term consequences of inflammation in health and fitness and for our knowledge of how tissue stem cells change in inflammation and cancer.

Canal of Hering functions as a pressure regulator for biliary excretion

Lingyu Sun (China)
PhD Institute: Southeast University, China
HFSP Cross-Disciplinary Fellowship at the National University of Singapore, Singapore
Host Supervisor: Hanry Yu

Regeneration of the liver is initiated in the canals of Hering that connect the bile canaliculi to the interlobular bile ducts, but it has remained unclear which exact functions they serve. We have previously discovered that bile canaliculi contracts in a cell autonomous manner driven by the bile salt excretion from the surrounding hepatocytes. We hypothesize that the canals of Hering function as pressure regulators for bile canaliculi to propel bile salt into the bile duct.

I will test this hypothesis by developing an *in vitro* model of hepatobiliary connection to dissect the steps of the pressure-driven bile canaliculi contraction and the transportation of bile salt into the bile duct. The aim is to establish an *in vitro* hepatobiliary connection model. I will induce the spatial alignment and polarization of cholangiocytes on a tubular structured scaffold to form a bile duct with barrier function in a microfluidic chip, followed by the co-cultivation of hepatocytes with the cholangiocyte-composed bile duct. To induce the formation of the desired connection between bile canaliculi and bile duct, I will modify the scaffold with cell adhesion molecules such as cadherin, together with extracellular matrix overlay such as collagen and Matrigel on hepatocytes to provide the necessary biochemical and mechanical cues. I also plan to dissect the pressure build up process for triggering bile canaliculi contraction. Using the developed model, I will combine fluorescent chemosensors and imaging techniques to visualize and monitor pressure-related behaviors, including but not limited to the accumulation of pericanalicular actin, the activation of Piezo 1, the dynamics of intracellular calcium, and the fluctuation of canalicular membrane. My third aim is to build an *in vivo* model to study the pressure regulation process by the canals of Hering. To verify key findings observed from the *in vitro* model, I will use an established transgenic mouse model and modulators of contraction machinery to compare the contraction process in the canals of Hering with different diameters. I anticipate that the hepatobiliary connection serves as constricted narrow channel similar to a pressure valve leading to osmotic pressure build up in bile canaliculi. When the pressure exceeds a threshold, it will trigger Piezo 1-mediated calcium influx into the surrounding hepatocytes to enable the bile canaliculi contraction and squeezing of bile salt into the bile duct.

Understanding exactly how the pressure is regulated will enable therapies for diseases such as cholestasis, evaluate supplements claiming to cleanse the liver, and help to establish a fundamental understanding of how the liver detoxifies the human body. The cells in the pressure valve are pre-mature and divide very fast. Upon liver injury, these putative pressure-sensitive cells are the first cells involved in liver regeneration. Thus, this study will pave the way to understand the earliest signals and events leading to liver regeneration.

05 Development: from cell to organism

Dissecting the composition and function of highly abundant crystals in mammalian oocytes

Jurgita Paukstyte (Lithuania)
PhD Institute: University of Helsinki, Finland
HFSP Long-Term Fellowship at MPI for Multidisciplinary Sciences, Göttingen, Germany
Host Supervisor: Melina Schuh

Life begins with fertilization, where the embryo inherits most of its cellular contents from the oocyte, a large maternal egg cell. During their development, oocytes grow extensively and store the essential biomolecules needed for early embryonic development. Storing these materials, even in a large cell such as an oocyte, is a major challenge. To overcome this, oocytes use proteins that can change their three-dimensional structure to neatly assemble into compartments, efficiently collecting and storing the components needed for later use. Disruption of these structures can lead to failure of embryonic development, highlighting their critical role in reproduction. The molecular mechanisms that regulate this unique organization of cellular components have remained largely unknown. When we examined mouse oocytes using cryo-electron tomography (cryo-ET), we discovered a previously unrecognized compartment. Some proteins in the oocytes were stacked in well-organized intracellular crystals. The high number of these crystals, up to 10,000 per cell, suggests that they are composed of abundant proteins and may play an important role in oocyte and embryo development. However, the identity and function of these protein crystals in mammalian oocytes are still unknown.

In this project, I aim to identify the proteins that form these crystals and understand their role in oocyte and embryo development. To do this, I will isolate crystals from mouse ovaries and analyze their composition and structure using microcrystal electron diffraction, a technique that uses electron beams, similar to X-rays, to reveal the atomic arrangement of very small crystals. Next, I will study when these crystals form and how they change during oocyte and embryo development using advanced imaging techniques such as second harmonic generation microscopy, which highlights ordered structures such as these crystals without the need for additional labeling. To understand the role of these crystals, I will deplete the crystallizing protein in mouse oocytes and observe the effects on oocyte and embryo development. I hypothesize that protein crystallization may support development by serving as a storage compartment, regulating the activity of metabolic enzymes, or protecting the cell by packaging harmful metabolic by-products into compact crystals that isolate them from other cellular components. Finally, I will use cryo-ET to investigate whether similar crystals exist in human oocytes and whether mutations in crystallizing proteins are linked to early menopause or infertility.

This project will provide novel insights into the composition and function of protein crystals in oocytes. My findings will deepen our understanding of oocyte biology and could lead to advances in reproductive health and in vitro fertilization technologies. This project also has implications for the study of protein crystals in other cell types, including those associated with diseases such as asthma, cataracts, and muscle disorders, offering opportunities for their prevention.

Mesoscale and Microscale Organization in *C. elegans* embryo

Yuri Hong (Republic of Korea)
PhD Institute: Pohang University of Science and Technology, Republic of Korea
HFSP Cross-Disciplinary Fellowship at MPI of Molecular Cell Biology and Genetics, Dresden, Germany
Host Supervisor: Tony Hyman

Our cells are not just a jumble of molecules—they are highly organized environments where precise positioning and interactions are essential for proper function. Understanding how cells achieve this internal organization is one of the great challenges of biology. My project focuses on a key aspect of this process known as "polarity," which refers to the way cells establish distinct regions with different molecular compositions. This is crucial for many cellular activities, such as division, movement, and development. I am studying these processes in the tiny roundworm *Caenorhabditis elegans*. Despite its simplicity, this organism shares many biological mechanisms with humans, making it an ideal model for understanding fundamental aspects of cell biology. During early development, *C. elegans* embryos create a "polarity" that determines the future organization of cells. A protein called MEX-5 plays a central role in this process by forming two different regions within the cell: high concentration in the anterior (front) and low concentration in the posterior (back). This gradient is crucial for setting up the embryo's body plan and ultimately for the formation of specialized cells, including those that will become the germ cells, which give rise to eggs and sperm. MEX-5 does not work alone; it interacts with RNA molecules to form clusters of various sizes that move through the cell differently depending on where they are.

My project aims to explore how these MEX-5 clusters form, what controls their size and movement, and how these properties contribute to the establishment of polarity in the developing embryo. Using advanced imaging techniques, I will observe MEX-5 in live *C. elegans* embryos, tracking its distribution and behavior in real time. We will also create and analyze mutant versions of MEX-5 that have altered abilities to bind RNA, helping us understand how these interactions regulate the protein's behavior in living cells. I will also recreate MEX-5 clusters in a test tube to study their physical properties and interactions with RNA in a controlled setting. By combining these *in vivo* (in living organisms) and *in vitro* (in the lab) approaches, I aim to uncover the detailed mechanics of how these clusters form and function.

This project could have far-reaching implications. Understanding the principles of cellular organization at the molecular level could inform new strategies for treating diseases where cellular organization goes awry. Additionally, the techniques we develop for studying protein-RNA clusters could be applied to other biological systems, advancing our understanding of cell biology more broadly. This project is an exciting step forward in the quest to understand how cells build their internal landscapes and maintain order amidst the chaos of thousands of interacting molecules. Through this work, I hope to contribute to a deeper understanding of the fundamental principles that make life possible.

Mechanisms of translation reprogramming during embryonic diapause

Ida Jentoft (Norway)
PhD Institute: MPI for Multidisciplinary Sciences, Göttingen, Germany
HFSP Long-Term Fellowship at the Research Institute of Molecular Pathology, Vienna, Austria
Host Supervisor: Andrea Pauli

Animal life has evolved various strategies to survive and reproduce during periods of unfavourable conditions. One of them is embryonic diapause. Diapause is a reversible, dormant state in which development of a healthy embryo is paused awaiting reestablishment of a favourable environment. Although it has been described in a wide range of species, our mechanistic understanding of diapause remains poor. For example, diapause is associated with a reduction in protein synthesis, but it is not known how the protein synthesis machinery, the ribosomes, are temporarily rewired to support a prolonged dormant state. It is neither understood whether different cell types or tissues in the same organism adapt differently to diapause.

The main goal of this research project is to understand how regulation of protein synthesis and organization of proteins within the cell are rewired during diapause in the model organism *Nothobranchius furzeri*, the African Turquoise Killifish. Embryos of this fish species enter diapause in response to the periodic drying out of their habitats. The embryos survive the dry season in their dormant, developmentally arrested state and are ready to continue development once water returns to the pond. To study diapause-induced changes to protein synthesis, I will assess alterations to the ribosome itself, the factors that act on the ribosome, and the messenger RNA (mRNA) from which proteins are synthesized. I will also investigate changes in how proteins interact with each other during diapause. If proteins change conformation and interaction partners during diapause, this may change their activity and localization, ultimately influencing the state of the cell. A killifish embryo in diapause is composed of around 30,000 cells with different cell type identities that build different tissues. With such a heterogeneous composition of cells, it is likely that different tissues adopt slightly different responses when diapause is induced.

To test this hypothesis, I will analyze the proteins and mRNAs within single tissues and even single cells. If the hypothesis is correct, the changes that occur between active development and diapause differ between cell types. Understanding whether and how various tissues adopt a dormant state could have impacts far beyond the field of diapause and cellular dormancy. For example, cancer cells can enter a dormant state in which they are unresponsive to therapeutics. These dormant cells can later be activated and repopulate the tissue causing the tumor to reoccur. If the dormant state of the cell is related to the tissue in which it resides, then knowing the potential factors at play could be crucial in identifying new drug targets. Thus, the outcomes of this project hold promise for the discovery of novel and potentially universal regulators of diapause that control cellular and organismal dormancy.

Characterization of the human Notch-ligand synapse

Michael Currie (New Zealand (Aotearoa))
PhD Institute: University of Canterbury, New Zealand
HFSP Long-Term Fellowship at Harvard Medical School, Boston, USA
Host Supervisors: Stephen Blacklow and Tomas Kirchhausen

In the human body, tissues and organs are formed by the development of specialized structures made up of different types of cells. The cells need to adopt the desired cell identities for their functions (e.g. muscle or neuron) and need to know when to divide or die.

The goal of this project is to visualize a biological process called Notch signaling, which plays an essential role in human development by guiding many of these cell fate decisions. In normal Notch signaling, Delta or Jagged proteins on signal-sending cells bind to and pull on Notch proteins present on signal-receiving cells. By pulling on Notch, Delta or Jagged renders Notch susceptible to precise processing by molecular scissors. The processed Notch then enters the receiver cell nucleus, acting as an effector to stimulate changes in gene expression that specify cell fate. Aberrant Notch signaling, on the other hand, can result in cancer or other diseases. For example, mutations of the human Notch1 protein are causal in more than half of human T-cell acute lymphocytic leukemias. Mutations of human Notch2 or human Jagged1 cause a devastating developmental disorder called Alagille syndrome that is often lethal at an early age. The Delta and Notch molecules that perform Notch signaling are enriched on the cell surface at the sites of contact between signal-sending and receiving cells, so called “Notch synapses”. To better understand and see fine details of the interaction at the subcellular level requires the high magnification of electron microscopy.

This project thus aims to use electron microscopy to image synapses between Notch and Delta cells at a resolution that can discern the molecular interactions taking place. This will provide information on the arrangement of cell surface molecules and whether they cluster or use auxiliary systems for stability. This project will also study the role of the cytoskeleton in Notch signaling. The area directly inward from the synapse will be examined to determine the influence of the cell cytoskeleton in creating or maintaining synapses. Lastly, the project aims to move beyond single cell pair interactions to organoid models. Organoids are three-dimensional clusters of cells that can be formed in a laboratory, outside of a host. Under optimized conditions, they can be stimulated to mimic human tissues and even the full complexity of an organ. It is not yet known whether Notch synapses form in organoids, and if so, to which extent, as these cells have much more complex contacts with adjacent cells than the cell pairs.

This project thus aims to utilize three avenues of research to increase our understanding of the Notch synapse, ranging from the molecular level to the complexity of an organoid. Because Notch signaling is required for the development and function of many tissues and organs such as heart, brain, muscle, intestine, liver, or the immune system, the discoveries made in this project will have implications for many areas of human biology, including developmental biology and immunology, and also for the many diseases associated with aberrant Notch signaling, including cardiovascular disease and cancer.

Studying the structure and function of cortical lamination in the developing brain with MRI

Shir Filo (Israel)
PhD Institute: The Hebrew University of Jerusalem, Israel
HFSP Long-Term Fellowship at the MPI for Human Cognitive and Brain Sciences, Leipzig, Germany
Host Supervisors: Evgeniya Kirilina and Kalanit Grill-Spector

As a parent, there's nothing quite like the joy of watching your baby master a new skill. During the first year of life, a baby's brain undergoes extraordinary changes to support the rapid learning of new abilities. One of the most fascinating questions in neuroscience is how structure and molecular composition of the brain develop to support its complex functions. Some of the most profound structural changes occur in the cortex, the outer layer responsible for many cognitive functions. The cortex is organized into six distinct layers, each playing a specific role in processing information. These layers mature during development, and myelin and iron are playing crucial roles in this process. Myelin, which insulates nerve fibers, ensures efficient communication between different brain regions. Iron supports the production of energy required for brain function and contributes to myelin production.

In this project I will investigate how myelin and iron accumulate and distribute in the cortical layers of the infant brain during the critical period of the first years of life. For hundreds of years, research on myelin and iron in the brain was limited to post mortem studies with histological techniques such as microscopy, and studying molecular changes in the developing brain was impossible. I will design state of the art magnetic resonance imaging (MRI) techniques for studying myelin and iron dynamics non invasively in the brain of living infants. Compared to traditional weighted MRI, quantitative MRI (qMRI) techniques have revolutionized the field by providing biophysical parametric measurements of brain tissue that can be quantified in physical units and compared across subjects, sites, and time points. Unlike the images produced with weighted MRI, qMRI generates parametric brain maps that quantify physical tissue properties. As qMRI is extremely sensitive to the interaction of water molecules with their molecular environment, it can detect the statistics of the microstructure of brain tissue. I will develop novel biophysical qMRI models for encoding information on the iron and myelin composition in the cortex of infants. This will allow me to map the distribution of myelin and iron across different cortical layers and monitor their changes over the first years of life. This will help in understanding whether changes in these substances are specific to certain layers or regions, and how these changes influence brain development. I will also investigate the relationship between structural changes and functional brain networks, assessing how alterations in myelin and iron impact cognitive development and network formation.

This project will provide a deeper understanding of how myelin and iron contribute to functional brain development during infancy. These insights will address critical gaps in our knowledge of how structural changes in the brain support functional development.

Role of DNA topology in regulating early mammalian development

Jose Terron Bautista (Spain)
PhD Institute: University of Sevilla, Spain
HFSP Long-Term Fellowship at the Institute of Epigenetics and Stem Cells, Helmholtz Munich, Germany
Host Supervisor: Maria-Elena Torres-Padilla

Mammalian development requires highly precise control of gene expression in space and time, ensuring that each cell adopts their correct identity and function. This tight control of transcriptional programs begins with the embryonic genome activation (EGA). EGA is a critical step in early development following oocyte fertilization, in which the embryo undergoes dramatic epigenomic remodeling starting its first own transcription. EGA is commonly described as a burst of transcription throughout the genome, characterized by an initial wave in which the transcription of specific transposable elements (TEs) is crucial for embryo progression. These elements, which include sequences like Endogenous Retroviruses (ERVs) and Long Interspersed Nuclear Elements (LINEs), are embedded in our DNA due to evolutionary processes and their transcription, rather than the transcribed products, is essential for early development. Despite progress in understanding how TEs influence early development, the precise molecular mechanisms underlying TEs activation and the effect of this vast and unique transcriptional wave remain elusive. One intriguing aspect of TE function and EGA is the way early embryos deal with the topological stress that results from these transcriptional waves. Transcription generates topological stress in the DNA double-helix, leading to twists and turns known as DNA supercoiling, which have profound effects on any aspect of genome dynamics. DNA supercoiling has long been considered as a mere byproduct of transcription, but recent works suggest it plays an active role in controlling processes like 3D genome architecture or transcription process itself. How this specific DNA topology is established in early developmental stages or its influence on EGA remains unexplored.

In this project, I hypothesize that TE-derived supercoiling during EGA might provide the initial wave of DNA supercoiling in the embryonic genome, actively contributing to developmental complexity. This project will explore the contribution of DNA supercoiling and DNA topology in early embryo development. To test the my hypothesis, I will apply a range of cutting-edge methods to characterize and map DNA supercoiling in mouse embryo models from fertilization to blastocyst stage, with focus on EGA and TE dynamics (Aim 1). The project will generate maps of DNA supercoiling in a developmental process in vivo for the first time. I will also disrupt DNA supercoiling using the CRISPR-Cas technology during EGA to establish causality between DNA supercoiling and early developmental processes (Aim 2). While DNA supercoiling is well-established as a key regulator of transcriptional and replication programs in prokaryotes, its potential role as a regulatory mechanism in mammalian development remains unexplored. This project will address this question by identifying a potential connection between DNA topology and the regulation of transcriptional and epigenetic programs during early mammalian development, increasing our understanding of the mechanisms driving embryogenesis and early development.

06 Plants and their symbionts

Shedding light on rhodopsin-mediated microbial phototrophy at the single-cell level

Ariel Chazan (Israel)
PhD Institute: Technion - Institute of Technology, Israel
HFSP Long-Term Fellowship at Swiss Federal Institute of Technology Zürich, Switzerland
Host Supervisor: Roman Stocker

Sunlight is a crucial energy source that drives the functioning of aquatic environments. At the core of these ecosystems are phototrophic microbes—tiny organisms that "capture" sunlight and convert it into biochemical energy to support their metabolic needs. This vital process, known as light harvesting, is central to aquatic food webs, enabling microbes to funnel energy into the microbial community. Phototrophic microbes use specialized protein complexes to absorb light energy, initiating a series of chemical reactions that culminate in the production of adenosine tri-phosphate (ATP), a molecule commonly referred to as the universal energy currency of most organisms. Only two types of protein complexes are known to govern this capture of sunlight energy by microbes. One major group of microbes uses a form of chlorophyll to perform photosynthesis in a manner similar to plants. This process is well understood and plays a significant role in shaping microbial communities. However, during the past two decades, discoveries hint at another significant player in these light-harvesting processes: rhodopsin-bearing microbes. These microbes use the rhodopsin protein to pump protons (H+) across their membrane to generate a proton gradient, which is used to produce ATP molecules. Rhodopsin-bearing microbes are tremendously abundant in aquatic environments and can constitute more than half of the microbial population in marine and freshwater ecosystems. They may therefore represent a major source of energy entering microbial communities. However, due to a lack of sensitive methods to measure light harvesting mediated by rhodopsins, we know very little about their ecological contribution. Understanding how much light is captured by rhodopsin-bearing microbes will allow us to measure their ecological impact and offer insights into their roles in the flow of energy and elements in aquatic environments.

This project is dedicated to developing tools to develop innovative measurement techniques to investigate the contribution and impact of rhodopsin-bearing microbes to microbial light-energy acquisition. We will develop cutting-edge technology to measure light-harvesting at the single microbe level, and to sort those microbes for identification and further analysis. This project will result in a deeper understanding of the fundamental process of light harvesting and its impact on aquatic microbial populations by bringing the ecological contribution of rhodopsin-bearing microbes to light harvesting into the scientific spotlight. By uncovering their ecological significance and providing novel tools to measure their impact, this research holds the potential to make a significant contribution to our understanding of microbial ecosystems.

Artificial selection and the rapid evolution of a plant-viral mutualism

Jason Chen (USA)
PhD Institute: Emory University, USA
HFSP Long-Term Fellowship at Netherlands Institute of Ecology, Wageningen, Netherlands
Host Supervisor: Mark Zwart

In Darwin's tangled bank, organisms of different species make their living not only by exploiting, but also by cooperating with each other. Many species interactions are ecologically specialized, with partners engaging in cooperative and exploitative relationships with just a few other species, and evolving remarkable adaptations which they rely on to maintain those associations. However, these specialized interactions can also evolve in different ways, with parasitic interactions evolving into mutualistic interactions and vice versa, sometimes with surprising rapidity. This is particularly common in host-microbe interactions, in which microbes can rapidly evolve to become either pathogenic or beneficial for plants and animals. In the early 17th century, parts of Dutch society were transfixed by "tulip mania", a cultural and financial craze over this exotic bulb that had been recently imported from the Ottoman empire. Driving this fad, in part, were tulips that spontaneously and unpredictably sported delicately feathered, multicolored streaks and spots in their flowers, which could not be inherited by seed and was associated with a gradual decline in plant vigor, making the plants that developed these traits particularly rare and valuable. Today, we know this phenomenon, known as color breaking, is a symptom of infection with a plant virus. Though viral infections weaken tulips and are often fatal, a few cultivars dating back as early as the era of tulip mania survive to this day: They harbor the virus, but nonetheless continue to be cultivated and asexually propagated as rare curiosities for their color-broken flowers. The careful maintenance of these cultivars coexisting with the virus living inside their tissues thus constitutes a possible artificial selection experiment on the evolution of viral mutualism, commencing centuries before viruses were even known to science.

In this project I ask whether surviving color-broken tulips harbor viral mutualists that rapidly evolved during tulip domestication and breeding in Europe, and examine the genomic and ecological mechanisms underpinning viral mutualism. To do so, I will combine multiple approaches, ranging from the reconstruction of tulip virus evolution to the introduction of mutations into engineered tulip virus genomes. My research will address a fundamental question on the emergence of novel host-microbe mutualisms, which has consequences for our understanding of the ecological role of viruses in natural populations, and more broadly the evolutionary flexibility of host-microbe interactions. Beyond its importance for understanding how we can manipulate viruses to benefit agriculture and horticulture in a model organism of commercial & cultural value, my work at the interface of biology and history, will also illustrate the role of evolutionary phenomena in shaping human history and culture.

Phyto-Umwelt: Decoding the multisensory world of plants

Noori Choi (Republic of Korea)
PhD Institute: University of Nebraska-Lincoln, USA
HFSP Long-Term Fellowship at University of Canterbury, New Zealand (Aotearoa)
Host Supervisors: Ximena Nelson and Lloyd Stringer

Plants are often thought of as stationary and less responsive than animals, but recent research reveals they are much more perceptive than previously believed. Plants have a sophisticated way of sensing their perceptual world—"phyto-umwelt." In the phyto-umwelt, plants can detect and react to a variety of signals, such as smells, sounds, and vibrations, which help them interact with and adapt to fluctuating environments in complex ways.

This project focuses on understanding how plants perceive and respond to different and complex sensations, using apple trees as study system. I will examine how apple trees react to environmental changes such as attacks from herbivores, by integrating information from sensory inputs including chemical signals released by nearby plants, vibrations caused by insects, and other stimuli in their phyto-umwelt. By studying these responses, the project aims to uncover how plants have developed these sensory abilities and how they use them to adapt and survive. The research will begin with data collection on various sensory inputs in apple orchards. For example, plants and insects release chemicals called volatile organic compounds into the air and soil, which can signal different conditions or threats. I will also record environmental sounds and vibrations from the environment and nearby insects. By analyzing these data, I will investigate what apple trees experience in their phyto-umwelt and how the different signals, for instance buzzing sounds and insect-released chemicals interact. Laboratory experiments will investigate how apple saplings respond to these stimuli, using advanced molecular techniques to observe their reactions at the cellular level. In particular, I will investigate whether and how a plant's response differs between exposure to single versus combined sensory inputs. Saplings may show faster or more specific responses to a combination of signals from herbivorous insects than to just one signal alone. In the next phase, I will test whether a plant's ability to sense multiple signals is influenced by its environment, comparing wild and domesticated apple trees. It has been debated whether domestication weakens plant defenses. It is possible that domesticated plants, living in controlled environments, have specialized in responding to fewer types of stimuli, potentially losing their ability to handle a broader range of sensory events such as invasive insects. To study this question, I will expose apple trees both in natural and controlled environments to familiar and new stimuli and study how they react. By comparing their responses to familiar and new signals, this research will shed light on how plants adapt their sensory systems over time, especially in environments shaped by humans.

Understanding how plants process sensory information without a centralized nervous system, might offer new insights into information processing in technology and it could lead to new strategies for sustainable agriculture by improving plant resistance to pests and environmental stressors.

Decoding GPCR signaling in insect physiology and interspecies conflict

Caroline Martin (USA)
PhD Institute: Massachusetts Institute of Technology, USA
HFSP Long-Term Fellowship at the University of Copenhagen, Denmark
Host Supervisors: Alexander Hauser and Staffan Persson

Plants and insects have coevolved for millennia, and their relationship is defined by opposing interactions: many insects are herbivourus, but pollinating insects are necessary for reproduction for many plant species. Sophisticated molecular mechanisms have evolved on both sides. For example, insects are attracted to plants by volatile compounds and deterred by defense proteins released by wounded plant cells. This complex relationship, which can be described as both an arms race and pact for mutual reproduction, may contribute to the great diversity observed in plant and insect clades. While plant-insect interactions have shaped much of the terrestrial world, only a small number of the molecular mechanisms mediating this exchange have been elucidated. As a result, there is not enough data to establish general principles of plant-insect coevolution.

I believe that evolutionary genomics together with new experimental and computational tools for predicting protein-protein interactions in high throughput will help illuminate some of these principles. I hypothesize that plant-derived peptides are important signaling conduits in plant-insect interactions, and that both plant and insect species have receptors for these signals. Plant-derived peptides might, for instance, serve defensive roles by interacting with receptors in insects or modulate plant immunity in response to insect herbivore attack. In this project, I will focus on the molecular dialogue between the flowering plants and Lepidoptera (butterflies and moths). These groups are exemplary of the dualism of plant-insect interactions: Lepidopteran larvae are herbivorous, while Lepidopteran adults are pollinators. To clarify the role of peptide signaling in plant response to Lepidopteran herbivory, I will computationally match plant peptides with plant and insect receptors using AI tools, and then test experimentally whether predicted peptide-receptor pairs cause receptor activation.

The identification of new axes of interspecies communication and plant immune activation may have far-reaching implications for the evolution of ecosystems. While plant peptides are appreciated for their roles in plant physiology and defense, the full repertoire of proteins that transduce peptide signals into cellular responses is unknown. A group of intracellular proteins in plants, the extra-large G proteins, likely play a role in peptide signal transduction, but it is unclear which cell surface receptors they interact with. I will use a new method for detecting the “interactome” of proteins to identify these receptors. These experiments will reveal how G protein signaling functions in plants and highlight their distinct evolutionary trajectories from animal G proteins.

Overall, this study aims to uncover new avenues of interspecies communication, as well as the fundamental mechanisms of plant-specific signal transduction pathways. This research has implications for plant immune activation and interspecies coevolution, which may provide a basis for new approaches to sustainable agriculture and underlines the interconnectivity of our living planet.

The dynamic regulation of coral-dinoflagellate symbiosis by protein glycosylation

Fabian Ruperti (Germany)
PhD Institute: EMBL and University of Heidelberg, Germany
HFSP Long-Term Fellowship at the University of Queensland, Brisbane, Australia
Host Supervisors: Benjamin Schulz and Cheong Xin Chan

Coral reefs are one of the most biologically diverse ecosystems worldwide. They are home to about one third of all known marine species and sustain livelihoods of over 1 billion people through fisheries, tourism and more. However, they are increasingly threatened by climate change, leading to significant ecological, economic, and societal problems. In particular, ocean warming disrupts the essential yet vulnerable symbiotic relationship between corals and small, photosynthetic algae called dinoflagellate. Living inside coral tissues, they exchange essential nutrients with the coral while receiving safe harbour. This “coral bleaching” prevents the transfer of key nutrients, often resulting in the death of the host and eventually the collapse of the dependent ecosystem.

My project aims to deepen our understanding of this essential partnership between corals and dinoflagellates at a molecular level. To do so, I will focus on protein glycosylation, a biochemical mechanism in which sugars attach to proteins and influence their properties and functions. I hypothesise that protein glycosylation plays a holistic role in reef coral symbiosis, however, due to its complexity, has thus far evaded detailed investigations. To address this, I will leverage novel technological approaches to identify, track and quantify dynamic protein glycosylation features that occur during the different stages of symbiosis lifetime—from the initial recognition between corals and symbionts to the maintenance and finally breakdown of this partnership during bleaching events. I will examine how symbiosis progression is affected by these changes and how they might serve as a “switch”, indicating successful symbiosis establishment. These experiments will be conducted in laboratory settings on the anemone Aiptasia, a model organism for coral symbiosis. To assess whether the findings are of ecological relevance, I will compare them to Great Barrier Reef coral samples curated by the Reef Restoration and Adaptation Program (RRAP) during natural bleaching events. These samples will offer an unprecedented view into the environmental reality of corals in the Great Barrier Reef.

My research will provide critical insights into the molecular foundations of coral symbiosis biology and will reveal new strategies to protect and restore reefs, thereby addressing an urgent environmental problem of global importance. Efforts to engineer bleaching-resistant corals or dinoflagellates could be advanced and innovative approaches, e.g. promoting efficient re-establishment of symbiosis, could be developed. Beyond these direct implications, the results of this project will have a translatable impact on other areas of science, including the symbiotic human microbiome, central to human health.

Integrating symbiosis and immunity: uncovering new signaling pathways in plant-microbe interactions

Yerisf Carla Torres Ascurra (Peru)
PhD Institute: Wageningen University, Netherlands
HFSP Long-Term Fellowship at the Salk Institute for Biological Studies, San Diego, USA
Host Supervisors: Lena Müller and Tony Hunter

All living organisms, including plants, are in constant contact with a myriad of microbes, and must respond appropriately to avoid diseases. While promoting beneficial partnerships, they must prevent pathogenic associations.

This project aims to explore this delicate equilibrium using the symbiosis of the plant *Medicago truncatula* and arbuscular mycorrhizal (AM) fungus *Rhizophagus irregularis* as a model. AM fungi form a vital partnership with most land plants. Plants provide organic carbon to the fungus, and fungi supply essential minerals like phosphorus and nitrogen to the plant. This partnership not only boosts plant growth but also helps plants to thrive under adverse environmental conditions. For successful AM fungus engagement, plants must initiate symbiosis signaling that helps form a beneficial partnership while also preventing them from pathogen attack. Once AM symbiosis is established, plants switch their immune system back on, allowing them to defend themselves against pathogen attack without disrupting the beneficial fungus.

How plants perceive multiple inputs, “decide” and transduce specific signals to trigger appropriate responses, is largely unknown. I aim to uncover new signaling pathways by which plants modulate their responses to beneficial and pathogenic microbes. Recent studies have shown that plants control AM symbiosis through small signaling molecules, CLE peptides, that regulate growth and development, and their receptors including CRN. Symbiotic AM fungi and parasitic nematodes produce CLE-like peptides to manipulate plant signaling to their advantage. However, CLE-like peptides from other pathogens remain elusive. Our data suggest that CRN is a key player in symbiosis and defense, but we do not know how CRN specifically responds to different CLE peptides.

In this project, I aim to first identify and characterize CLE peptides from both plants and microbes that are involved in the interplay of symbiosis and immunity. Using bioinformatics, I will mine genomes and proteomes of pathogens to identify their CLE-like peptides and study their role during AM symbiosis and during infection by pathogens. Second, I will examine how the CRN protein interacts with these CLE peptides. I will use advanced biochemical techniques to map CRN interactors and identify novel signaling pathways that mediate the interplay of beneficial and pathogenic interactions.

The project aims to elucidate the molecular mechanisms underlying plant-microbe interactions and identify new targets for engineering crops with enhanced disease resistance and symbiotic efficiency. This will lay the groundwork for the creation of crops that are more efficient in forming beneficial symbiotic relationships and fighting against pathogens. Such advances will not only enhance agricultural productivity but also contribute to environmental sustainability by reducing the need for fertilizer or pesticide inputs.

Exploring the evolution and optimization of the auxin signaling pathway

Gil Wiseglass (Israel)
PhD Institute: Tel Aviv University, Israel
HFSP Long-Term Fellowship at Wageningen University, Netherlands
Host Supervisor: Dolf Weijers

Plants originated in aquatic environments, where survival depended on the constant availability of water and nutrients. The move to land was a monumental leap in evolution, requiring plants to develop a series of adaptations that allowed them to survive and thrive in drier, more variable environments. These adaptations included structures to retain water, anchor themselves in soil, and efficiently transport nutrients throughout their bodies.

A key player in this evolutionary success is auxin, a plant hormone that regulates growth, development, and environmental responses. Auxin enables plants to bend toward light, grow roots, and respond to stress. The nuclear auxin response pathway (NAP) functions as a communication channel within the cell nucleus, relaying auxin's instructions to the rest of the plant and triggering specific actions. As plants evolved from simple ancestors to the diverse species we see today, the NAP also evolved. In ancient plants, this pathway was relatively straightforward, involving only a few components. In more advanced plants like flowering species, the pathway has become highly intricate, with numerous specialized interacting parts. This complexity allows plants to fine-tune their growth and development in response to a wide range of environmental cues, aiding their adaptation to changing habitats. Despite our growing understanding of auxin's role in plant biology, a crucial question remains: How did the NAP evolve from a simple system in early plants to the complex network found in today's land species?

To explore this, my project will use two plant models representing different stages of this evolutionary journey: *Marchantia polymorpha*, a simple liverwort, and *Ceratopteris richardii*, a more complex fern. In *Marchantia*, I will introduce new components into its simple NAP to observe how added complexity affects the plant's response to auxin, shedding light on the early steps in the pathway's evolution. In *Ceratopteris*, I will simplify its more complex NAP by removing specific components. By studying how these changes impact the fern's growth and development, we can understand how the pathway's complexity enhances its functionality.

The outcomes of this research could have far-reaching implications. By unraveling how plants evolved sophisticated control over their growth and development, we may gain insights that help improve crop resilience—an urgent need as climate change threatens global food security. Understanding how plants naturally adapt to diverse environments could inform strategies to develop crops better equipped to withstand stress, to ensure a stable food supply for the future.

Index

By nationality of researcher, host institutions and countries given after each name

Australia

Bangladesh

Belgium

Brazil

Canada

China

Egypt

France

Germany

Ghana

Hong Kong, China

India

Israel

Italy

Japan

Republic of Korea

Lithuania

Netherlands

New Zealand (Aotearoa)

Norway

Peru

Romania

Spain

UK

USA

Acknowledgements

HFSPO is grateful for the support of its Management Supporting Parties and other organizations (*):

Australia
National Health and Medical Research Council (NHMRC)

Canada
Canadian Institutes of Health Research (CIHR)
Natural Sciences and Engineering Research Council (NSERC)

European Commission
Directorate-General for Research and Innovation (DG RTD)

France
Ministry of Higher Education, Research and Innovation (MESRI)
Strasbourg Eurométropole*
Région Grand Est*

Germany
Federal Ministry of Education and Research (BMBF)
German Research Foundation (DFG)*

India
Department of Biotechnology (DBT), Ministry of Science and Technology

Israel
Ministry of Science and Technology

Italy
Ministry of Education, University and Research
National Research Council of Italy (CNR)*

Japan
Japan Agency for Medical Research and Development (AMED)
Ministry of Economy, Trade and Industry (METI)
Ministry of Education, Culture, Sports, Science and Technology (MEXT)

Republic of Korea
Ministry of Science and ICT

New Zealand
Ministry of Business, Innovation and Employment
Royal Society Te Apārangi*

Norway
Research Council of Norway

Singapore
National Research Foundation, Singapore (NRF)
Agency for Science, Technology and Research (A*STAR)*
National University of Singapore (NUS)*
Nanyang Technological University (NTU)*

South Africa
National Research Foundation
South African Medical Research Council

Switzerland
Swiss National Science Foundation (SNF)

United Kingdom of Great Britain and Northern Ireland
UKRI-Biotechnology and Biological Sciences Research Council (BBSRC)
UKRI-Medical Research Council (MRC)

United States of America
National Institutes of Health (NIH)
National Science Foundation (NSF)

International Human Frontier Science Program Organization (HFSPO)
12 quai Saint Jean
67000 Strasbourg, France
e-mail: info@hfsp.org
Website: www.hfsp.org