



European Research Council
Executive Agency

Established by the European Commission

ERC Implementing Arrangements Call for Expression of Interest 2019



European Research Council
Executive Agency

Established by the European Commission

Project ID:

759661

Project Acronym:

SPOCKS MS

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr CHARLOTTE UETRECHT**

Host Institution: HEINRICH-PETTE INSTITUT LEIBNIZ INSTITUT FUER EXPERIMENTELLE
VIROLOGIE - DE

Sampling Protein cOMplex Conformational Space with native top down Mass Spectrometry

The main question to be addressed by SPOCK'S MS is how protein complex conformation adapts to local changes, such as processing of polyproteins, protein phosphorylation or conversion of substrates. While labelling strategies combined with mass spectrometry (MS), such as hydrogen deuterium exchange and hydroxyl footprinting, are very versatile in studying protein structure, these techniques are employed on bulk samples averaging over all species present. SPOCK'S MS will remedy these by studying the footprinting and therefore exposed surface area on conformation and mass selected species. Labelling still happens in solution avoiding gas phase associated artefacts. The labelling positions are then read out using newly developed top-down MS technology. Ultra-violet and free-electron lasers will be employed to fragment the protein complexes in the gas phase. In order to achieve the highest possible sequence and thus structural coverage, lasers will be complemented by additional dissociation and separation stages to allow MS^N. SPOCK'S MS will allow sampling conformational space of proteins and protein complexes and especially report about the transient nature of protein interfaces. Constraints derived in MS will be fed into a dedicated software pipeline to derive atomistic models. SPOCK'S MS will be used to study intracellular viral protein complexes, especially coronaviral replication/transcription complexes, which are highly flexible and often resist crystallisation and are barely accessible by conventional structural biology techniques.

Objectives:

- Integrate labelling with complex species selective native MS for time-resolved structural studies
 - Combine fragmentation techniques to maximise information content from MS
 - Develop software suite to analyse data and model protein complex structures based on MS constraints
 - Apply SPOCK'S MS to protein complexes of human pathogenic viruses
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Link to the ERC project webpage:

Keywords of the ERC project: structural mass spectrometry, structural virology, coronavirus, soft X-rays

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
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Project ID:

789267

Project Acronym:

REPLICHROMA

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr NYNKE DEKKER**

Host Institution: **TECHNISCHE UNIVERSITEIT DELFT - NL**

Eukaryotic DNA replication: a single-molecule approach to the study of yeast replication on chromatin

DNA replication is essential to cellular function. During a lifetime, each of us synthesizes a light-year's length of DNA, but this process is so robust that few of us will develop cancer. In eukaryotes, DNA is packed into chromatin, a hierarchical DNA-protein assembly of which the nucleosome forms the basic unit. Chromatin replication convolves DNA replication with the duplication and reassembly of all DNA-associated proteins. Understanding the coupling between these processes has fundamental implications for epigenetic inheritance and cancer.

The goal of this proposal is to gain spatiotemporal insight into chromatin replication by using our biophysical expertise in replication and chromosomal dynamics to build up a mechanistic timeline of the process. We will harness recent advances in the reconstitution of the yeast replisome alongside our novel, high-throughput single-molecule approach to visualize and quantify the collaboration between a single yeast replisome and the histone chaperones to achieve chromatin replication. We will:

- Monitor the assembly of the replisome on chromatin and visualize how nucleosomes impact its progression.
- Quantify how the replisome and histone chaperones disrupt nucleosomes and retain histones for further processing.
- Detect the deposition of newly synthesized histones behind the replisome and reveal the interactions between replisome components and histone chaperones that couple replication to nucleosome assembly.
- Report on the phenomenon of epigenetic inheritance by imaging histone recycling between parental and daughter DNA. We will examine its timing and efficiency, the conformations of reassembled nucleosomes, and any preferential recycling to either daughter DNA.

This proposal places us in a unique position to make major contributions to the field of chromatin replication, and to provide the field with a powerful tool to investigate topics from fundamental questions in molecular biology to the performance of new cancer drugs.

Link to the ERC project webpage: <http://nynkedekkerlab.tudelft.nl>

Keywords of the ERC project: DNA replication, eukaryotic replication, yeast replication, chromatin replication, histones, single-molecule fluorescence, single-molecule studies

Keywords that characterize the scientific profile of the potential visiting researcher/s: DNA replication, chromatin, biochemistry, biophysics



European Research Council
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Established by the European Commission

Project ID:

805230

Project Acronym:

ORGASOME

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr ALEXEY AMUNTS**

Host Institution: **STOCKHOLMS UNIVERSITET - SE**

Protein synthesis in organelles

Protein synthesis in mitochondria is essential for the bioenergetics, whereas its counterpart in chloroplasts is responsible for the synthesis of the core proteins that ultimately converts sunlight into the chemical energy that produces oxygen and organic matter. Recent insights into the mito- and chlororibosomes have provided the first glimpses into the distinct and specialized machineries that involved in synthesizing almost exclusively hydrophobic membrane proteins. Our findings showed: 1) mitoribosomes have different exit tunnels, intrinsic GTPase in the head of the small subunit, tRNA-Val incorporated into the central protuberance; 2) chlororibosomes have divaricate tunnels; 3) ribosomes from both organelles exhibit parallel evolution. This allows contemplation of questions regarding the next level of complexity: How these ribosomes work and evolve? How the ribosomal components imported from cytosol are assembled with the organellar rRNA into a functional unit being matured in different compartments in organelles? Which trans-factors are involved in this process? How the chlororibosomal activity is spatiotemporally coupled to the synthesis and incorporation of functionally essential pigments? What are the specific regulatory mechanisms?

To address these questions, there is a need to first to characterize the process of translation in organelles on the structural level. To reveal molecular mechanisms of action, we will use antibiotics and mutants for pausing in different stages. To reconstitute the assembly, we will systematically pull-down pre-ribosomes and combine single particle with tomography to put the dynamic process in the context of the whole organelle. To understand co-translational operations, we will stall ribosomes and characterize their partner factors. To elucidate the evolution, we will analyze samples from different species.

Taken together, this will provide fundamental insights into the structural and functional dynamics of organelles.

Link to the ERC project webpage:

Keywords of the ERC project: cryo-EM, ribosome, ATP synthase, membrane proteins, mitochondria, chloroplast, photosystem

Keywords that characterize the scientific profile of the potential visiting researcher/s: cryo-EM



European Research Council
Executive Agency

Established by the European Commission

Project ID:

851564

Project Acronym:

EpiRep

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr FRANCESCA MATTIROLI**

Host Institution: **KONINKLIJKE NEDERLANDSE AKADEMIE VAN WETENSCHAPPEN - KNAW - NL**

Mechanism of nucleosome assembly during DNA replication

Proper inheritance of the epigenetic information during cell division controls cell fate decisions, tissues homeostasis and development, ensuring disease avoidance. We have little understanding however of the mechanisms by which epigenetic information, specifically histone post-translational modifications in nucleosomes, are replicated in parallel to the DNA prior to cell division. This process strictly depends on proper nucleosome formation on the newly synthesized DNA strands. Here, I will study the molecular mechanism of nucleosome assembly during DNA replication. Nucleosome dynamics during DNA replication is controlled by an interconnected network of histone chaperones that converges on the key Chromatin Assembly Factor 1 (CAF-1). I recently elucidated the molecular mechanism of CAF-1-mediated nucleosome assembly, in absence of any other replication components. I developed a quantitative (NAQ) assay that allows, for the first time, the quantification of nucleosome assembly activity in vitro. In cells, CAF-1 is recruited to replication forks by the DNA polymerase processivity factor PCNA. Here, I will capitalize and expand on the assays above to integrate structural data, quantitative biochemical and biophysical measurements, and functional analyses, to elucidate how CAF-1 crosstalks to PCNA, DNA polymerases and other components of the DNA replication machinery in S phase. Specifically, the proposed research will 1) uncover how CAF-1 recruitment by PCNA affects its function in nucleosome assembly, and 2) examine how CAF-1 activity is regulated during ongoing DNA replication. This work will reveal the mechanism of nucleosome assembly during DNA replication and its interplay with S phase signaling. A mechanistic understanding of this pathway will uncover the fundamental principles that control genome and epigenome stability, thus cell fate decisions and disease avoidance.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
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Project ID:

852915

Project Acronym:

CRYTOCOP

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr GIULIA ZANETTI**

Host Institution: **BIRKBECK COLLEGE - UNIVERSITY OF LONDON - UK**

Coat assembly and membrane remodelling: understanding regulation of protein secretion

Eukaryotic cells are organised in membrane-bound compartments, which have defined chemical identities and carry out specific essential functions. Exchange of material between these compartments is necessary to maintain cell functionality, and is achieved in a highly specific and regulated manner by vesicular transport. To mediate protein trafficking, coat complexes assemble on membranes and couple bilayer deformation with cargo capture into transport carriers. How coat assembly can deliver the flexibility necessary to accommodate a wide variety of cargo proteins, and how the process can be regulated, are outstanding questions in the field. This is exemplified by the COPII coat, which mediates export from the ER of about a third of newly synthesized proteins. COPII assembles into two concentric layers and can form transport carriers of a variety of shapes and sizes, including tubules and spherical vesicles. This is important for export of large cargoes and is a process targeted by cargo-specific regulatory factors. The aim of this project proposal is to shed light on the molecular interactions between coat components, and understand their role in determination of coat architecture and membrane shape. We will use a combination of structural and functional approaches to characterise COPII coat assembly, and its relationship with membranes in systems of increasing complexity, ranging from in vitro reconstitutions to cells. In particular, we will use cryo-electron tomography and subtomogram averaging to understand the architecture of the coat layers in these systems. These are fast-developing techniques that uniquely target complex structures while achieving high resolutions. With my lab at the forefront of current advances, we are perfectly placed to obtain a complete view of the COPII coat assembled on membranes. Our research will answer outstanding questions in the membrane trafficking field and open new perspectives to tackle ill-characterised regulation systems.

Link to the ERC project webpage: <http://www.zanettilab.co.uk>

Keywords of the ERC project: cryo-EM, cryo-tomography, subtomogram averaging, coat proteins, COPII, membrane trafficking

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
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Project ID:

715024

Project Acronym:

RAPID

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr SIMON ELSÄSSER**

Host Institution: **KAROLINSKA INSTITUTET - SE**

Chromatin dynamics resolved by rapid protein labeling and bioorthogonal capture

Histone proteins provide a dynamic packaging system for the eukaryotic genome. Chromatin integrates a multitude of signals to control gene expression, only some of which have the propensity to be maintained through replication and cell division. For our understanding of cellular memory and epigenetic inheritance we need to know what features characterize a stable, heritable chromatin state throughout the cell cycle. State-of-the-art methods such as ChIP-Seq provide population-based snapshots of the epigenomic landscape but little information on the stability and relative importance of each studied feature or modification. This project pioneers a rapid, sensitive and selective protein labeling method (termed RAPID) for capturing genome-wide chromatin dynamics resolved over a period of time ranging from minutes to days. RAPID introduces a flexible time dimension in the form of pulse or pulse-chase experiments for studying genome-wide occupancy of a protein of interest by next-gen sequencing. It can also be coupled to other readouts such as mass spectrometry or microscopy. RAPID is uniquely suited for studying cell cycle-linked processes, by defining when and where stable 'marks' are set in chromatin. I will employ mouse embryonic stem cell (mESC) as a model system for pluripotency and lineage specification. RAPID will define fundamental rules for inheritance of histone and other chromatin-associated proteins and how they are modulated by the fast cell cycle of pluripotent cells. Using RAPID in combination with other state-of-the art genetics and epigenomics, I will collect multi-dimensional descriptions of the dynamic evolution and propagation of functionally relevant chromatin states, such as interstitial heterochromatin and developmentally regulated Polycomb domains.

Link to the ERC project webpage: <http://www.elsaesserlab.org>

Keywords of the ERC project: Chromatin, Epigenetics, Stem Cells

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
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Project ID:

759120

Project Acronym:

TransTryp

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr YASER HASHEM**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Structural differences in mRNA translation machineries between eukaryotic pathogens and their mammalian hosts

mRNA translation consists on translating the genetic code to proteins by the ribosome that is universally conserved in all cells. However, its structure presents significant differences between bacteria and eukaryotes. Partly because of these differences, the bacterial ribosome can be targeted specifically by a number of antibiotics without affecting the eukaryotic host cells. However, the conservation of the ribosome among eukaryotes complicates the search for specific drugs against eukaryotic pathogens such as certain protozoa like plasmodium and kinetoplastids.

Our work along with other studies demonstrates the existence of significant structural differences between ribosomes of protozoa and mammals. Using Cryogenic electron microscopy, we endeavor to investigate such structural differences that are anticipated to affect some of the vital steps of mRNA translation, especially the initiation process, because of their position on the ribosome. 1. Thus we will focus on the structural differences in translation initiation between kinetoplastids and their mammalian hosts (i) by characterizing initiation complexes from several plasmodium and kinetoplastids species and compare them to their mammalian counterparts. (ii) We will also follow up on our previous works in solving the structures of various conventional, but also unconventional mammalian initiation complexes, in interaction with special mRNAs. 2. We will focus on the structure of protozoa-specific features characterized from elongating ribosomal complexes and (i) attempt to fish for regulators that they interact with from cell extracts. In addition, (ii) we will investigate the ribosomal structures from plasmodium at different stages of the parasite life cycle, as they vary according to the latter.

Our results will significantly advance our understanding of protein synthesis regulation in protozoa and will represent a promising step in the search for more efficient treatments against these eukaryotic pathogens

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

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Project ID:

820187

Project Acronym:

EXCHANGE

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr DAVID DREW**

Host Institution: **STOCKHOLMS UNIVERSITET - SE**

Dynamic Complexes and Allosteric Regulation of Small Molecule Transporters

Solute Carrier (SLC) transporters mediate the translocation of substrates across membranes and after GPCRs represent the second-largest fraction of the human membrane proteome. SLC transporters are critical to cell homeostasis, which is reflected in the fact that more than a quarter is associated with Mendelian disease. Despite a few exceptions, however, they have been under-utilized as drug targets and most of the mechanistic understanding has been derived from bacterial homologues of these medically important proteins. In addition to subtle differences, bacterial homologues will not enable us to establish how the activities of many SLC transporters are allosterically regulated through the binding of accessory factors, e.g., hormones, to their non-membranous globular domains. Understanding the mechanisms by which their activities can be allosterically regulated through these complex and dynamic assemblies is critical to human physiology and important for future drug design.

Our model system is a family of transporters known as sodium/proton exchangers (NHEs), which exchange sodium for protons across membranes to aid many fundamental processes in the cell. NHEs are important to the cell cycle, cell proliferation, cell migration and vesicle trafficking and are associated with a wide-spectrum of diseases. Their diverse portfolio is connected to the importance of pH homeostasis, and the binding of many different factors to a large, globular cytosolic domain exquisitely regulates them. To date, we have no structural information for any of the NHE's, functional assays in liposomes are lacking, and many interaction partners are yet to be validated by in vitro studies. Determining the structure, dynamics, and allosteric regulation of NHEs will be an enormous challenge. However, we envisage that by achieving our objectives, we will reveal important mechanistic insights relevant not just to NHEs, but to many types of SLC transporters.

Link to the ERC project webpage:

Keywords of the ERC project: membrane protein, transporter, cryo EM, kinetics

Keywords that characterize the scientific profile of the potential visiting researcher/s: enzymologist, cell biologist, nanobody-screening



European Research Council
Executive Agency

Established by the European Commission

Project ID:

834394

Project Acronym:

TENDO

Evaluation Panel:

LS1

Molecular and Structural
Biology and Biochemistry

Principal Investigator: **Dr ROBBIE LOEWITH**

Host Institution: **UNIVERSITE DE GENEVE - CH**

Tension of ENDOMembranes maintained by TORC1

The target of the bacterial macrolide rapamycin, TOR, is a ser/thr protein kinase that assembles into two distinct protein complexes, conserved from yeast to human, we named TORC1 and TORC2. TORC1 is directly bound and inhibited by rapamycin and studies with rapamycin have revealed that TORC1 plays a central role in coupling nutrient cues to biomass synthesis and turnover. The lack of a specific inhibitor for TORC2 has made the study of this complex much more challenging. We overcame this challenge by solving the structure of yeast TORC2 which revealed why it is insensitive to rapamycin and enabled us to create a rapamycin-sensitive TORC2 variant. We also developed two small molecules, one that dissipates plasma membrane (PM) tension and the other that serves as a biosensor of PM tension. With this suite of chemical-biology tools we confirmed that TORC2 functions in a mechanotransduction pathway to maintain tension homeostasis of the PM. Concurrently, solving the structure of TORC1 revealed that its activity is regulated via assembly into a huge, inactive helix which we named a TOROID – TORC1 Organized in an Inactive Domain. In this grant, we ask if these major advances are transferable; i.e. can lessons learned regarding TORC2 be applied to TORC1, and vice versa? Our major aim is to determine if and how TORC1 regulates vacuolar membrane (VM) tension. To this end, we will develop novel chemical probes to monitor VM tension and we will use genetic screens, quantitative phosphoproteomics, in vitro assays, high-throughput compound screens, STORM and FRAP imaging, and state-of-the-art cryo-EM to learn how TORC1 senses and regulates VM tension. Our other aim, prompted by our TOROID discovery, is to solve the TOROID-like structure that TORC2 forms upon glucose depletion. This work will reveal new mechanisms in growth control, and details in TORC1 and TORC2 regulation that may inform future therapeutic interventions for these medically relevant signalling complexes.

Link to the ERC project webpage:

Keywords of the ERC project: TOR/mTOR, signaling, kinase, membrane

Keywords that characterize the scientific profile of the potential visiting researcher/s: metabolism, signaling, membrane, biophysics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

694282

Project Acronym:

Lysosomics

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr ANDREA BALLABIO**
Host Institution: FONDAZIONE TELETHON - IT

Functional Genomics of the Lysosome

For a long time the lysosome has been viewed as a “static” organelle that performs “routine” work for the cell, mostly pertaining to degradation and recycling of cellular waste. My group has challenged this view and used a systems biology approach to discover that the lysosome is subject to a global transcriptional regulation, is able to adapt to environmental clues, and acts as a signalling hub to regulate cell homeostasis. Furthermore, an emerging role of the lysosome has been identified in many types of diseases, including the common neurodegenerative disorders Parkinson's and Alzheimer's. These findings have opened entirely new fields of investigation on lysosomal biology, suggesting that there is a lot to be learned on the role of the lysosome in health and disease. The goal of LYSOSOMICS is to use “omics” approaches to study lysosomal function and its regulation in normal and pathological conditions. In this “organellar systems biology project” we plan to perform several types of genetic perturbations in three widely used cell lines and study their effects on lysosomal function using a set of newly developed cellular phenotypic assays. Moreover, we plan to identify lysosomal protein-protein interactions using a novel High Content FRET-based approach. Finally, we will use the CRISPR-Cas9 technology to generate a collection of cellular models for all lysosomal storage diseases, a group of severe inherited diseases often associated with early onset neurodegeneration. State-of-the-art computational approaches will be used to predict gene function and identify disease mechanisms potentially exploitable for therapeutic purposes. The physiological relevance of newly identified pathways will be validated by in vivo studies performed on selected genes by using medaka and mice as model systems. This study will allow us to gain a comprehensive understanding of lysosomal function and dysfunction and to use this knowledge to develop new therapeutic strategies.

Link to the ERC project webpage:

Keywords of the ERC project: lysosomes, autophagy

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

757411

Project Acronym:

PUNCTUATION

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr SEBASTIAN MARQUARDT**

Host Institution: **KOBENHAVNS UNIVERSITET - DK**

Pervasive Upstream Non-Coding Transcription Underpinning Adaptation

Genomic DNA represents the blueprint of life: it instructs solutions to challenges during life cycles of organisms. Curiously DNA in higher organisms is mostly non-protein coding (e.g. 97% in human). The popular “junk-DNA” hypothesis postulates that this non-coding DNA is non-functional. However, high-throughput transcriptomics indicates that this may be an over-simplification as most non-coding DNA is transcribed. This pervasive transcription yields two molecular events that may be functional: 1.) resulting long non-coding RNA (lncRNA) molecules, and 2.) the act of pervasive transcription itself. Whereas lncRNA sequences and functions differ on a case-by-case basis, RNA polymerase II (Pol II) transcribes most lncRNA. Pol II activity leaves molecular marks that specify transcription stages. The profiles of stage-specific activities instruct separation and fidelity of transcription units (genomic punctuation). Pervasive transcription affects genomic punctuation: upstream lncRNA transcription over gene promoters can repress downstream gene expression, also referred to as tandem Transcriptional Interference (tTI). Even though tTI was first reported decades ago a systematic characterization of tTI is lacking. Guided by my expertise in lncRNA transcription I recently identified the genetic material to dissect tTI in plants as an independent group leader. My planned research promises to reveal the genetic architecture and the molecular hallmarks defining tTI in higher organisms. Environmental lncRNA transcription variability may trigger tTI to promote organismal responses to changing conditions. We will address the roles of tTI in plant cold response to test this hypothesis. I anticipate our findings to inform on the fraction of pervasive transcription engaging in tTI. My proposal promises to advance our understanding of genomes by reconciling how the transcription of variable non-coding DNA sequences can elicit equivalent functions.

Link to the ERC project webpage:

Keywords of the ERC project: long non-coding RNA (lncRNA), epigenetics, chromatin, RNA polymerase II transcription, genomics

Keywords that characterize the scientific profile of the potential visiting researcher/s: long non-coding RNA (lncRNA), epigenetics, chromatin, RNA polymerase II transcription, genomics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

759139

Project Acronym:

TarMyc

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr ELMAR WOLF**

Host Institution: **JULIUS-MAXIMILIANS-UNIVERSITÄT WÜRZBURG - DE**

Targeting the Oncogenic Function of Myc in vivo

The transcription factor Myc plays a central role in tumorigenesis but was deemed undruggable due to it being an essential protein. However, recent proof-of-principle studies in mice using a dominant negative allele of Myc demonstrated the dependency of established tumours on Myc function and showed that mice tolerated Myc inhibition to a degree that allowed tumour regression. In line with these observations my group found Myc to regulate distinct sets of genes at low, physiological and high, oncogenic levels, because promoters differ in their affinity for Myc. This notion implies the compelling possibility to specifically target the oncogenic functions of Myc.

TarMyc aims to address four key questions required to bring this new concept from bench to bedside. Firstly, TarMyc will estimate the therapeutic window of Myc inhibition in vivo by expressing shRNAs against Myc in mice with established solid tumours. Secondly, TarMyc aims to identify in vivo Myc target genes crucial for tumorigenesis. Thirdly, this proposal aims to elucidate the role of Myc's differential promoter affinity in untransformed cells. Analysis of published gene expression datasets revealed Myc binding to low-affinity promoters during the process of tissue regeneration. Thus, by characterizing the regeneration programme induced by Myc we hope to gain further insight on the therapeutic window of Myc inhibition and assess potential side-effects in a Myc-targeting anticancer therapy. Fourthly, we aim to develop strategies to interfere with the oncogenic functions of Myc by (i) developing a novel class of drugs that reduce Myc's cellular concentrations, and (ii) by testing the therapeutic potential of Myc target genes by inhibiting their function in tumour models.

Taken together, TarMyc takes on the challenge of inhibiting the oncogenic functions of Myc in a highly multidisciplinary approach using state-of-the-art molecular biology, advanced tumour models and new concepts in drug development.

Link to the ERC project webpage: <https://www.biozentrum.uni-wuerzburg.de/molbio/research-groups/ag-wolf/>

Keywords of the ERC project: Myc, Cancer, transcription, medical chemistry

Keywords that characterize the scientific profile of the potential visiting researcher/s: medical chemistry, medicinal chemistry, biological chemistry, drug development



European Research Council
Executive Agency

Established by the European Commission

Project ID:

773089

Project Acronym:

METACELL

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr THEODORE ALEXANDROV**

Host Institution: **EUROPEAN MOLECULAR BIOLOGY LABORATORY - DE**

Metabolism of a cell pictured by single-cell approach

Every cell is unique. Metabolites define the composition of each cell and play key roles in essential intracellular processes of energy production and uptake, signaling, regulation, and cell death. Obtaining metabolite signatures of individual cells and linking them to cellular phenotypes is of paramount importance for a holistic understanding of these processes. This requires high-throughput single-cell metabolomics that is not generally attainable due to the limited sensitivity, low throughput, and disruptiveness of state-of-the-art metabolomics methods.

I propose to develop a spatial single-cell metabolomics approach for human cell culture systems. The approach will be based on using metabolite imaging mass spectrometry and will provide metabolite profiles of individual cells and metabolite signatures of single-cell phenotypes identified by light microscopy. With this approach developed, I will investigate the link between the intracellular metabolism and single-cell phenotype and focus on the following questions: How is the intracellular metabolism linked to cellular heterogeneity? How high is the variation of essential metabolites in a cell population? How do the energy metabolism and lipids biosynthesis change through the cell cycle and infection stages? What is the metabolic response to inflammatory signals?

I will scale up the analysis to discover novel cell phenotypes both in the cell culture systems and in big metabolite imaging mass spectrometry data from various biological systems provided to us by our collaborators and the community, and representing billions of cells.

My project will enable spatial single-cell metabolomics on a large scale and will provide yet lacking capacity for investigating and visualizing the intracellular metabolism on a single-cell level. It will advance our molecular understanding of key biological processes and pave the way to discoveries of molecular mechanisms of inflammation, cancer, and infection.

Link to the ERC project webpage: <https://cordis.europa.eu/project/rcn/213785/factsheet/en>

Keywords of the ERC project: single-cell, metabolomics, spatial, omics, mass spectrometry, imaging, machine learning

Keywords that characterize the scientific profile of the potential visiting researcher/s: single-cell, omics, microscopy, mass spectrometry, machine learning



European Research Council
Executive Agency

Established by the European Commission

Project ID:

803852

Project Acronym:

Mito-recombine

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr HANSONG MA**

Host Institution: THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF
CAMBRIDGE - UK

Homologous recombination and its application in manipulating animal mitochondrial DNA

Mitochondrial DNA (mtDNA) is a multi-copy genome that works with the nuclear genome to control energy production and various cellular processes. To date, disorders associated with mutations in mtDNA are among the most common genetically inherited metabolic diseases¹. However, our knowledge regarding many aspects of mtDNA biology remains limited, and we know even less about how it influences development and organismal traits. This is largely due to our inability to manipulate mtDNA. Recently, a colleague and I developed novel genetic tools in *Drosophila* that allowed us to isolate animal mitochondrial mutants for the first time, and to create heteroplasmic organisms containing two mitochondrial genotypes^{2,3}. These advances make *Drosophila* a powerful system for mtDNA studies. Importantly, I showed that *Drosophila* mtDNA could undergo homologous recombination. Furthermore, I established a system to induce recombination at specific sites and select for progeny containing only the recombinant genome⁴. Thus, my work has demonstrated the existence of recombination in animal mitochondria, and opens up the possibility of developing a recombination system for functional mapping and manipulating animal mtDNA. Here I propose to 1) identify components of the mitochondrial recombination machinery by a candidate RNAi screen; 2) develop a recombination toolkit to map trait-associated mtDNA sequences/SNPs; and 3) build a site-directed mutagenesis system by establishing robust ways to deliver DNA into fly mitochondria. Given the essential functions of mitochondria and their involvement in incurable diseases, the genetic tools developed in this proposal will transform the field by making it possible to link mtDNA variations to phenotypic differences and introduce specific mutations into mtDNA for functional studies at organismal level. These advances will open many possibilities to accelerate our understanding on how mtDNA impacts health, disease and evolution.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
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Project ID:

851054

Project Acronym:

DyNAMEcs

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr MAXIM GREENBERG**

Host Institution: **CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS - FR**

Early embryonic events, life-long consequences: DNA methylation dynamics in mammalian development

Immediately after fertilization, mammalian genomes undergo a dramatic reshaping of the epigenome as the embryo transitions from the zygote into the pluripotent cells primed for lineage commitment. This is best exemplified by DNA methylation reprogramming, as the gametic patterns are largely erased, and the embryonic genome undergoes a wave of de novo DNA methylation. Moreover, once DNA methylation patterns are established, mechanisms faithfully maintain the mark across cell division. Thus, there is latent potential for DNA methylation deposited in the early embryo to exhibit a lifelong effect.

DNA methylation is a modification that is typically associated with gene repression at repetitive elements and at a minority of protein coding genes. I previously described the regulation of the *Zdbf2* gene in mice, which is programmed during the de novo DNA methylation program. Challenging the paradigm, in this case DNA methylation is required for activation of a gene via antagonism of the polycomb-group of silencing proteins. If the DNA methylation fails to occur, the gene stays silent throughout life, resulting in a reduced growth phenotype.

For my proposed research I will utilize both a cell-based system that recapitulates these early embryonic events as well as an in vivo mouse model to investigate the extent and mechanisms of non-canonical DNA methylation functions. I plan to use a combinatorial approach of genomics, genetics, and proteomics in order to ascertain novel insights into DNA methylation-based regulation. Furthermore, I plan to employ precision epigenome editing tools to address the locus-specific impact of DNA methylation. Ultimately, I strive to gain a clear understanding of the profound epigenetic consequences of DNA methylation on this window of development, which occurs in the first week of mouse embryogenesis, and the second of human, but the repercussions of which can ripple throughout life.

Link to the ERC project webpage:

Keywords of the ERC project: DNA methylation, epigenetics, polycomb, stem cells

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

679146

Project Acronym:

EpigenomeProgramming

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr CHRISTOPH BOCK**

Host Institution: **CEMM - FORSCHUNGSZENTRUM FUER MOLEKULARE MEDIZIN GMBH - AT**

An experimental and bioinformatic toolbox for functional epigenomics and its application to epigenetically making and breaking a cancer cell

Epigenetic alterations can be detected in all cancers and in essentially every patient. Despite their prevalence, the concrete functional roles of these alterations are not well understood, for two reasons: First, cancer samples tend to carry many correlated epigenetic alterations, making it difficult to statistically distinguish relevant driver events from those that co-occur for other reasons. Second, we lack tools for targeted epigenome editing that could be used to validate biological function in perturbation and rescue experiments.

The proposed project strives to overcome these limitations through experimental and bioinformatic methods development, with the ambition of making and breaking cancer cells in vitro by introducing defined sets of epigenetic alterations. We will focus on leukemia as our “model cancer” (given its low mutation rate, frequent defects in epigenetic regulators, and availability of excellent functional assays), but the concepts and methods are general. In Aim 1, we will generate epigenome profiles for a human knockout cell collection comprising 100 epigenetic regulators and use the data to functionally annotate thousands of epigenetic alterations observed in large cancer datasets. In Aim 2, we will develop an experimental toolbox for epigenome programming using epigenetic drugs, CRISPR-assisted recruitment of epigenetic modifiers for locus-specific editing, and cell-derived guide RNA libraries for epigenome copying. Finally, in Aim 3 we will explore epigenome programming (methods from Aim 2) of candidate driver events (predictions from Aim 1) with the ultimate goal of converting cancer cells into non-cancer cells and vice versa.

In summary, this project will establish a broadly applicable methodology and toolbox for dissecting the functional roles of epigenetic alterations in cancer. Moreover, successful creation of a cancer that is driven purely by epigenetic alterations could challenge our understanding of cancer as a genetic disease.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s: Medical Epigenomics, Bioinformatics, Machine Learning / Artificial Intelligence, Single-cell Sequencing, Cancer Immunology, CRISPR Technology



European Research Council
Executive Agency

Established by the European Commission

Project ID:

716344

Project Acronym:

TREATCilia

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr MIRIAM SCHMIDTS**

Host Institution: **UNIVERSITAETSKLINIKUM FREIBURG - DE**

Novel Therapeutic Avenues for dynein-related Ciliopathies

Background: Cilia are hair-like, microtubule-based organelles protruding from most quiescent mammalian cells. They play essential roles in cell signalling (primary cilia) as well as movement of fluid (motile cilia). Although individually rare, cilia dysfunction affects up to 1 in 500 people in Europe, significantly reducing quality of life and lifespan due to dysfunction of multiple organs, including the kidneys, liver, heart, brain, retina, airways and the skeleton. To date, treatment is purely symptomatic.

Aim and Approach: TREATCilia aims to decipher novel treatment avenues and improve clinical management for dynein-related ciliopathies. Next-generation sequencing based gene identification for dynein-related ciliopathies (ciliary chondrodysplasias and Primary Ciliary Dyskinesia, PCD) is employed to dissect the molecular basis and identify new therapeutic targets. Revealing genotype-phenotype mechanisms and their underlying cell signalling defects provides further insight into potential treatment options. Novel innovative curative approaches include high-throughput substance screening in model organisms such as the green algae *Chlamydomonas* and mammalian cells specially adapted for this purpose.

Impact: Identification of novel ciliopathy genes will not only improve the biological understanding, but also reveal new treatment candidates. Furthermore, scrutinizing the molecular mechanisms of disease yields pharmacological entry points. TREATCilia develops a pre-clinical pipeline towards gene and mutation-specific treatments for hereditary conditions resulting from dynein-related ciliary dysfunction.

Link to the ERC project webpage:

Keywords of the ERC project: Cilia, kidney, development, genetics, pediatrics, CRISPR/Cas9, *chlamydomonas*

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

787611

Project Acronym:

DeCRyPT

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr EILEEN FURLONG**

Host Institution: **EUROPEAN MOLECULAR BIOLOGY LABORATORY - DE**

Deciphering Cis-Regulatory Principles of Transcriptional regulation: Combining large-scale genetics and genomics to dissect functional principles of genome regulation during embryonic development

Understanding how genomic information is organised and interpreted to give rise to robust patterns of gene expression is a long-standing problem in genome biology, with direct implications for development, evolution and disease. Despite recent advances in locating regulatory elements in animal genomes, there is a general lack of functional data on elements in their endogenous setting – the bulk of our current knowledge comes from reporter assays examining elements out of context, giving insights on sufficiency but not necessity. The functional requirement of very few individual enhancers, and other elements, has been assessed by deletion, with even less known about how the action of multiple elements is integrated. To understand the functional effects of genetic variants, and how they are buffered during embryogenesis, it is imperative to genetically dissect regulatory domains to uncover functional rules of genome regulation within a well-characterised animal model. Here, by combining *Drosophila* population genetics, developmental genetics, and novel multiplexed genomic methods we will perform the first large-scale functional dissection of cis-regulatory landscapes during embryogenesis.

Extensive resources make *Drosophila* a unique model organism for this task, including (a) 500 fully sequenced inbred wild isolates for population genetics, (b) over 20,000 fly strains custom-built for genome engineering & (c) a wealth of cis-regulatory information on the location of enhancers. The proposal has three Aims: 1) Use population genetics as a perturbation tool to functionally link regulatory elements to their target genes; 2) Systematically delete cis-regulatory elements to dissect their role in gene expression and genome topology; 3) Manipulate cis-regulatory domains to generate new regulatory environments for developmental genes. These Aims will provide unique functional insights, enabling us to move from correlation to causation in our understanding of genome regulation.

Link to the ERC project webpage:

Keywords of the ERC project: Developmental enhancers, Genetics, Population Genetics, Genome topology, Genomics (Hi-C, CRISPR, RNA-seq)

Keywords that characterize the scientific profile of the potential visiting researcher/s: One or more of the following expertise: Strong molecular Biology, Population Genetics, Genomics, *Drosophila* genetics, Bioinformatics, computer science



European Research Council
Executive Agency

Established by the European Commission

Project ID:

852865

Project Acronym:

EmbryoMethFunc

Evaluation Panel:

LS2

Genetics, Genomics,
Bioinformatics and
Systems Biology

Principal Investigator: **Dr YONATAN STELZER**

Host Institution: **WEIZMANN INSTITUTE OF SCIENCE - IL**

Cell-Type Specific DNA Methylation Changes During Mammalian Development: Beyond Mapping

DNA methylation is essential for normal mammalian development. While seminal work has provided tremendous insight into the dynamic regulation of DNA methylation throughout embryogenesis, comprehensive understanding of how cell-specific methylation programs are established and maintained, and how they are involved in defining cell states in vivo through regulation of target genes, remains a formidable task. Revolutionary technologies now offer unprecedented opportunities for understanding the function of DNA methylation in specifying, memorizing and modulating embryonic programs. These powerful tools motivate further development of novel experimental systems, to integrate single-cell monitoring with flexible engineering of markers, reporters and perturbations. This will make it possible to precisely target key rare embryonic cell populations for in-depth analysis.

Here, combining cutting-edge methods for single cell mapping of DNA methylation and gene expression, and by developing a novel approach for inferring spatial information from single cell genomic data, we propose to comprehensively chart the post-implantation embryo, at unprecedented resolution. To move to functional studies, we will implement our recently established reporter system that enables monitoring and isolation of cells based on endogenous locus-specific changes in DNA methylation. Together with site-specific methylation editing tools, mouse genetics, and in vitro differentiation of pluripotent stem cells, we will study the developmental potential of rare epiblast cells that we identified that exhibit lower-than-expected genome-wide methylation levels. We will further study the effects of cell-specific methylation changes at an imprinted control region on gene dosage by genetic and epigenetic perturbation, during mouse development. Our combined approach will open new avenues for elucidating the contribution of cell-specific DNA methylation changes to cell-state and function following implantation

[Link to the ERC project webpage:](#)

[Keywords of the ERC project:](#) Epigenetics, Embryonic Development, DNA methylation, Parental Imprinting, Single-Cell Genomics, Germ Cells

[Keywords that characterize the scientific profile of the potential visiting researcher/s:](#) Epigenetics, Embryonic Development, DNA methylation, Parental Imprinting, Single-Cell Genomics, Germ Cells



European Research Council
Executive Agency

Established by the European Commission

Project ID:

679140

Project Acronym:

CentSatRegFunc

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr ELIF NUR FIRAT-KARALAR**

Host Institution: **KOC UNIVERSITY - TR**

Dissecting the function and regulation of centriolar satellites: key regulators of the centrosome/cilium complex

Centrosomes are the main microtubule-organizing centers of animal cells. They influence the morphology of the microtubule cytoskeleton and function as the base of primary cilium, a nexus for important signaling pathways. Structural and functional defects in centrosome/cilium complex cause a variety of human diseases including cancer, ciliopathies and microcephaly. To understand the relationship between human diseases and centrosome/cilium abnormalities, it is essential to elucidate the biogenesis of centrosome/cilium complex and the control mechanisms that regulate their structure and function. To tackle these fundamental problems, we will dissect the function and regulation of centriolar satellites, the array of granules that localize around the centrosome/cilium complex in mammalian cells. Only recently interest in the satellites has grown because mutations affecting satellite components were shown to cause ciliopathies, microcephaly and schizophrenia. Remarkably, many centrosome/cilium proteins localize to these structures and we lack understanding of when, why and how these proteins localize to satellites. The central hypothesis of this grant is that satellites ensure proper centrosome/cilium complex structure and function by acting as transit paths for modification, assembly, storage, stability and trafficking of centrosome/cilium proteins. In Aim 1, we will identify the nature of regulatory and molecular relationship between satellites and the centrosome/cilium complex. In Aim 2, we will elucidate the role of satellites in proteostasis of centrosome/cilium proteins. In Aim 3, we will investigate the functional significance of satellite-localization of centrosome/cilium proteins during processes that go awry in human disease. Using a multidisciplinary approach, the proposed research will expand our knowledge of the spatiotemporal regulation of the centrosome/cilium complex and provide new insights into pathogenesis of ciliopathies and primary microcephaly.

Link to the ERC project webpage: <http://mysite.ku.edu.tr/ekaralar/projects/>

Keywords of the ERC project: centrosomes, cilia, ciliopathies, retinal degeneration, microtubules, proteomics

Keywords that characterize the scientific profile of the potential visiting researcher/s: centrosomes, cilia, ciliopathies, retinal degeneration, microtubules, proteomics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

694236

Project Acronym:

COREMA

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr JAN ELLENBERG**

Host Institution: **EUROPEAN MOLECULAR BIOLOGY LABORATORY - DE**

Cell division and the origin of embryonic aneuploidy in preimplantation mouse development

Cell division is fundamental for development. In the early mammalian embryo it drives the rapid proliferation of totipotent cells, the basis for forming the fetus. Given its crucial importance, it is surprising that cell division is particularly error-prone at the beginning of mammalian life, resulting in spontaneous abortion or severe developmental retardation, the incidence of which is increasing with age of the mother. Why aneuploidy is so prevalent and how early embryonic development nevertheless achieves robustness is largely unknown. The goal of this project is a comprehensive analysis of cell divisions in the mouse preimplantation embryo to determine the molecular mechanisms underlying aneuploidy and its effects on normal development. Recent technological breakthroughs, including light sheet microscopy and rapid loss-of-function approaches in the mouse embryo will allow us for the first time to tackle the molecular mechanisms of aneuploidy generation and establish the preimplantation mouse embryo as a standard cell biological model system. For that purpose we will develop next generation light sheet microscopy to enable automated chromosome tracking in the whole embryo. Mapping of cell division errors will reveal when, where, and how aneuploidy occurs, what the fate of aneuploid cells is in the embryo, and how this changes with maternal age. We will then perform high resolution functional imaging assays to identify the mitotic pathways responsible for aneuploidy and understand why they do not fully function in early development. Key proteins will be functionally characterised in detail integrating light sheet imaging with single molecule biophysics in embryos from young and aged females to achieve a mechanistic understanding of the unique aspects of cell division underlying embryonic aneuploidy. The achieved knowledge gain will have an important impact for our understanding of mammalian, including human infertility.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

694918

Project Acronym:

ReLIVE

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr MICHALIS AVEROF**

Host Institution: **CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS - FR**

Unraveling complex organ regeneration through live imaging and molecular profiling approaches

Many animals have the ability to regenerate parts of their body following injury or amputation. While there is great biological and medical interest in this process, many fundamental questions remain unanswered, because complex organ regeneration is poorly represented in classic model organisms; flies, nematodes and mammals have limited regenerative abilities, in contrast to flatworms, crustaceans and fish.

reLIVE explores fundamental questions on regeneration in an emerging crustacean model, *Parhyale hawaiiensis*, which combines extensive regenerative abilities, advanced genetic tools and live imaging.

The project will address the following fundamental, centuries-old questions on regeneration:

- 1) Which are the progenitors that underpin complex organ regeneration? Do epidermis, tendons, neurons, glia and muscle arise de novo from undifferentiated adult stem cells, or do they emerge from differentiated cell types? Are the progenitors unipotent/committed or multipotent? Which are their molecular responses and behaviors during the course of regeneration?
- 2) Do diverse animal groups regenerate in the same way? Do the regenerative progenitors of crustaceans have common molecular and functional properties with those of vertebrates and flatworms? Do they have a shared evolutionary history?
- 3) How does regeneration differ from development? Are these processes operating on comparable temporal and spatial scales? How similar are the transcriptional responses and cell behaviors that underpin embryonic and regenerative morphogenesis of the limb?

To answer these questions, reLIVE will take advantage of the unique opportunities offered by *Parhyale* limb regeneration and, for the first time, combine four cutting-edge approaches: a) CRISPR-mediated marking of specific cell types, b) continuous live imaging and cell tracking in regenerating limbs over week-long periods, c) a novel method of cell lineage reconstruction, and d) transcriptional profiling on individual cells.

Link to the ERC project webpage:

Keywords of the ERC project: regeneration, progenitors, comparative developmental biology, live imaging, transcriptional profiling

Keywords that characterize the scientific profile of the potential visiting researcher/s: genetic tools, live imaging, comparative transcriptomics, cis-regulatory sequences, live imaging, image analysis



European Research Council
Executive Agency

Established by the European Commission

Project ID:

726049

Project Acronym:

InPhoTime

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr DAVID DOLEZEL**

Host Institution: **Biologické centrum AV ČR, v. v. i. - CZ**

Insect Photoperiodic Timer

Daylength measuring devices such as the photoperiodic timer enable animals to anticipate and thus survive adverse seasons. This ability has contributed to the great success of insects living in temperate regions. Yet the basis of photoperiodic sensing remains elusive, because of the lack of suitable genetic models expressing photoperiod-dependent seasonal phenotypes. We have developed the linden bug, *Pyrrhocoris apterus*, into a genetically tractable model with a robust, photoperiod-dependent reproductive arrest (diapause). With the available tools, this insect has become ideal for deciphering the regulation of seasonality. The project has 3 clear and ambitious objectives: 1). Our goal is to define the molecular and anatomical bases of the photoperiodic timer. To achieve this, we propose to identify photoperiodic timer genes, genes regulating input to the timer, and early output markers, through an RNA interference screen(s). To define the molecular mechanism of the timer, we will employ genome editing to precisely alter properties of the key players. 2). Next, we will combine techniques of neuronal backfilling, in-vivo fluorescent reporters, and microsurgery to define the photoperiodic timer anatomically and to examine its spatial relationship to the circadian clock in the insect brain. 3). We will exploit the great natural geographic variability of photoperiodic timing in *P. apterus* to explore its genetic basis. Genetic variants correlating with phenotypic differences will be causally tested by genome editing within the original genetic backgrounds. Both the established and the innovative strategies provide a complementary approach to the first molecular characterization of the seasonal photoperiodic timer in insects. The proposed research aspires to explain mechanisms underlying the critical physiological adaptation to changing seasons. Deciphering mechanisms underpinning widespread adaptation might bring general implications for environment-friendly pest control.

Link to the ERC project webpage:

Keywords of the ERC project: insect; circadian clock; diapause; photoperiodic timing; reverse genetics

Keywords that characterize the scientific profile of the potential visiting researcher/s: population genetics; genomics; bioinformatics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

772437

Project Acronym:

CHROMABOLISM

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr STEFAN KUBICEK**

Host Institution: **CEMM - FORSCHUNGSZENTRUM FUER MOLEKULARE MEDIZIN GMBH - AT**

Chromatin-localized central metabolism regulating gene expression and cell identity

Epigenetics research has revealed that in the cell's nucleus all kinds of biomolecules—DNA, RNAs, proteins, protein posttranslational modifications—are highly compartmentalized to occupy distinct chromatin territories and genomic loci, thereby contributing to gene regulation and cell identity. In contrast, small molecules and cellular metabolites are generally considered to passively enter the nucleus from the cytoplasm and to lack distinct subnuclear localization. The CHROMABOLISM proposal challenges this assumption based on preliminary data generated in my laboratory. I hypothesize that chromatin-bound enzymes of central metabolism and subnuclear metabolite gradients contribute to gene regulation and cellular identity.

To address this hypothesis, we will first systematically profile chromatin-bound metabolic enzymes, chart nuclear metabolomes across representative leukemia cell lines, and develop tools to measure local metabolite concentrations at distinct genomic loci. In a second step, we will then develop and apply technology to perturb these nuclear metabolite patterns by forcing the export of metabolic enzymes for the nucleus, aberrantly recruiting these enzymes to selected genomic loci, and perturbing metabolite patterns by addition and depletion of metabolites. In all these conditions we will measure the impact of nuclear metabolism on chromatin structure and gene expression. Based on the data obtained, we will model for the effects of cellular metabolites on cancer cell identity and proliferation. In line with the recent discovery of oncometabolites and the clinical use of antimetabolites, we expect to predict chromatin-bound metabolic enzymes that can be exploited as druggable targets in oncology. In a final aim we will validate these targets in leukemia and develop chemical probes against them.

Successful completion of this project has the potential to transform our understanding of nuclear metabolism in control of gene expression and cellular identity.

Link to the ERC project webpage: <https://cemm.at/research/funding/international-funding/erc-consolidator-grant-chromabolism/>

Keywords of the ERC project: chromatin, epigenetics, chemical biology, nuclear metabolism

Keywords that characterize the scientific profile of the potential visiting researcher/s: chromatin, epigenetics, chemical biology, nuclear metabolism



European Research Council
Executive Agency

Established by the European Commission

Project ID:

801669

Project Acronym:

EVOSELFATE

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr JOSE M MARTIN-DURAN**

Host Institution: **QUEEN MARY UNIVERSITY OF LONDON - UK**

Evolution of cell fate specification modes in spiral cleavage

Spiral cleavage is a highly stereotypical early embryonic program, and the ancestral, defining feature to Spiralia, a major phylogenetic clade including almost half of the animal phyla. Remarkably, spiral-cleaving embryos specify homologous cell fates (e.g. the progenitor cell of posterodorsal structures) conditionally –via cell interactions– or autonomously –via segregation of maternal inputs. This variation occurs naturally, even between closely related species, and has been related to the precocious formation of adult characters (adultation) in larvae of autonomous spiral-cleaving species. How spiralian lineages repeatedly shifted between these two cell fate specification modes is largely unexplored, because the mechanisms controlling spiral cleavage are still poorly characterized.

This project tests the hypothesis that maternal chromatin and transcriptional regulators differentially incorporated in oocytes with autonomous spiral cleavage explain the evolution of this mode of cell fate specification. Through a comparative and phylogenetic-guided approach, we will combine bioinformatics, live imaging, and molecular and experimental techniques to: (i) Comprehensively identify differentially supplied maternal factors among spiral cleaving oocytes with distinct cell fate specification modes using comparative RNA-seq and proteomics; (ii) Uncover the developmental mechanisms driving conditional spiral cleavage, which is the ancestral embryonic mode; and (iii) Investigate how maternal chromatin and transcriptional regulators define early cell fates, and whether these factors account for the repeated evolution of autonomous specification modes.

Our results will fill a large gap of knowledge in our understanding of spiral cleavage and its evolution. In a broader context, this project will deliver fundamental insights into two core questions in evolutionary developmental biology: how early embryonic programs evolve, and how they contribute to phenotypic change.

Link to the ERC project webpage:

Keywords of the ERC project: evo-devo, annelids, spiral cleavage, epigenomics, comparative developmental biology, comparative genomics

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational biology, developmental biologist, microscopy, epigenomics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

834580

Project Acronym:

MiniEmbryoBlueprint

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr ALFONSO MARTINEZ ARIAS**

Host Institution: **THE CHANCELLOR MASTERS AND SCHOLARSO OF THE UNIVERSITY OF
CAMBRIDGE - UK**

The mammalian body plan blueprint, an in vitro approach

The development of an embryo requires the spatially structured emergence of tissues and organs. This process relies on the early establishment of a coordinate system in the form of three orthogonal axes that act as a reference for laying down the body plan, a template for the organism. Genetic analysis of this process has revealed an underlying transcriptional blueprint that links the coordinate system and the body plan. However, the way in which the gene products contribute to the emergence of the body plan remains an open question. A reason for this is that this process involves feedbacks and integration between the activity of Gene Regulatory Networks (GRNs) and the mechanics of multicellular ensembles, and that probing this relationship is experimentally challenging. In the case of mammalian embryos, which are particularly important as models for human development, our gaps in knowledge of these events are larger than in other organisms. This is partly due to the challenges associated with uterine development but also, and increasingly, because of the cost of mice and the difficulty of obtaining large numbers of embryos, as required for mechanistic experiments. In this project we shall use gastruloids, a novel and versatile Pluripotent Stem Cells based experimental system that we have developed for the study of mammalian development, to gain insights into the molecular and cellular basis underlying the emergence of the mammalian body plan. Gastruloids lack anterior neural structures and over a period of five days become organized in the fashion of a midgestation mouse embryo. We shall use the experimental versatility of the Gastruloid system to probe into the functional relationships between the mechanical activities of multicellular ensembles and the dynamics of GRNs that underlie the emergence of the mammalian body plan.

Link to the ERC project webpage:

Keywords of the ERC project: Gastruloid, organ engineering, developmental systems biology

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

835322

Project Acronym:

CENGIN

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr PIERRE GÖNCZY**

Host Institution: **ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE - CH**

Deciphering and engineering centriole assembly

Deciphering and engineering the assembly of cellular organelles is a key pursuit in biology. The centriole is an evolutionarily conserved organelle well suited for this goal, and which is crucial for cell signaling, motility and division. The centriole exhibits a striking 9-fold radial symmetry of microtubules around a likewise symmetrical cartwheel containing stacked ring-bearing structures. Components essential for generating this remarkable architecture from alga to man have been identified. A next critical step is to engineer assays to probe the dynamics of centriole assembly with molecular precision to fully understand how these components together build a functional organelle. Our ambitious research proposal aims at taking groundbreaking steps in this direction through four specific aims:

- 1) Reconstituting cartwheel ring assembly dynamics. We will use high-speed AFM (HS-AFM) to dissect the biophysics of SAS-6 ring polymer dynamics at the root of cartwheel assembly. We will also use HS-AFM to analyze monobodies against SAS-6, as well as engineer surfaces and DNA origamis to further dissect ring assembly.
 - 2) Deciphering ring stacking mechanisms. We will use cryo-ET to identify SAS-6 features that direct stacking of ring structures and set cartwheel height. Moreover, we will develop an HS-AFM stacking assay and a reconstituted stacking assay from human cells.
 - 3) Understanding peripheral element contributions to centriole biogenesis. We will dissect the function of the peripheral centriole pinhead protein Cep135/Bld10p, as well as identify and likewise dissect peripheral A-C linker proteins. Furthermore, we will further engineer the HS-AFM assay to include such peripheral components.
 - 4) Dissecting de novo centriole assembly mechanisms. We will dissect de novo centriole formation in human cells and water fern. We will also explore whether de novo formation involves a phase separation mechanism and repurpose the HS-AFM assay to probe de novo organelle biogenesis
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Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

788363

Project Acronym:

HITSCIL

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr ERWIN PETERMAN**

Host Institution: **STICHTING VU - NL**

How intraflagellar transport shapes the cilium: a single-molecule systems study

Sensory cilia are organelles extending like antennas from many eukaryotic cells, with crucial functions in sensing and signalling. Cilia consist of an axoneme built of microtubules, enveloped by a specialized membrane. Ciliary development and maintenance depend critically on a specific, microtubule-based intracellular transport mechanism, intraflagellar transport (IFT). In my laboratory, we study the chemosensory cilia of *C. elegans*, which sense water-soluble molecules in the animal's environment for chemotaxis. Over the past years, we have developed a unique set of quantitative, single-molecule fluorescence microscopy tools that allow us to visualize and quantify IFT dynamics with unprecedented detail in living animals. So far, our focus has been on the cooperation of the motor proteins driving IFT. The overall objective of my current proposal is to zoom out and shed light on the connection between ciliary structure, chemosensory function and IFT, from a systems perspective. Recent work has indicated that axoneme length is controlled by IFT. Preliminary results from my laboratory show that axoneme length changes dynamically in response to perturbations of IFT or cilia. Furthermore, we have shown that IFT is substantially affected upon exposure of animals to known repellent solutions. The four major aims in my proposal are to:

- determine how directional changes in IFT are regulated and are affected by external disturbances,
- understand the dynamics of the axonemal microtubules and how IFT affects these dynamics and vice versa,
- study how sensory ciliary function affects IFT and ciliary structure,
- further develop our (single-molecule) fluorescence microscopy toolbox by improving instrumentation and using better fluorescent probes and sensors.

These experiments will place my lab in a unique position to push forward our understanding of the relationship between structure, function and dynamics of transport of this fascinating and fundamental organelle.

Link to the ERC project webpage: www.nat.vu.nl/~erwinp

Keywords of the ERC project: *C. elegans*, cilia, chemosensing, intraflagellar transport

Keywords that characterize the scientific profile of the potential visiting researcher/s: bit more senior visiting scientist, sabbatical, skills in *C. elegans* or advanced fluorescence microscopy



European Research Council
Executive Agency

Established by the European Commission

Project ID:

788442

Project Acronym:

INPHORS

Evaluation Panel:

LS3
Cellular and
Developmental Biology

Principal Investigator: **Dr ANDREAS MAYER**

Host Institution: **UNIVERSITE DE LAUSANNE - CH**

Intracellular phosphate reception and signaling: A novel homeostatic system with roles for an orphan organelle?

Cells face a phosphate challenge. Growth requires a minimal concentration of this limiting resource because intracellular phosphate (Pi) is a compound of nucleic acids and modifies most cellular proteins. At the same time, cytosolic Pi may not rise much, because elevated cytosolic Pi can stall metabolism. It reduces the free energy that nucleotide triphosphate hydrolysis can provide to drive energetically unfavorable reactions.

I will undertake a pioneering study to elucidate how cells strike this critical balance. We will identify a novel pathway for intracellular phosphate reception and signaling (INPHORS) and explore the role of acidocalcisomes in it. These studies may identify a key function of these very poorly understood organelles, provide one reason for their evolutionary conservation and elucidate a novel homeostatic system of critical importance for cellular metabolism.

We recently provided first hints that a dedicated pathway for sensing and signaling intracellular Pi might exist, which regulates multiple systems for import, export and acidocalcisomal storage of Pi, such that cytosolic Pi homeostasis is guaranteed 1. Yeast cells will serve as a powerful model system for exploring this pathway and its physiological relevance. Yeast Pi transport and storage proteins are known. Furthermore, we can establish cell-free in vitro systems that reconstitute Pi-regulated transport and storage processes, providing an excellent basis for identifying signaling complexes and studying their dynamics.

We will (A) generate novel tools to uncouple, individually manipulate and measure key parameters for the INPHORS pathway; (B) identify its components, study their interactions and regulation; (C) elucidate how acidocalcisomes are targeted by INPHORS and how they contribute to Pi homeostasis; (D) study the crosstalk between INPHORS and Pi-regulated transcriptional responses; (E) test the relevance of INPHORS for Pi homeostasis in mammalian cells.

Link to the ERC project webpage:

Keywords of the ERC project: nutrient signaling, phosphate homeostasis, SPX domains

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

678119

Project Acronym:

SiCMetabol

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr GRZEGORZ SUMARA**

Host Institution: **JULIUS-MAXIMILIANS-UNIVERSITÄT WÜRZBURG - DE**

Signaling Cascades in Metabolic Diseases

Over 380 million people suffer from diabetes worldwide, with majority of cases being attributed to type 2 diabetes (T2D). Obesity is a major risk factor predisposing to the development of this disease. T2D is characterized by peripheral insulin resistance in combination with relative insulin deficiency that results in hyperglycemia and hyperlipidemia. Liver and adipose tissue are central for regulation of glucose and lipids levels. However, during T2D the hepatic glucose uptake is reduced while rates of gluconeogenesis and lipogenesis are increased. In the adipose tissue, T2D leads to decreased glucose uptake, perturbations in secretion of adipokines and increased lipolysis. Importantly, dysfunction of the liver and the adipose tissue during T2D is caused by defective phosphorylation signaling cascades and normalization of these pathways was shown to attenuate the course of T2D. However, the specific roles of different classes of signaling molecules in these organs remain poorly characterized. We hypothesize that the cross-talk of different classes of signaling molecules determines regulation of metabolism.

Thus, we aim to identify the signaling networks regulating metabolism. The results generated in my own laboratory suggest that the Pkd family kinases are the crucial regulators of metabolic homeostasis. Specifically, Pkd1 and Pkd2 promote obesity and diabetes while Pkd3 controls liver function. Thus, we plan to characterize the molecular mechanisms controlling Pkds signaling. In parallel, we will utilize screening approaches to identify novel, non-canonical signaling modules (phosphatases and components of the ubiquitin system) regulating abundance, localization and phosphorylation of targets of Pkds and, in the long term, also other kinases implicated in T2D.

By identifying and characterizing the essential signaling networks in liver and adipose tissue the project will contribute to more targeted pharmacological strategies for the treatment of T2D.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

694717

Project Acronym:

Immunobile

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr BART STAELS**

Host Institution: **UNIVERSITE DE LILLE - FR**

Bile acid, immune-metabolism, lipid and glucose homeostasis

The role of chronic inflammation in obesity, metabolic and cardiovascular diseases is increasingly recognized. Bile acids (BA), synthesized in the liver and modified by the gut flora, facilitate lipid absorption in the intestine. BA modulate lipid and glucose homeostasis by activating the nuclear receptor FXR and the GPCR TGR5. Intriguingly, peripheral BA concentrations are elevated in type 2 diabetes (T2D) and FXR mediates the beneficial metabolic response to gastric bypass in mice. The immune system plays an important role in the cross-talk with metabolic tissues, such as liver, intestine and adipose tissues. However, whether BA modulate immune cell function is unknown. Our unpublished results identifying FXR and TGR5 expression in lymphoid cells, prompt us to study their role in the regulation of glucose and lipid metabolism through immune cell modulation. Using reporter mice and specific ligands, we will characterize the immune cells expressing active FXR and TGR5. We will determine their role in metabolism and inflammation by immune cell-specific gene inactivation in models of obesity, T2D and elevated peripheral blood BA concentrations. Mass cytometry, cell sorting and single cell transcriptomic analysis will allow the identification of gene networks regulated by BA and their receptors. As microbiota generate biologically active secondary BA, we will assess the impact of microbiota depletion and subsequent BA acid pool modifications on immune cell populations. Translational studies in humans with altered BA metabolism and pharmacological treatment with anti-diabetic BA sequestrants will allow assessment of alterations in immune functions. This project aims to identify an hitherto unexplored role of BA through modulation of the immune system on T2D, NAFLD and dyslipidemia. Success of the project critically depends on an integrative approach uniquely undertaken in my laboratory through its unique multidisciplinary expertise in basic and translational biology.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s: nuclear receptors; bile acids; epigenetics; immunology; animal models



European Research Council
Executive Agency

Established by the European Commission

Project ID:

771486

Project Acronym:

MetaRegulation

Evaluation Panel:

LS4
Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr SARAH-MARIA FENDT**

Host Institution: **VIB - BE**

Metabolic regulation of metastatic growth

Metastatic growth of cancer cells requires extracellular matrix (ECM) production. The current understanding is that transcription factors regulate ECM production and thus metastatic growth by increasing the expression of collagen prolyl 4-hydroxylase (CP4H). In contrast, we recently discovered that metabolism regulates CP4H activity independently of the known transcription factors. Specifically, we found that loss of pyruvate metabolism inhibits CP4H activity and consequently ECM-dependent breast cancer cell growth. Based on this discovery we propose the novel concept that metabolism regulates metastatic growth by increasing ECM production.

In this project we will investigate the following questions: 1) What is the mechanism by which pyruvate regulates CP4H activity in breast cancer cells? To address this question we will investigate pyruvate metabolism and ECM production in 3D cultures of various breast cancer cell lines using ¹³C tracer analysis, metabolomics, and two-photon microscopy based ECM visualization. 2) How can this novel metabolic regulation be exploited to inhibit breast cancer-derived lung metastases growth? To address this question we will inhibit pyruvate metabolism in metastatic breast cancer mouse models using genetically modified cells and small molecules in combination with immuno- and chemotherapy. 3) How can this novel regulation be translated to different metastatic sites and cancers of different origin? To address this question we will determine the in vivo metabolism of breast cancer-, lung cancer-, and melanoma-derived liver and lung metastases (using metabolomics and ¹³C tracer analysis), and link it to ECM production (using two-photon microscopy based ECM visualization).

With this project we will deliver a novel concept by which metabolism regulates metastatic growth. In a long-term perspective we expect that targeting this novel metabolic regulation will pave the way for an unexplored approach to treat cancer metastases.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

771704

Project Acronym:

NoMePaCa

Evaluation Panel:

LS4
Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr GUIDO BOMMER**

Host Institution: **UNIVERSITE CATHOLIQUE DE LOUVAIN - BE**

Novel Metabolic Pathways in Cancer

Metabolic adaptations in central carbon metabolism play a key role in cancer. Yet, the success of therapeutic interventions in major pathways has been limited, although some of the changes have been known to exist for almost 100 years.

Biochemical textbooks present intermediary metabolism as something canonical, and the molecular identity of most enzymes required for the production of known intermediary metabolites is indeed known. Yet, the function of many putative enzymes is still unknown, indicating that novel metabolic pathways containing so far unknown metabolites exist.

We have recently discovered a novel metabolic pathway containing two metabolites that have never been described before. Preliminary data indicate that this pathway might play an important role in a group of cancers sharing specific mutations. Furthermore, genetic inactivation of a component of this pathway in mice is compatible with normal development, indicating that pharmacological inhibition should be well tolerated.

In the present project, we will use a multi-dimensional approach combining biochemical, genetic and pharmacological techniques, to identify missing components of this metabolic pathway and assess its role in cellular metabolism and cancer development. In the process of this, we will develop tools that will allow us to test whether this pathway can be targeted in vivo. Thus, our work will lead to the description of a novel metabolic pathway, should reveal novel regulatory circuits and might open novel therapeutic avenues in cancer and beyond.

Link to the ERC project webpage:

Keywords of the ERC project: metabolism, cancer, mass spectrometry, novel biochemical pathways, mouse models

Keywords that characterize the scientific profile of the potential visiting researcher/s: Strong interest or experience in the following areas would be desirable:

- bioinformatics
- biochemistry
- mouse models of cancer; bone marrow transplantation in mice
- mass spectrometry of small molecules



European Research Council
Executive Agency

Established by the European Commission

Project ID:

773208

Project Acronym:

ImmunoFit

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr MASSIMILIANO MAZZONE**

Host Institution: **VIB - BE**

Harnessing tumor metabolism to overcome immunosuppression

Anti-cancer immunotherapy has provided patients with a promising treatment. Yet, it has also unveiled that the immunosuppressive tumor microenvironment (TME) hampers the efficiency of this therapeutic option and limits its success. The concept that metabolism is able to shape the immune response has gained general acceptance. Nonetheless, little is known on how the metabolic crosstalk between different tumor compartments contributes to the harsh TME and ultimately impairs T cell fitness within the tumor.

This proposal aims to decipher which metabolic changes in the TME impede proper anti-tumor immunity. Starting from the meta-analysis of public human datasets, corroborated by metabolomics and transcriptomics data from several mouse tumors, we ranked clinically relevant and altered metabolic pathways that correlate with resistance to immunotherapy. Using a CRISPR/Cas9 platform for their functional in vivo selection, we want to identify cancer cell intrinsic metabolic mediators and, indirectly, distinguish those belonging specifically to the stroma. By means of genetic tools and small molecules, we will modify promising metabolic pathways in cancer cells and stromal cells (particularly in tumor-associated macrophages) to harness tumor immunosuppression. In a mirroring approach, we will apply a similar screening tool on cytotoxic T cells to identify metabolic targets that enhance their fitness under adverse growth conditions. This will allow us to manipulate T cells ex vivo and to therapeutically intervene via adoptive T cell transfer. By analyzing the metabolic network and crosstalk within the tumor, this project will shed light on how metabolism contributes to the immunosuppressive TME and T cell maladaptation. The overall goal is to identify druggable metabolic targets that i) reinforce the intrinsic anti-tumor immune response by breaking immunosuppression and ii) promote T cell function in immunotherapeutic settings by rewiring either the TME or the T cell itself.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

787171

Project Acronym:

POLICE

Evaluation Panel:

LS4
Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr ANDREAS VILLUNGER**

Host Institution: **MEDIZINISCHE UNIVERSITÄT INNSBRUCK - AT**

The PIDDosome in Centrosome and Ploidy-Surveillance

Tight control of the number of chromosome sets in a cell (ploidy) is fundamental for normal development and organismal health. Most cells in our body are diploid, yet, some cells, including cardiomyocytes or hepatocytes require a balanced increase in ploidy for proper function. Polyploidization is accompanied by an accumulation of centrosomes, structures needed for nucleating the mitotic spindle and ciliogenesis. Extra centrosomes, however, promote aneuploidy in proliferating cells by causing errors in chromosome segregation, underlying a series of human pathologies, most notably cancer and premature ageing. How polyploidization is controlled in organogenesis and how errors in ploidy control contribute to disease is poorly understood.

We recently demonstrated that the “PIDDosome” complex polices centrosome numbers in mammalian cells, alerting the tumor suppressor p53 in response to extra centrosomes. This is achieved by inactivating MDM2, the key-inhibitor of p53, by targeted proteolysis. MDM2-processing is mediated by caspase-2, a neglected member in a protease family that controls cell death and inflammation, activated in the PIDDosome.

This exciting finding allows examining the consequences of deregulated ploidy and centrosome number in development and disease without interfering with p53, nor the cell fusion or cytokinesis machineries. This puts us in pole position to carry out an integrative study that aims to develop the PIDDosome as a new therapeutic target in cancer, related inflammation and in regenerative medicine. To meet this aim, we will define

(i) the relevance of the PIDDosome in aneuploidy tolerance of cancer

(ii) the role of the PIDDosome in controlling sterile inflammation and immunity

(iii) the PIDDosome as a key-regulator of organ development and regeneration

POLICE will open new lines of research at the interface of cell cycle, cell death & inflammation control and promote the PIDDosome as new target in our efforts to improve human health.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802644

Project Acronym:

LeukemiaEnviron

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr MAREK MRÁZ**

Host Institution: **Masarykova univerzita - CZ**

SIGNALING PROPENSITY IN THE MICROENVIRONMENT OF B CELL CHRONIC LYMPHOCYTIC LEUKEMIA

B cell chronic lymphocytic leukemia (CLL) is the most frequent leukemia in adults. CLL cells are characterized by their universal dependency on pro-survival and pro-proliferative signals from immune niches. To achieve this they constantly re-circulate between blood and lymph nodes, which is inhibited by novel microenvironment-targeting therapies such as “BCR inhibitors”. We aim to reveal how the malignant B cells change the propensity of their signalling pathways in response to the different microenvironments such as peripheral blood vs lymph node to obtain the proliferative signals. This is of major relevance for CLL, but also transferable to the biology of some other B cell malignancies and/or normal B cells. We analyzed the “finger print” of microenvironmental interactions in many CLL samples at various times during the disease course or during therapy. The obtained data led us to hypothesize on the mechanisms of regulation of signalling propensity of two pathways that are responsible for proliferation and survival of CLL cells, namely B Cell Receptor (BCR) signalling and signals from T-cells mediated by CD40/IL4. In aim 1 we hypothesize that CD20 is one of the key proteins involved in CLL cell activation, and influences BCR and interleukin signalling (see figure). This has important therapeutic implication since CD20 is used as a therapeutic target for 20 years (rituximab), but its function in CLL/normal B cells is unknown. In aim 2 we hypothesize that miR-29 acts a key regulator of T-cell signalling from CD40 and downstream NFkB activation (see figure). This represents the first example of miRNAs’ role in the propensity of T-cell interaction, and could be also utilized therapeutically. In aim 3 we will integrate our data on microenvironmental signaling (aim 1+2) and develop a first mouse model for PDX that would allow stable engraftment of primary CLL cells. Currently, CLL is non-transplantable to any animal model which complicates studies of its biology.

Link to the ERC project webpage: ceitec.cz/mrazlab

Keywords of the ERC project: BCR signalling; T cell interactions; development of targeted therapy for CLL; biomarkers of resistance to therapy; mouse model for PDX in chronic lymphocytic leukemia; ibrutinib; B cells; chronic lymphocytic leukemia; BCR inhibitors

Keywords that characterize the scientific profile of the potential visiting researcher/s: BCR signalling; B cells; CLL; chronic lymphocytic leukemia; lymphoma; BCR inhibitors



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802825

Project Acronym:

EnDeCAD

Evaluation Panel:

LS4
Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr MINNA KAIKKONEN-MÄÄTTÄ**

Host Institution: **ITA-SUOMEN YLIOPISTO - FI**

Enhancers Decoding the Mechanisms Underlying CAD Risk

In recent years, genome-wide association studies (GWAS) have discovered hundreds of single nucleotide polymorphisms (SNPs) which are significantly associated with coronary artery disease (CAD). However, the SNPs identified by GWAS explain typically only small portion of the trait heritability and vast majority of variants do not have known biological roles. This is explained by variants lying within noncoding regions such as in cell type specific enhancers and additionally 'the lead SNP' identified in GWAS may not be the 'the causal SNP' but only linked with a trait associated SNP. Therefore, a major priority for understanding disease mechanisms is to understand at the molecular level the function of each CAD loci. In this study we aim to bring the functional characterization of SNPs associated with CAD risk to date by focusing our search for causal SNPs to enhancers of disease relevant cell types, namely endothelial cells, macrophages and smooth muscle cells of the vessel wall, hepatocytes and adipocytes. By combination of massively parallel enhancer activity measurements, collection of novel eQTL data throughout cell types under disease relevant stimuli, identification of the target genes in physical interaction with the candidate enhancers and establishment of correlative relationships between enhancer activity and gene expression we hope to identify causal enhancer variants and link them with target genes to obtain a more complete picture of the gene regulatory events driving disease progression and the genetic basis of CAD. Linking these findings with our deep phenotypic data for cardiovascular risk factors, gene expression and metabolomics has the potential to improve risk prediction, biomarker identification and treatment selection in clinical practice. Ultimately, this research strives for fundamental discoveries and breakthrough that advance our knowledge of CAD and provides pioneering steps towards taking the growing array of GWAS for translatable results.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

805201

Project Acronym:

METANICHE

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr ANJALI KUSUMBE**

Host Institution: THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF
OXFORD - UK

Regulation of bone metastases by age-associated angiocrine signals

Blood vessels form a versatile transport network and provide inductive signals called angiocrine factors to regulate tissue-specific functions. Blood vessels in bone are heterogeneous with distinct capillary subtypes that exhibit remarkable alterations with age. Bone is the most prevalent site of metastasis, and ageing is linked to the reactivation of dormant tumor cells (dorTCs) and metastatic relapse. Bone remodeling processes are also associated with metastatic relapse. Here, I will define the role of distinct vascular niches in regulating the fate of DTCs in bone. Finally, I will unravel the age-related angiocrine factors and identify key angiocrine signals that drive the reactivation of dorTCs. I will employ a powerful combination of advanced 3D, intravital, and whole body imaging, cell specific-inducible mouse genetics, transcriptional profiling and bioinformatics in an unprecedented manner to achieve my goals. New cutting-edge techniques such as advanced 3D and 4D bone imaging are important aspects of my proposal. I will also define the role of highly promising novel candidate age-related angiocrine signals with sophisticated inducible endothelial-specific humanised mouse models. My work will break new ground by unraveling a repertoire of age-related angiocrine factors and will contribute to a wider scientific community in bone, blood, and age-related diseases. This interdisciplinary work at the frontiers of bone, cancer and vascular biology will provide the first conceptual link between vascular ageing and bone metastasis and will contribute towards the development of therapeutic strategies for targeting DTCs in bone.

Link to the ERC project webpage:

Keywords of the ERC project: bone marrow microenvironment, ageing, angiogenesis, bone metastasis

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

819600

Project Acronym:

FIRM

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr MICHELANGELO CAMPANELLA**

Host Institution: **THE ROYAL VETERINARY COLLEGE - UK**

Form and Function of the Mitochondrial Retrograde Response

The molecular communication between mitochondria and nucleus is an integrated bi-directional crosstalk - anterograde (nucleus to mitochondria) and retrograde (mitochondria to nucleus) signalling pathways. The mitochondrial retrograde response (MRR) is driven by defective mitochondrial function, which increases cytosolic reactive oxygen species (ROS) and Ca^{2+} . Metabolic reprogramming is a key feature in highly proliferative cells to meet the energy needs for rapid growth by generating substrates for cellular biogenesis. In these mitochondria retro-communicate with the nucleus to induce wide-ranging cytoprotective effects exploited to develop resistance against treatment and sustain uncontrolled growth. Recently, the mitochondrial management of cholesterol-derived intermediates for the synthesis of steroids has been demonstrated as a determinant in the oncogenic reprogramming of cellular environment.

We hypothesise that cholesterol-enriched domains facilitate the communication between remodelled mitochondria and nucleus to expedite MRR. This mechanism may be exploited during abnormal cell growth in which cholesterol metabolism and associated molecules are increased.

This application capitalizes on expertise in cell signalling and metabolism to interrogate core pathways and unveil molecular sensors and effectors that define form and function of the MRR by:

- I. Elucidating the mechanism of metabolic regulation of MRR, describing the role exerted by cholesterol trafficking;
- II. Unveiling microdomains for mito-nuclear communication established by remodelled, autophagy escaped, mitochondria;
- III. Validating protocols to modulate and target MRR for diagnostic and therapeutic benefit;

The experimental plan will (i) define a molecular signalling axis that currently stands uncharacterized, (ii) provide mechanistic knowledge for preventive, and (iii) therapeutic applications to counteract deficiencies associated with stressed, dysregulated mitochondria.

Link to the ERC project webpage:

Keywords of the ERC project: Mitochondria, Quality Control, Contact Sites, Pharmacology, Signalling

Keywords that characterize the scientific profile of the potential visiting researcher/s: Mitochondria, Autophagy, Pharmacology Inter-organelles Communication, Signalling



European Research Council
Executive Agency

Established by the European Commission

Project ID:

850622

Project Acronym:

MOLEC ANTI-ARRHYT

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr SARA LIIN**

Host Institution: LINKOPINGS UNIVERSITET - SE

Resilience and Trigger Factors in Cardiac Arrhythmia: Risk Stratification and Drug Design

Up to 30% of individuals with inherited cardiac arrhythmias such as Long QT syndrome are not protected from sudden cardiac death despite state-of-the-art treatment. A major hurdle for effective risk stratification and treatment of inherited cardiac arrhythmias is the poor correlation between genetic variant and clinical manifestations. Affected individuals, who harbour the same arrhythmia-causative mutation, paradoxically display a spectrum of clinical phenotypes ranging from a lifelong asymptomatic state to sudden death in infancy. Up to 40% of genotype-positive individuals, depending on type of arrhythmia, do not display clinical manifestation. Based on our unpublished observations, I propose that an important, yet unexplored, underlying cause of the diverse clinical manifestations are endogenous resilience and trigger factors, which interact with mutated cardiac ion channels to alter arrhythmia severity. MOLEC ANTI-ARRHYT utilizes front-line experimental and computational approaches and the cardiac IKs potassium channel, which is strongly linked to lethal arrhythmias and sudden cardiac death, as a prototype. We aim to: (i) identify major classes of endogenous ligands with therapeutic (resilience factors) or pathological (trigger factors) effects on the IKs channel, (ii) provide proof of mechanism for how the effect of resilience and trigger factors is determined by arrhythmia-causative mutations in the IKs channel, (iii) utilize resilience mechanisms to develop a fundamentally novel concept of anti-arrhythmic drug development: Resilience-Mimetic Drug Development. The successful completion of this project will open up new avenues for personalized risk stratification and clinical management, which ultimately will improve the clinical outcome for individuals with inherited arrhythmias.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

852343

Project Acronym:

EPICAMENTE

Evaluation Panel:

LS4
Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr SARA SDELCI**

Host Institution: **FUNDACIO CENTRE DE REGULACIO GENOMICA - ES**

At the epigenetics-cancer metabolism interface

Epigenetic regulation and metabolism are of great interest in cancer research. However, physical and functional connections between these two areas remain largely unexplored. While it is commonly believed that metabolites can randomly distribute inside the cell, recent evidence rather favors the hypothesis that production of certain metabolites in specific subcellular compartments orchestrates different cellular processes. EPICAMENTE aims at exploring whether the localization of enzymatic activities on chromatin can integrate cancer metabolism with chromatin remodeling to control epigenetic regulation and tumor progression. First, I aim at providing a dataset of chromatin-bound metabolic enzymes in a comprehensive panel of cancer cell lines. By combining a chromatin fluorescent reporter cell line strategy with epigenomic approaches, I will define the epigenetic and transcriptional scenarios orchestrated by chromatin-bound metabolic enzymes, and investigate their relevance in cancer cell proliferation. Performing genetic screenings with the chromatin fluorescent reporter cell lines will allow the identification of genetic interactors mediating the epigenetic role of chromatin-bound metabolic enzymes. In parallel, I aim to screen for small molecules able to counteract the epigenetic states mediated by those metabolic enzymes. Finally, I will validate my results in in vivo cancer models, thus adding an important translational aspect to the project, and opening up new opportunities for cancer therapy. The success of this project can impact our fundamental understanding of cellular and cancer biology. In most cases, the belief is that intracellular materials reside inside steady-state membrane-based compartments, which limit the interactions between different molecular pathways. By describing the role of chromatin-bound metabolic enzymes and discovering direct connections between cancer metabolism and epigenetic regulation, I will scrutinize this belief.

Link to the ERC project webpage:

Keywords of the ERC project: epigenetic, cancer, metabolism, screening, compounds, reporter, Warburg, transcription, chromatin

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

716379

Project Acronym:

MetResistance

Evaluation Panel:

LS4
Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr BINZHI QIAN**

Host Institution: **THE UNIVERSITY OF EDINBURGH - UK**

The role of tumour microenvironment in metastatic hormone-refractory prostate cancer

The goal of this proposal is to investigate the role of tumor microenvironment in metastatic hormone-refractory prostate cancer (mHRPC). Prostate Cancer (PC) is the most common malignancy in men in Europe while mHRPC is the most lethal form of the disease, causing over 95% of PC related deaths. Extensive clinical and preclinical research using state-of-the-art tumour models has led to the development of several new therapeutics that, unfortunately, provide only marginal patient benefit. One key element missing in standard preclinical models is the relevant metastasis microenvironment associated with mHRPC that may dramatically affect disease outcome. Here, I plan to significantly advance our understanding in mHRPC associated microenvironment with the first androgen dependent PC bone metastasis model I developed that mimics both the pathology and disease progression in patients. My preliminary data indicate that metastasis associated stromal cells may form a unique bone metastasis microenvironment that promotes mHRPC. I aim to identify the underlying molecular mechanisms using a multidisciplinary approach combining intra-vital microscopy, dynamic ADT resistance reporter system, innovative adoptive transfer approach and genetic tools of lineage specific knockout. This work is also designed to translate findings made in mouse models into human disease using innovative humanized in vivo models of mHRPC. The findings generated in this project will lead to innovative therapeutic approaches that can effectively treat mHRPC thus relieve this lethal threat on European societies. MetResistance will make a step change in the field of cancer medicine research by providing new standards to study therapy resistance of metastatic cancer an area representing the number one challenge in cancer research and patient care.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

804135

Project Acronym:

INVADERS

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr BENOIT CHASSAING**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Mucus-Penetrating Microbiota: Characterization, Mechanism and Therapeutic in Metabolic Disease

Mucus-Penetrating Microbiota: Characterization, Mechanism and Therapeutic in Metabolic Disease

Humanity is facing an epidemic of inter-related metabolic disorders, including obesity, insulin resistance, hyperglycemia, hyperlipidemia, and hepatic steatosis, that altogether have major impact on the promotion of cardiovascular diseases. The increasing incidence of these complex metabolic disorders and their highly morbid, chronic and costly downstream diseases threatens to overwhelm the world's health care systems and economies, making it a top public health priority in dire need of investigation.

The intestinal tract is inhabited by a large and diverse community of bacteria, collectively referred to as the intestinal microbiota. When stably maintained at an appropriately safe distance from the epithelial cell monolayer, the microbiota provides important benefits to its host. However, disturbance of the microbiota-host relationship, promoted by genetic or non-genetic factors, can alter intestinal homeostasis and drive chronic low-grade intestinal inflammation, ultimately leading to metabolic abnormalities. We previously reported that a ubiquitous class of food additives, emulsifiers, detrimentally impact the microbiota resulting in its encroachment into the mucus layer that associated with low-grade inflammation and development of metabolic disorders.

The central goal of this proposal is to investigate the hypothesis that bacteria that penetrate the inner part of the mucus layer, referred as invaders, promote development of metabolic alterations.

We herein propose to identify mucus-invaders, in preclinical models and clinical conditions, and investigate mechanisms by which they promote inflammatory and metabolic abnormalities. Furthermore, we propose to define original approaches to modulate the intestinal microbiota in order to counteract microbiota encroachment and protect against associated metabolic abnormalities.

Link to the ERC project webpage: <https://www.chassainglab.com/>

Keywords of the ERC project: Microbiota, Inflammation, Mucus

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

804418

Project Acronym:

The Matrix

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr EMMA BORGESON**

Host Institution: **GOETEBORGS UNIVERSITET - SE**

Inflammatory resolution and remodelling of the adipose extracellular matrix: key determinants of a metabolically healthy phenotype?

Obesity and its affiliated metabolic diseases pose serious public-health challenges. However, certain patient subgroups appear protected. To halt the socio-economic burden of metabolic disease, we urgently need to understand what distinguishes the Metabolically-Healthy-Lean (MHL), Metabolically-Unhealthy-Lean (MUL), Metabolically-Healthy-Obese (MHO) and Metabolically-Unhealthy-Obese (MUO) phenotypes, and which factors promote metabolic health. Inflammation has been proposed as a target, as it is a key driver of metabolic disease. However, clinical trials show limited evidence that anti-inflammatory drugs reduce diabetes. Why is that?

Inflammation consists of a pro-inflammatory phase followed by a pro-resolving phase, which are regulated by different cells/pathways. This is critical to consider when attempting a therapeutic approach. Based on my preliminary data, I hypothesise that what separates MHL/MHO from MUL/MUO are not pro-inflammatory triggers, but rather the endogenous ability of individuals to resolve inflammation. Adipose extracellular-matrix remodelling appears critical, and pro-resolving lipids promote a MUO-to-MHO switch.

My overall goal is to determine molecular pathways that differentiate the MHL/MUL/MHO/MUO phenotypes (Aim 1-4), and to investigate the therapeutic potential of pro-resolving lipids (Aim 5). This multi-disciplinary project combines cutting-edge techniques with state-of-the-art translational approaches. Through my unique access to human biobanks, I will generate patient-specific cell-lines and test drug-targets *ex vivo*. Novel bioinformatics pipelines will produce protein/lipid/metabolite fingerprints associated with respective patient groups, ultimately providing a new approach to tackle obesity-related comorbidities. My experience in the specialised field of pro-resolving lipid biology, coupled with my lab's unique placement at a translational site, makes me the right candidate to lead this research program.

Link to the ERC project webpage: <https://www.borgesonlab.org/>

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s: Inflammation, resolution, lipoxin, metabolic disease, obesity



European Research Council
Executive Agency

Established by the European Commission

Project ID:

819543

Project Acronym:

MetaboSENS

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr GANNA PANASYUK**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Metabolic integration by nutrient SENSing

Nutrient sensing enables metabolic homeostasis by matching energy use with fuel availability. The vast body of knowledge on pro-anabolic nutrient sensors, such as insulin and class 1 phosphoinositide-3 kinase (PI3K) signalling exposed the missing links in molecular coordination of catabolism. The cellular catabolism relies on mitochondrial activities and on lysosomal pathway of autophagy, both paced by the biological clock. However, how pro-catabolic nutrient sensors synchronize these catabolic activities is not well understood. We discovered that class 3 PI3K, the only PI3K present in all eukaryotes, is essential for catabolic homeostasis in vivo, but the mechanisms of its metabolic functions are still lacking. We found novel roles for class 3 PI3K in metabolic adaptation to fasting and mitochondrial activity, beyond its established functions in autophagy and endosomal trafficking. These findings form the basis of our innovative interdisciplinary research program that will investigate the molecular bases of Metabolic integration in vivo by a nutrient SENSing pathway of class 3 PI3K (MetaboSENS). In the MetaboSENS research program, we seek to identify transcription factor networks and regulatory complexes of class 3 PI3K that serve its catabolic integrator function. We aim to reveal the physiological oscillation of class 3 PI3K signalling and its reciprocal impact on metabolic timekeeping. Finally, the MetaboSENS project will combine patient analyses and the medical expertise of my team to reveal, for the first time, genetic alterations in class 3 PI3K signalling in inborn metabolic disease. The new mechanisms that we discover may provide therapeutic targets that we will test in the pre-clinical models. Altogether, the MetaboSENS project will redefine our view of systemic catabolism.

Link to the ERC project webpage: www.panasyuklab.fr

Keywords of the ERC project: metabolic homeostasis, nutrient sensing, catabolism, class 3 phosphoinositide 3-kinase, Vps15/Vps34, nuclear receptor transcription factors, autophagy, lysosome, endocytic trafficking, human rare liver disease

Keywords that characterize the scientific profile of the potential visiting researcher/s: motivated, pro-active, creative early career researcher (MD or PhD) with experience in cell biology, molecular biology, animal models and/or human genetics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

833440

Project Acronym:

IMMUNOTHROMBOSIS

Evaluation Panel:

LS4

Physiology,
Pathophysiology and
Endocrinology

Principal Investigator: **Dr STEFFEN MASSBERG**

Host Institution: **LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN - DE**

Cross-talk between platelets and immunity - implications for host homeostasis and defense

The overall aim of the IMMUNOTHROMBOSIS project is to clarify the mechanisms underlying the recently identified synergism between thrombosis and inflammation. Thrombus formation and inflammation are vital host responses that ensure homeostasis, but can also drive cardiovascular disease, including myocardial infarction and stroke, the major causes of death in Europe. My group and others discovered, that thrombosis and inflammation are not to be considered separate processes. They are tightly interrelated and synergize in immune defence, but also in inflammatory and thrombotic diseases in a process we termed immunothrombosis. Targeting this synergism has great potential to identify innovative and unconventional strategies to more specifically prevent undesired activation of thrombotic and inflammatory pathways. However, this requires a deeper mechanistic understanding of immunothrombosis. I recently identified two ground-breaking novel immunothrombotic principles: I discovered that platelets have the ability to migrate autonomously, which assists immune cells in fighting pathogens. Further, I revealed that immune cells play a central role in controlling the production of platelets from their megakaryocyte precursors. The physiological and pathophysiological relevance of both processes is unclear. This is the starting point and focus of the IMMUNOTHROMBOSIS project. My aim is to define how platelets use their ability to migrate to support immune cells in protection of vascular integrity (objective 1) and to identify the contribution of platelet migration to different cardiovascular diseases involving immunothrombotic tissue damage (objective 2). Finally, I will clarify how inflammatory responses feedback to the production of thrombotic effectors and dissect inflammatory mechanisms that control platelet production (objective 3). IMMUNOTHROMBOSIS will identify new options for specific prevention or treatment of thrombotic and inflammatory cardiovascular diseases.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

678307

Project Acronym:

WIRELESS

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr LUCA BONINI**

Host Institution: **UNIVERSITA DEGLI STUDI DI PARMA - IT**

Motor and cognitive functions of the monkey premotor cortex during free social interactions

A number of studies demonstrated that the primates' premotor cortex (PM) plays a crucial role not only in organizing movement, but also in perceptual and socio-cognitive functions. However, these studies have been carried out in laboratory settings, which deeply limit the possibility to understand the neural mechanisms underlying natural behaviours. To solve this problem, I propose a new approach consisting in a two-steps chronic recording of monkey PM neurons: first, single neurons response properties will be characterized in a traditional, head-restrained laboratory setting; then, in the same session, the same neurons activity will be recorded wirelessly during free interactions of the monkey with its physical and social environment. The project will initially focus on neurons belonging to the forelimb representation of the ventral (i.e. areas F4 and F5) and dorsal (area F2vr) PM, putatively well known for their role in sensorimotor transformations, goal coding, representation of space, and recognition of other's observed actions. The same paradigm will then be applied to the study of the mesial pre-supplementary area F6, a crucial bridge between prefrontal and PM regions whose role in socio-cognitive functions remains still virtually unknown. Finally, by simultaneous, chronic recording of neuronal activity from lateral and mesial PM, we will first assess the functional interactions between these areas in both laboratory and natural settings, and then we will probe causality in these interactions by chemically manipulating neuronal activity of one region (i.e. F6) while recording from the other one (i.e. F5). The project will reveal the role of premotor cortex in motor and social functions during natural behaviours. In addition, it might open up new possibilities for future studies of neural plasticity and reorganization of ethologically-relevant motor, cognitive and social functions following chemical manipulation of neural activity and virtual brain lesions.

Link to the ERC project webpage: www.boninilab.unipr.it

Keywords of the ERC project: mirror neurons; peripersonal space; motor control; monkey; social interaction

Keywords that characterize the scientific profile of the potential visiting researcher/s: neurophysiology; data analysis; neuroethology; animal behaviour



European Research Council
Executive Agency

Established by the European Commission

Project ID:

681607

Project Acronym:

SolutionSleep

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr PENNY LEWIS**

Host Institution: **CARDIFF UNIVERSITY - UK**

Understanding creativity and problem solving through sleep-engineering

Innovative problem solving is critical for all spheres of organised endeavour, including science and industry, and thus forms the cornerstone of a successful society. Such creative thinking often requires suppression of preconceptions and restructuring of existing knowledge. Pioneering work has shown that sleep facilitates problem solving, but exactly how, and which sleep characteristics are important, remain to be determined. We know that recent experiences are replayed in sleep, and that in Slow Wave Sleep (SWS) this replay integrates new knowledge with old. The role of such replay in Rapid Eye Movement (REM) sleep, a stage which is strongly linked to creativity, is unknown. Here, I propose a model which combines physiology, behavioural studies, and computational modelling to make testable predictions about the complimentary contributions of memory replay in REM and SWS to problem solving. I will test this model through explicit manipulation of memory replay in sleep. I will use a very recently developed technique to explicitly trigger memory replay, a pioneering method for quantifying this replay, and cutting-edge approaches for manipulation of neural oscillations during sleep. I expect two key results: first, I will uncover the principles of how memory replay in REM and SWS combines with specific neural oscillations to promote both long-term memory and creative problem solving. This will involve development of a computational model which will enable optimised experimental design, paving the way for efficient future investigation of how to enhance innovation through manipulation of sleep. Second, I will develop methods for boosting key sleep processes in a selective, targeted manner. Immediate consequences will include a translational project to facilitate everyday problem solving. My findings will revolutionise the understanding of sleep and how it impacts upon some of our most important cognitive abilities—memory and problem solving.

Link to the ERC project webpage: <https://www.cardiff.ac.uk/research/explore/research-units/neuroscience-and-psychology-of-sleep-lab-naps>

Keywords of the ERC project: sleep, memory, consolidation, creativity, abstraction, replay

Keywords that characterize the scientific profile of the potential visiting researcher/s: EEG, sleep, memory, creativity, MEG, fMRI



European Research Council
Executive Agency

Established by the European Commission

Project ID:

683154

Project Acronym:

AstroWireSyn

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr NATHALIE ROUACH**

Host Institution: **COLLEGE DE FRANCE - FR**

Wiring synaptic circuits with astroglial connexins: mechanisms, dynamics and impact for critical period plasticity

Brain information processing is commonly thought to be a neuronal performance. However recent data point to a key role of astrocytes in brain development, activity and pathology. Indeed astrocytes are now viewed as crucial elements of the brain circuitry that control synapse formation, maturation, activity and elimination. How do astrocytes exert such control is matter of intense research, as they are now known to participate in critical developmental periods as well as in psychiatric disorders involving synapse alterations. Thus unraveling how astrocytes control synaptic circuit formation and maturation is crucial, not only for our understanding of brain development, but also for identifying novel therapeutic targets.

We recently found that connexin 30 (Cx30), an astroglial gap junction subunit expressed postnatally, tunes synaptic activity via an unprecedented non-channel function setting the proximity of glial processes to synaptic clefts, essential for synaptic glutamate clearance efficacy. Our work not only reveals Cx30 as a key determinant of glial synapse coverage, but also extends the classical model of neuroglial interactions in which astrocytes are generally considered as extrasynaptic elements indirectly regulating neurotransmission. Yet the molecular mechanisms involved in such control, its dynamic regulation by activity and impact in a native developmental context are unknown. We will now address these important questions, focusing on the involvement of this novel astroglial function in wiring developing synaptic circuits.

Thus using a multidisciplinary approach we will investigate:

- 1) the molecular and cellular mechanisms underlying Cx30 regulation of synaptic function
- 2) the activity-dependent dynamics of Cx30 function at synapses
- 3) a role for Cx30 in wiring synaptic circuits during critical developmental periods

This ambitious project will provide essential knowledge on the molecular mechanisms underlying astroglial control of synaptic circuits.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

758604

Project Acronym:

ENTRAINER

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr RAFAEL POLANIA**

Host Institution: **EIDGENOESSISCHE TECHNISCHE HOCHSCHULE ZUERICH - CH**

Enhancing brain function and cognition via artificial entrainment of neural oscillations

Neural oscillations are ubiquitous in the human brain and have been implicated in diverse cognitive functions to support both neural communication and plasticity. Their functional relevance is further supported by a large number of studies linking various cognitive deficits (e.g., attention deficit hyperactivity disorder, ADHD) with abnormal neural oscillations. However, this field of research faces two important problems: First, there is only correlative, but no causal evidence linking cognitive deficits to abnormal neural oscillations in humans. Second, there is virtually no theory-driven mechanistic approach that generates insights into how oscillations within and across neural networks are linked to human behavior. In this project, I propose to take decisive steps to provide a long-needed neurophysiological characterization—via (1) computational modelling, (2) electrophysiological measures, and (3) novel non-invasive manipulations of cortical rhythms—on how neural oscillations contribute to two types of cognitive processes that are fundamental for many aspects of human behavior: attention and short-term memory. I will go a step further by demonstrating that it is possible to augment performance in these cognitive functions with the design of non-invasive brain stimulation protocols individually tailored to the theory-driven neurocomputational characterizations and electrophysiological signatures of each individual. This will result in the applied goal of deriving new neuro-computational assays that can detect deviant network interactions causally related to cognitive functions, which is key for then renormalizing those functions in neuropsychological conditions such as ADHD. Thus, if successful, my proposed work will ultimately result in novel, low-cost, and painless non-invasive neural interventions for a wide range of neuropsychological disorders tied to abnormal neural oscillations.

Link to the ERC project webpage: <https://decision.ethz.ch/>

Keywords of the ERC project: decision making, brain stimulation

Keywords that characterize the scientific profile of the potential visiting researcher/s: neuro-computational modeling, programming (R, C++, Matlab)



European Research Council
Executive Agency

Established by the European Commission

Project ID:

770951

Project Acronym:

CLAUSTRUM

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr AMI CITRI**

Host Institution: **THE HEBREW UNIVERSITY OF JERUSALEM - IL**

The Claustrum: A Circuit Hub for Attention

Our senses face a constant barrage of information. Hence, understanding how our brain enables us to attend to relevant stimuli, while ignoring distractions, is of increasing biomedical importance. Recently, I discovered that the claustrum, a multi-sensory hub and recipient of extensive neuromodulatory input, enables resilience to distraction.

In my ERC project, I will explore the mechanisms underlying claustral mediation of resilience to distraction and develop novel approaches for assessing and modulating attention in mice, with implications for humans. Transgenic mouse models that I identified as enabling selective access to claustral neurons overcome its limiting anatomy, making the claustrum accessible to functional investigation. Using this novel genetic access, I obtained preliminary results strongly suggesting that the claustrum functions to filter distractions by adjusting cortical sensory gain.

My specific aims are: 1) To delineate the mechanisms whereby the claustrum achieves sensory gain control, by applying in-vivo cell-attached, multi-unit and fiber photometry recordings from claustral and cortical neurons during attention-demanding tasks. 2) To discriminate between the functions of the claustrum in multi-sensory integration and implementation of attention strategies, by employing multi-sensory behavioral paradigms while modulating claustral function. 3) To develop validated complementary physiological and behavioral protocols for adjusting claustral mediation of attention via neuromodulation.

This study is unique in its focus and aims: it will provide a stringent neurophysiological framework for defining a key mechanism underlying cognitive concepts of attention, and establish a novel platform for studying the function of the claustrum and manipulating its activity. The project is designed to achieve breakthroughs of fundamental nature and potentially lead to diagnostic and therapeutic advances relevant to attention disorders.

Link to the ERC project webpage: www.citrilab.com

Keywords of the ERC project: claustrum physiology anatomy reward attention photometry neuropixels patch-clamp mice behavior

Keywords that characterize the scientific profile of the potential visiting researcher/s: physiologist behaviourist attention prefrontal



European Research Council
Executive Agency

Established by the European Commission

Project ID:

786949

Project Acronym:

HOWPER

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr EHUD AHISSAR**

Host Institution: **WEIZMANN INSTITUTE OF SCIENCE - IL**

An open or closed process: Determining the global scheme of perception

Despite decades of intensive research, there is no agreement about the general scheme of perception: Is the external object a trigger for a brain-internal process (open-loop perception, OLP) or is the object included in brain dynamics during the entire perceptual process (closed-loop perception, CLP)? HOWPER is designed to provide a definite answer to this question in the cases of human touch and vision. What enables this critical test is our development of an explicit CLP hypothesis, which will be contrasted, via specific testable predictions, with the OLP scheme. In the event that CLP is validated, HOWPER will introduce a radical paradigm shift in the study of perception, since almost all current experiments are guided, implicitly or explicitly, by the OLP scheme. If OLP is confirmed, HOWPER will provide the first formal affirmation for its superiority over CLP.

Our approach in this novel paradigm is based on a triangle of interactive efforts comprising theory, analytical experiments, and synthetic experiments. The theoretical effort (WP1) will be based on the core theoretical framework already developed in our lab. The analytical experiments (WP2) will involve human perceivers. The synthetic experiments (WP3) will be performed on synthesized artificial perceivers. The fourth WP will exploit our novel rat-machine hybrid model for testing the neural applicability of the insights gained in the other WPs, whereas the fifth WP will translate our insights into novel visual-to-tactile sensory substitution algorithms.

HOWPER is expected to either revolutionize or significantly advance the field of human perception, to greatly improve visual to tactile sensory substitution approaches and to contribute novel biomimetic algorithms for autonomous robotic agents.

Link to the ERC project webpage:

Keywords of the ERC project: perception, active-sensing, robotics, sensory-substitution, brain-machine-interface

Keywords that characterize the scientific profile of the potential visiting researcher/s: perception, active-sensing, robotics, sensory-substitution, brain-machine-interface



European Research Council
Executive Agency

Established by the European Commission

Project ID:

789054

Project Acronym:

Myel-IN-Crisis

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr DAVID ROWITCH**

Host Institution: THE CHANCELLOR MASTERS AND SCHOLARSOFTHE UNIVERSITY OF
CAMBRIDGE - UK

Myelin at the crossroads of Development and Disease

The oligodendrocyte, the largest cell in mammalian biology, greatly enables central nervous system (CNS) function through production of a single substance: myelin. Oligodendrocytes undergo a dramatic 1-2 day metamorphosis during myelination, increasing their cell surface area ~6500-fold with proteolipid extensions to nerve axons in the CNS white matter. How is this synthetic feat accomplished? We lack a comprehensive understanding of machinery that precisely coordinates transcription, translation, lipid synthesis and energy production. Moreover, how do these mechanisms become so intensively upregulated during myelination? Does this extraordinary transient state put the myelinating oligodendrocyte at risk of death in diseases of white matter? These questions underlie the Aims of the proposal “Myel-IN-crisis.”

I propose (Aim 1) testing whether an “Integrated Synthetic Programme (ISP)” controls oligodendrocyte differentiation, metabolic and synthetic requirements of developmental myelination. In Aim 2, I will investigate roles for “smart sensor” oxygen (HIF) and nutrient (mTOR) pathways in regulating initiation and termination of the ISP. During development, extrinsic white matter injury in preterm infants leads to cerebral palsy, while intrinsic defects in myelin protein PLP1 cause the fatal human leukodystrophy, Pelizaeus-Merzbacher disease (PMD). Preliminary studies indicate transcriptional and translational dysregulation in human PLP1-mutant oligodendrocytes, which become iron overloaded leading to apoptotic cell death. In Aim 3, I propose that either extrinsic (e.g., hypoxia) or intrinsic (e.g., PLP1 mutation) factors promote a “Universal Stress Response (USR)” in the pre-myelinating oligodendrocyte that leads to toxic dysregulation of the ISP. Finally, in Aim 4 we will identify the key pathways of the USR to generate strategies for rescue of myelination with potential translational impact in cerebral palsy and leukodystrophy, multiple sclerosis and stroke.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

789128

Project Acronym:

SENSATIONAL TETHERS

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr GARY LEWIN**

Host Institution: **MAX DELBRUECK CENTRUM FUER MOLEKULARE MEDIZIN IN DER
HELMHOLTZ-GEMEINSCHAFT (MDC) - DE**

Tethers for sensory mechanotransduction: from molecules to perception

Touch sensation is built upon the ability of sensory neurons to detect and transduce nanometer scale mechanical displacements. The underlying process has been termed mechanotransduction: the high sensitivity and speed of which is enabled by direct gating (opening) of ion channels by mechanical force. Force detection is functionally compartmentalized and only takes place at the peripheral endings of sensory neurons in vivo. Two molecules are known to be genetically necessary for touch in many sensory neurons, the force gated ion channel PIEZO2 and its modulator STOML3. However, mechanotransduction complexes in all touch receptors absolutely require tethering to the extracellular matrix for function. Tethering is dependent on large extracellular proteins that are sensitive to site-specific proteases. Here we will not only identify the nature of these tethers, but will develop technology to acutely and reversibly abolish tethers and other mechanotransducer components. We will use genome engineering to tag tether and mechanotransduction components in order to visualize and manipulate these proteins at their in vivo sites of action. By engineering de novo cleavage sites for site-specific proteases we will render tethers and ion channels newly sensitive to normally ineffective proteases in the skin. We will engineer mutations into candidate ion channels that dramatically alter biophysical properties to physiologically "mark" function in vivo. Finally we will develop new behavioural paradigms in mice that allow us to measure touch perception from the forepaw. Psychometric curves for different vibrotactile tasks can then be precisely compared between humans and mice. Furthermore, the impact of acute and reversible manipulation of mechanotransduction on touch perception can be measured. Understanding how molecules assemble to function in a mechanotransduction complex in the skin will open up avenues to develop therapeutic strategies to modulate touch.

Link to the ERC project webpage:

Keywords of the ERC project: mechanotransduction, sensory, touch, pain

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802371

Project Acronym:

DISCONN

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr ALESSANDRO GOZZI**

Host Institution: **FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA - IT**

Neural drivers of functional disconnectivity in brain disorders

A rapidly expanding approach to understanding neural organization is to map patterns of spontaneous neural activity as an index of functional communication and connectivity across brain regions. Fostered by the advent of neuroimaging methods like resting-state fMRI (rsfMRI), this approach has revealed that functional connectivity is almost invariably disrupted in severe psychiatric disorders, such as autism or schizophrenia. However, the neural basis of such functional disconnectivity remains mysterious. What drives brain-wide functional synchronization? And are there shared pathophysiological mechanisms leading to impaired large-scale neural coupling?

This project aims to elucidate the neural drivers of macroscale functional connectivity, as well as its breakdown in brain connectopathies. To achieve this goal, I propose a multi-scale perturbational approach to establish causal relationships between specific neural events and brain-wide functional connectivity via a novel combination of rsfMRI and advanced neural manipulations and recordings in the awake mouse.

By directionally silencing functional hubs as well as more peripheral cortical regions, I will provide a hierarchical description of spontaneous network organization that will uncover regional substrates vulnerable to network disruption. I will also manipulate physiologically-distinct excitatory or inhibitory populations to probe a unifying mechanistic link between excitatory/inhibitory imbalances and aberrant functional connectivity. Finally, to account for the hallmark co-occurrence of synaptic deficits and functional disconnectivity in developmental disorders, I will link cellular mechanisms of synaptic plasticity and learning to the generation of canonical and aberrant spontaneous activity patterns. These studies will pave the way to a back-translation of aberrant functional connectivity into interpretable neurophysiological events and models that can help understand, diagnose or treat brain disorders.

Link to the ERC project webpage:

Keywords of the ERC project: connectivity, fMRI, chemogenetics, optogenetics, mouse, autism, schizophrenia

Keywords that characterize the scientific profile of the potential visiting researcher/s: neural computation, image analysis, neuroscience, electrophysiology



European Research Council
Executive Agency

Established by the European Commission

Project ID:

819496

Project Acronym:

PrefrontalMap

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr OFER YIZHAR**

Host Institution: **WEIZMANN INSTITUTE OF SCIENCE - IL**

Organization and learning-associated dynamics of prefrontal synaptic connectivity

How does experience alter the functional architecture of synaptic connections in neural circuits? This question is particularly pertinent for the complex circuits of the medial prefrontal cortex (mPFC), a high-order associative neocortical area that plays a crucial role in flexible, goal-directed behavior. The mPFC is densely interconnected with cortical and subcortical circuits, and its neurons were shown to undergo substantial experience-dependent structural remodeling that is thought to support learning and memory consolidation. However, little is known regarding the synaptic organization of this complex circuit, and of the functional implications of its experience-dependent structural remodeling. In this proposal, we aim to uncover the organization and learning-associated dynamics of functional connectivity in the mouse mPFC.

To obtain high-resolution maps of cell type-specific synaptic connectivity in the mPFC, we will combine single-cell optogenetic manipulation with calcium imaging and electrophysiology in vitro, and establish the circuit-wide organization of connectivity within and between defined projecting neuron populations. We will test the hypothesis that pyramidal neurons projecting to subcortical targets form tightly interconnected subnetworks, and that inhibitory inputs to these networks, through selective innervation, can modulate information output from the mPFC.

To understand how learning changes the functional synaptic organization of the mPFC, we will establish an all-optical system for interrogation of synaptic connectivity in vivo. We will utilize this powerful platform to test the hypothesis that prefrontal-dependent learning is associated with reorganization of local-circuit functional connectivity among identified subcortically-projecting cell assemblies.

Our innovative technology will be widely applicable for neural circuit analysis in a variety of systems, and allow us to gain new insights into the complex circuitry of the mPFC.

Link to the ERC project webpage:

Keywords of the ERC project: Synaptic connectivity, optogenetics, two-photon imaging, learning

Keywords that characterize the scientific profile of the potential visiting researcher/s: electrophysiology, imaging, patch-clamp



European Research Council
Executive Agency

Established by the European Commission

Project ID:

819814

Project Acronym:

RememberEx

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr BRYAN STRANGE**

Host Institution: **UNIVERSIDAD POLITECNICA DE MADRID - ES**

Human Subcortical-Cortical Circuit Dynamics for Remembering the Exceptional

Our memory system is optimised for remembering the exceptional over the mundane. We remember better those events that violate predictions generated by the prevailing context, particularly because of surprise or emotional impact. Understanding how we form and retrieve long-term memories for important or salient events is critical for combating the rapidly growing incidence of pathologies associated with memory dysfunction with huge socio-economic burden. Human lesion and non-invasive functional imaging data, motivated by findings from animal models, have identified subcortical structures that are critical for upregulating hippocampal function during salient event memory. However, mechanistic understanding of these processes in humans remains scarce, and requires better experimental approaches such as direct intracranial recordings from, and focal electrical stimulation of, these subcortical structures.

This project will characterise human subcortico-cortical neuronal circuit dynamics associated with enhanced episodic memory for salient stimuli by studying direct recordings from human hippocampus, amygdala, nucleus accumbens, ventral midbrain and cortex. Within this framework, I will elucidate the electrophysiological mechanisms underlying amygdala-hippocampal-cortical coupling that lead to better memory for emotional stimuli, extend the hippocampal role in detecting unpredicted stimuli to define its role in orchestrating cortical dynamics in unpredictable contexts, and discover the neuronal response profile of the human mesolimbic dopamine system during salient stimulus encoding. The predicted results, based on my own preliminary data, will offer several conceptual breakthroughs, particularly regarding hippocampal function and the role of dopaminergic ventral midbrain in memory. The knowledge gained from this project is a fundamental requirement for designing therapeutic interventions for patients with memory deficits and other neuropsychiatric disorders.

Link to the ERC project webpage: <http://www.thestrangelab.org/erc-cog-rememberex/>

Keywords of the ERC project: Memory, Emotion, Salience, Hippocampus; Amygdala; Nucleus accumbens; Ventral tegmental area; Human intracranial recordings; functional MRI (fMRI); magnetoencephalography (MEG)

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

682345

Project Acronym:

EPITOR

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr STÉPHANIE BAULAC**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

NEUROBIOLOGY OF EPILEPSY GENES

Ion channel genes have long been linked to Mendelian focal epilepsies, but my recent finding of frequent mutations in DEPDC5 opens completely new perspectives. DEPDC5 is an inhibitor of the mTORC1 (mammalian target of rapamycin) signaling pathway, the master regulator of cell proliferation and growth. Mutations of this gene are found in a wide spectrum of focal epilepsy syndromes, with or without cortical malformations. I propose to examine the links between DEPDC5 and the mTORC1 pathway in cortical development and the genesis of epileptic activity.

My proposal work will combine high-throughput sequencing, in vivo proteomics, biochemistry, electrophysiology, and animal behavior testing (video-EEG). Functional analyses will be made on human postoperative tissue and neuronal cultures from human iPSC and specific rodent models. These approaches will enable me to (1) ask if and how the mTORC1 signaling pathway may contribute to epileptogenesis and seizures in patients with DEPDC5 mutations, (2) attempt to explain the diversity of phenotypes, in particular the presence of cortical lesion by searching for somatic brain mutations in the gene, (3) explore neurobiology pathways and partners of DEPDC5, and (4) identify novel actors for inherited focal epilepsies.

Our results will help us understand the genesis of epileptic networks, and more generally how defects in mTORC1 signaling cascade cause neurologic conditions. We anticipate genetic studies on germline and somatic mutations will have a significant clinical impact for genetic counseling and improved prognosis. The molecules and pathways that will be studied in this proposal differ completely from ion channels and receptors that have been so far associated with focal epilepsies. Thus I hope to provide a new orientation for the field, to identify novel genetic mechanisms and to provide an unbiased route to new molecular therapeutic targets.

Link to the ERC project webpage:

Keywords of the ERC project: Neurogenetics, epilepsy, malformation of cortical development, mouse models682345

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

682622

Project Acronym:

ALS-Networks

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr KABASHI EDOR**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Defining functional networks of genetic causes for ALS and related neurodegenerative disorders

Brain and spinal cord diseases affect 38% of the European population and cost over 800 billion € annually; representing by far the largest health challenge. ALS is a prevalent neurological disease caused by motor neuron death with an invariably fatal outcome. I contributed to ALS research with the groundbreaking discovery of TDP-43 mutations, functionally characterized these mutations in the first vertebrate model and demonstrated a genetic interaction with another major ALS gene FUS. Emerging evidence indicates that four major causative factors in ALS, C9orf72, TDP-43, FUS & SQSTM1, genetically interact and could function in common cellular mechanisms. Here, I will develop zebrafish transgenic lines for all four genes, using state of the art genomic editing tools to combine simultaneous gene knockout and expression of the mutant alleles. Using these innovative disease models I will study the functional interactions amongst these four genes and their converging effect on key ALS pathogenic mechanisms: autophagy degradation, stress granule formation and RNA regulation. These studies will permit to pinpoint the molecular cascades that underlie ALS-related neurodegeneration. We will further expand the current ALS network by proposing and validating novel genetic interactors, which will be further screened for disease-causing variants and as pathological markers in patient samples. The power of zebrafish as a vertebrate model amenable to high-content phenotype-based screens will enable discovery of bioactive compounds that are neuroprotective in multiple animal models of disease. This project will increase the fundamental understanding of the relevance of C9orf72, TDP-43, FUS and SQSTM1 by developing animal models to characterize common pathophysiological mechanisms. Furthermore, I will uncover novel genetic, disease-related and pharmacological modifiers to extend the ALS network that will facilitate development of therapeutic strategies for neurodegenerative disorders

Link to the ERC project webpage:

Keywords of the ERC project: ALS, neurodegeneration, zebrafish, pathogenic pathways, multigenic, drug screening

Keywords that characterize the scientific profile of the potential visiting researcher/s: Drug screening, bioinformatics, omics, analysis



European Research Council
Executive Agency

Established by the European Commission

Project ID:

714762

Project Acronym:

LIFE synapses

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr SIMON WIEGERT**

Host Institution: **UNIVERSITAETSKLINIKUM HAMBURG-EPPENDORF - DE**

Long-term Investigation of Functional Excitatory Synapses: Linking Plasticity, Network Wiring and Memory Storage

The nature of the physical substrate of memory – or engram – is probably one of the longest studied mysteries in neuroscience, and yet it still remains elusive. In recent years, the search for the engram has gained new momentum due to the possibilities of optogenetic activation and silencing of specific neurons in the brain. Recent studies suggest that the engram could be defined as the subset of neurons that is necessary and sufficient to cause recall of a specific memory when activated. But where is the engram when the neurons are not active? Most likely, ‘lasting alterations’ during memory formation are encoded in synaptic connections, forming a specific circuit that is able to trigger memory recall when active. This raises the possibility that the engram could be encoded in a pattern of altered synapses, not a pattern of cell bodies.

Long-lasting potentiation or depression of synaptic efficacy is thought to underlie learning and memory formation suggesting that the engram could be stored in the strength of synapses. Yet, most excitatory synapses in the brain are highly plastic and show pronounced morphological dynamics. It is therefore not clear to what extent engrams can be stored in a network of synapses and how functional and structural changes of individual synapses contribute to the engram.

The central aim of this proposal is to identify synapses participating in the engram and to study their morphological stability and pre- and postsynaptic functional properties. With novel optogenetic approaches and molecular markers we will investigate functional synapses in their native circuit over the time scale of weeks. By connecting functional long-term analysis of single synapses with morphological observations the proposed project will fill a wide gap in our understanding of how synapses encode and store information. I anticipate that my work will transform our knowledge about the location and mechanism of memory storage in the brain.

Link to the ERC project webpage: simon-wiegert.com

Keywords of the ERC project: synapses, 2-photon imaging, optogenetics, neuroscience

Keywords that characterize the scientific profile of the potential visiting researcher/s: data analysis, neuroscience, optics, imaging



European Research Council
Executive Agency

Established by the European Commission

Project ID:

726280

Project Acronym:

Spontaneous Zebbrain

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr GERMAN SUMBRE**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Whole-brain dynamics underlying self-generated behaviour

The first behavioural theories conceived the organism as primarily driven by external sensory stimuli. However, the energy associated with momentary demands of the environment represent ~1% of the brain's total energy budget, implying that the intrinsic activity represents a major aspect of the brain's function. Indeed, more recent theories such as cognitivism and embodiment describe the organisms as capable of generating complex behaviours emerging from the brain's intrinsic dynamics.

Past and current studies that investigated the neuronal basis self-generated behaviours mainly focus on the readiness potential (RP) signal, a build-up ramping activity in the premotor cortex, occurring ~ 2 sec before the movement's onset. However, the neuronal mechanisms underlying the generation of self-generated behaviours (how RPs are generated), the involvement of other regions, and how the brain codes the impending movements (activity predictive of the onset and type of movement), still remain poorly understood.

The combination of light-sheet microscopy, optogenetics, and the zebrafish larva model enables monitoring whole-brain dynamics in an intact behaving vertebrate. Moreover, the diverse yet limited and well described repertoire of motor behaviours will enable to perform experiments in more natural unconstrained conditions, in comparison to previous studies, which were structured in trials and limited to one or two behavioural choices. These advantages will allow us to go beyond the current state-of-the-art in the field. More specifically, we propose to investigate the following specific aims:

- 1) Whole-brain dynamics basis and mechanisms underlying self-generated behaviours.
- 2) A comparison between the neuronal pathways underlying the initiation of self-generated and sensory induced behaviours.
- 3) The internal and external modulation of self-generated behaviours.

Link to the ERC project webpage: www.zebrain.biologie.ens.fr

Keywords of the ERC project: Neuronal circuit dynamics, motor behaviour, two-photon calcium imaging, light-sheet microscopy, computational neuroscience, zebrafish, criticality, neuroethology

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational neuroscience, neuroscience, physics, big data analysis, mathematics, computer science, quantitative biology



European Research Council
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Established by the European Commission

Project ID:

770244

Project Acronym:

CMTaaRS

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr ERIK STORKEBAUM**

Host Institution: **STICHTING KATHOLIEKE UNIVERSITEIT - NL**

Defective protein translation as a pathogenic mechanism of peripheral neuropathy

Familial forms of neurodegenerative diseases are caused by mutations in a single gene. It is unknown whether distinct mutations in the same gene or in functionally related genes cause disease through similar or disparate mechanisms. Furthermore, the precise molecular mechanisms underlying virtually all neurodegenerative disorders are poorly understood, and effective treatments are typically lacking.

This is also the case for Charcot-Marie-Tooth (CMT) peripheral neuropathy caused by mutations in five distinct tRNA synthetase (aaRS) genes. We previously generated *Drosophila* CMT-aaRS models and used a novel method for cell-type-specific labeling of newly synthesized proteins *in vivo* to show that impaired protein translation may represent a common pathogenic mechanism.

In this proposal, I aim to determine whether translation is also inhibited in CMT-aaRS mouse models, and whether all mutations cause disease through gain-of-toxic-function, or alternatively, whether some mutations act through a dominant-negative mechanism. In addition, I will evaluate whether all CMT-aaRS mutant proteins inhibit translation, and I will test the hypothesis, raised by our unpublished preliminary data shown here, that a defect in the transfer of the (aminoacylated) tRNA from the mutant synthetase to elongation factor eEF1A is the molecular mechanism underlying CMT-aaRS. Finally, I will validate the identified molecular mechanism in CMT-aaRS mouse models, as the most disease-relevant mammalian model.

I expect to elucidate whether all CMT-aaRS mutations cause disease through a common molecular mechanism that involves inhibition of translation. This is of key importance from a therapeutic perspective, as a common pathogenic mechanism allows for a unified therapeutic approach. Furthermore, this proposal has the potential to unravel the detailed molecular mechanism underlying CMT-aaRS, what would constitute a breakthrough and a requirement for rational drug design for this incurable disease.

Link to the ERC project webpage:

Keywords of the ERC project: Charcot-Marie-Tooth peripheral neuropathy - aminoacyl tRNA synthetase - *Drosophila* genetics - mouse genetics

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

804824

Project Acronym:

NeuroDevo

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr JULIJANA GJORGJEVA**

Host Institution: **MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN EV
- DE**

Spontaneous and sensory-evoked activity shape neural circuits in the developing brain

To generate brain circuits that are both flexible and stable requires the coordination of powerful developmental mechanisms acting at different scales. How does the brain prepare to efficiently compute information and reliably generate behavior during early development without any previous experience? A prominent transient feature of developing circuits is the ability to generate spontaneous activity before sensory organs mature. We know little about the detailed structure of this activity; however, blocking or perturbing this activity leads to miswiring defects, suggesting its powerful role in shaping local and brain-wide neural circuits. After the onset of sensory experience, ongoing activity continues to modify sensory circuits, and plays an important functional role in the mature brain. Together with advances in experimental techniques, we propose that theory and models are needed to establish a unifying framework of neural circuit development. Using quantitative data analysis, experiment-driven theory and computational modeling, we will derive key principles for how neural circuits are built and organized during early postnatal development into functional units, and how they are modified by intact and perturbed sensory-evoked activity. We will provide a quantitative analysis of longitudinal recordings of single neuron and network activity for the first time by synthesizing data from three collaborating labs. Our goal will be to reveal novel aspects of this activity that drive circuit refinement over a prolonged timescale during development, and to identify the powerful ways in which activity and circuit properties influence each other. Our models will generate and test hypotheses for how individual components affect different aspects of circuit organization during development. Therefore, the unique potential of our theoretical approach lies in dissecting the influence of each developmental process, making predictions to be tested in the real biological system.

Link to the ERC project webpage:

Keywords of the ERC project: cortical development, computational neuroscience, synaptic plasticity

Keywords that characterize the scientific profile of the potential visiting researcher/s: cortical development, synaptic plasticity, calcium imaging



European Research Council
Executive Agency

Established by the European Commission

Project ID:

852869

Project Acronym:

CN Identity

Evaluation Panel:

LS5
Neurosciences and
Neural Disorders

Principal Investigator: **Dr ZHENYU GAO**

Host Institution: **ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM - NL**

Comprehensive anatomical, genetic and functional identification of cerebellar nuclei neurons and their roles in sensorimotor tasks

How does the brain integrate diverse sensory inputs and generate appropriate motor commands? Our cerebellum is a key region for such a sensorimotor processing, empowered by its sophisticated neural computation and constant communication with other brain regions. The well-timed cerebellar information is integrated and funneled to other brain regions through the cerebellar nuclei (CN). Yet, how CN circuitry contributes to the cerebellar control of sensorimotor processing is unclear. My recent work indicates that the CN activity serves various functions ranging from the online motor control, the amplitude amplification of cerebellar outputs to the control of motor planning. Given these advances, I am now in a unique position to decipher the properties of CN neurons and identify their specific roles in different forms of sensorimotor processing. It is my central hypothesis that depending on the specific demands of the task, CN neurons can either facilitate or suppress the activity of downstream regions with millisecond precision; and the anatomical, genetic and functional properties of CN neurons are tailored to the particular task involved. To test this hypothesis, I will 1) identify the activity patterns of different CN modules during the acquisition and execution of two sensorimotor tasks and characterize the relevant extra-cerebellar inputs to these modules; 2) identify the connectivity-transcription logic of different CN modules and link them to their task-specific outputs; and 3) examine the impacts of manipulating anatomically and/or genetically defined CN neurons on the downstream regions during different sensorimotor tasks. I will accomplish these key objectives by developing various novel electrophysiological, optogenetic, molecular and imaging techniques. My research is likely to break new ground, demonstrating that the identity of CN neurons is determined by their differential temporal demands of sensorimotor tasks controlled by different brain structures.

Link to the ERC project webpage: <https://neuro.nl/research/gao>

Keywords of the ERC project: brain circuits, cerebro-cerebellar communication, sensorimotor function, cerebellar nuclei

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Project ID:

714175

Project Acronym:

PLAT-IL-1

Evaluation Panel:

LS6

Immunity and Infection

Established by the European Commission

Principal Investigator: **Dr BERNARDO FRANKLIN**

Host Institution: **UNIVERSITÄTSKLINIKUM BONN - DE**

Pathophysiology of platelet-derived Interleukin 1

The Interleukin (IL)-1 family of pro-inflammatory cytokines are among the most potent pyrogens, and their excessive production can cause several auto-inflammatory syndromes. Additionally, overabundance of IL-1 cytokines can trigger, or contribute to a range of inflammatory and metabolic disorders. The expression of the key members of the IL-1 family, such as IL-1 β and IL-18, is regulated at both the transcriptional and post-transcriptional levels. IL-1 β and IL-18, are produced as inactive precursors, which require activation of caspase-1 by the inflammasomes for their maturation and release by from cells, occasionally at the cost of caspase-1 mediated-cell death. We have recently discovered that inflammasomes are released into the extracellular space where they remain active after the demise of activated cells, and that extracellular inflammasomes can amplify inflammation by sustaining extracellular production of IL-1 β . However, the sources of extracellular pro-IL-1 β are not known. Recent advances in platelet proteomics have revealed that these non-nucleated cells are able to produce their own cytokines, including soluble IL-1 β and membrane-bound IL-1 α , and are able to significantly magnify IL-1 production by immune cells. As platelets outnumber leukocytes by several folds, they could potentially be the major source of extracellular inflammasomes in the body, or be a major producer of IL-1 precursors that are cleaved by extracellular inflammasomes released from dying immune cells. In this proposal, we will investigate the mechanism(s) by which platelets produce IL-1, and the specific contribution of platelet-derived IL-1 to sterile inflammation, or host resistance to bacterial and viral infection. We believe that a deeper understanding of platelet-IL-1 and their interaction with immune cells during sterile inflammation, or infection might help to uncover new targets for immune-therapies.

Link to the ERC project webpage: http://www.iii.uni-bonn.de/franklin_lab/the_ag_franklin_lab.html

Keywords of the ERC project: Inflammation, Inflammasomes, Platelets

Keywords that characterize the scientific profile of the potential visiting researcher/s: Innate Immunity, Pattern

Recognition

Receptors,

NLRP3,

Macrophages



European Research Council
Executive Agency

Project ID:

742195

Project Acronym:

HHMM-Neonates

Evaluation Panel:

LS6
Immunity and Infection

Established by the European Commission

Principal Investigator: **Dr ANDREW J. MACPHERSON**

Host Institution: **UNIVERSITAET BERN - CH**

DEVELOPMENT OF HEALTHY HOST-MICROBIAL MUTUALISM IN EARLY LIFE

Background

Humans and other animals harbour enormous microbial consortia, especially in the lower intestine. My group has now shown that effects of the microbiota on host are far earlier and more pervasive than previously appreciated, starting even before birth from exposure to defined maternal microbial metabolites.

Concept

There is a critical window for development of immunity and metabolism in early life. This shapes infectious resistance, lymphocyte repertoire development and the likelihood of later autoimmune or inflammatory disease. We will determine the molecular mechanisms of how the maternal microbiota prepares the newborn for the critical fetal/suckling/early-independent-nutrition transitions. The core hypothesis is that generally pervasive effects of maternal microbial influences, so-far investigated only for innate immunity and metabolism of germ-free offspring, can be defined in terms of a clear portfolio of maternal microbial molecular signatures and epigenetic marks as the newborn develops with its own microbiota.

Approach

Interdependence of microbial \rightleftharpoons host interactions during gestation and lactation will be dissected using reversible colonisation systems under axenic and precisely controlled gnotobiotic conditions. The flow and identity of maternal microbial metabolites driving development and shaping incoming colonisation shall be determined from high-resolution metabolomics and host strain combinations that reveal in vivo signalling and epigenetic marks.

Significance

The project will reveal mechanisms of the earliest phases of mammalian adaptation to a microbiota, the epigenetic effects of maternal microbial metabolites and the resulting potential protection from metabolic disease or immunopathology. Conversely, there are profound effects of early life adaptation on the dynamics of microbial colonisation and the potential blooms and extinctions for the incoming microbiota: the project will define the different mechanisms involved.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

759226

Project Acronym:

ANTIViR

Evaluation Panel:

LS6

Immunity and Infection

Principal Investigator: **Dr CAROLINE GOUJON**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Molecular mechanisms of interferon-induced antiviral restriction and signalling

Interferons (IFNs), which are signalling proteins produced by infected cells, are the first line of defence against viral infections. IFNs induce, in infected and neighbouring cells, the expression of hundreds of IFN-stimulated genes (ISGs). The ISGs in turn induce in cells a potent antiviral state, capable of preventing replication of most viruses, including Human Immunodeficiency Virus type 1 (HIV-1) and influenza A virus (FLUAV). Identifying the antiviral ISGs and understanding their mechanisms of action is therefore crucial to progress in the fight against viruses.

ISGs playing a role in the antiviral state have been identified, such as human MX1, a well-known antiviral factor able to restrict numerous viruses including FLUAV, and MX2, an HIV-1 inhibitor. Both proteins bind to viral components but their detailed mechanisms of action, as well as the consequences of restriction on the activation of the innate immune system, remain unclear. Moreover, our preliminary work shows that additional anti-HIV-1 and anti-FLUAV ISGs remain to identify.

In this context, this proposal seeks an ERC StG funding to explore 3 major aims: 1) unravelling the mechanisms of antiviral action of MX proteins, by taking advantage of their similar structure and engineered chimeric proteins, and by using functional genetic screens to identify their cofactors; 2) investigating the consequences of incoming virus recognition by MX proteins on innate immune signalling, by altering their expression in target cells and measuring the cell response in terms of gene induction and cytokine production; 3) identifying and characterizing new ISGs able to inhibit viral replication with a combination of powerful approaches, including a whole-genome CRISPR/Cas9 knock-out screen.

Overall, this proposal will provide a better understanding of the molecular mechanisms involved in the antiviral effect of IFN, and may guide future efforts to identify novel therapeutic targets against major pathogenic viruses.

Link to the ERC project webpage:

Keywords of the ERC project: antiviral restriction, interferon, HIV, influenza virus, crispr/cas9 screens

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

771714

Project Acronym:

FatTryp

Evaluation Panel:

LS6

Immunity and Infection

Principal Investigator: **Dr LUISA FIGUEIREDO**

Host Institution: **INSTITUTO DE MEDICINA MOLECULAR JOAO LOBO ANTUNES - PT**

Exploring the hidden life of African trypanosomes: parasite fat tropism and implications for disease

Background: The study of protozoan pathogens has been extensively explored often motivated to find suitable targets for new intervention strategies. However these studies have been mostly limited to those life-cycle stages that can be cultivated in vitro. Using a mouse model of African trypanosomiasis, we have recently discovered that the adipose tissue (fat) is a major reservoir for the extracellular protozoan *Trypanosoma brucei* and that, within this environment, parasites become phenotypically different from those in the blood. Our study exposed novel biology of the *T. brucei* life cycle, yet it remains unknown how parasites adapt to the fat and how parasite fat tropism affects disease.

Our first aim is to determine the molecular and cellular mechanisms underlying *T. brucei* fat tropism. We will perform a genetic screen in mice to identify key parasite genes required for establishing and maintaining chronic infection in the fat. Together with the information of the transcriptome and proteome, we will identify the mechanistic steps underlying parasite tissue-adaptation.

Our second aim is to identify the consequences of *T. brucei* fat tropism for the host and the importance for disease. We will first investigate if parasites can egress from the fat. We will also determine if parasites induce lipid breakdown in the host, leading to loss of fat mass. Finally, we will measure the impact of fat tropism in general traits of disease, including host survival and transmission potential.

Impact: This project represents a completely novel research avenue built on recent work from my laboratory. By uncovering fundamental aspects of the biology of *T. brucei*, we will also improve the understanding of clinically relevant features of African trypanosomiasis, including relapses and weight loss. In addition, since parasite fat tropism has also been observed in malaria and Chagas' disease, our findings will help elucidate disease mechanisms relevant to other infectious diseases.

Link to the ERC project webpage: <https://imm.medicina.ulisboa.pt/investigation/laboratories/luisa-figueiredo-lab/>

Keywords of the ERC project: Adipose tissue, metabolism, infection, parasite, mice

Keywords that characterize the scientific profile of the potential visiting researcher/s: Vascular biology, single cell, metabolism, immunology,



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802780

Project Acronym:

Sugar-Enable

Evaluation Panel:

LS6
Immunity and Infection

Principal Investigator: **Dr ROBERT DE VRIES**
Host Institution: **UNIVERSITEIT UTRECHT - NL**

Influenza Virus - Sugar Interactions, From Glycan Arrays To Better Vaccines

Our current assays to determine the receptor specificity and vaccine efficiency of influenza A virus fail as they do not represent receptors available in the human upper respiratory tract. The lack of these receptors in our laboratory hosts to create vaccines significantly dampen yields, the resulting mismatched vaccines do not afford proper protection and further drive antigenic drift.

The objective of this proposal is to elucidate the functional receptor of human influenza A viruses. By using antigenically drifted viruses, we expect to understand how glycan specificity changes due to immune pressure but it will also lead to the identification of a glycan that is utilized by all human IAV viruses. With this knowledge, better surveillance techniques, culture models and structure-based inhibitors can be developed. Using a novel and sophisticated cell-engineering tool, based on lipidated sugars, we will show functional glycan receptor usage. In addition, I will create cell lines in which human influenza A vaccine viruses grow to high titers without adaptation, thus providing superior protection.

To achieve this goal, I propose to enzymatically synthesize complex glycans (AIM 1), including sialic acid modifications that are found on the respiratory tract epithelial cells of humans and other IAV hosts. Several enzymatic methods and glycan array tools are in place, and thus the chance of success is high. I already set-up preliminary methods for the use of lipidated N-glycan structures and extensive knowledge on SEEL is present in the department (AIM 2). For creating super vaccine producing cell lines I will use genetic approaches that previously have shown to be successful (AIM3).

The systems dealing with sugars enabling function, either for infection or vaccine research, I term sugar-enable, will provide new endeavors to create glycan-analog inhibitors and will bring us steps closer to better vaccines.

Link to the ERC project webpage:

Keywords of the ERC project: influenza A virus, hemagglutinin, glycan array, sialic acid

Keywords that characterize the scientific profile of the potential visiting researcher/s: virology, glycobiology, immunology



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802899

Project Acronym:

VIRUSES AND RNA

Evaluation Panel:

LS6

Immunity and Infection

Principal Investigator: **Dr TROELS SCHEEL**

Host Institution: **KOBENHAVNS UNIVERSITET - DK**

RNA regulation during viral infection

Viral infections are responsible for significant morbidity and mortality and frequency and impact of epidemics are expected to increase. Thorough understanding of basic virology is critical for informed development of prevention and control. Most systematic studies of virus-host interactions have focused on proteins, however, with recent methodological advances the intersecting fields of viral infection and RNA biology hold great promise for basic and therapeutic exploration. The goal of this application therefore is to discover and dissect RNA-based virus-host interactions and related regulatory mechanisms of gene expression.

Micro-RNAs (miRNAs) fine-tune gene expression by repressing mRNA targets. However, cellular miRNAs increase translation and replication of certain viruses. Thus, hepatitis C virus (HCV) critically depends on the liver specific miR-122, which emerged as a therapeutic target. Further, HCV sequesters enough miR-122 to indirectly regulate cellular gene expression. I hypothesize that this RNA-based mechanism contributes to virus induced liver cancer, and aim to address this using our recently developed rodent model for HCV infection (Aim 1). Better understanding of viral RNA (vRNA) interactions could significantly contribute to basic infection biology and novel therapeutics. I therefore aim to systematically identify vRNA interactions with other cellular RNAs and proteins (Aim 2). I expect to identify interactions of value for functional regulation and therapeutic targeting. I finally hypothesize that translation of certain cellular mRNAs – similarly to viruses – increase upon miRNA binding, and aim to systematically screen for such virus-like alternative regulation, with potential to change understanding of post-transcriptional regulation (Aim 3).

In conclusion, this high-risk high-gain project has potential to shape novel dogmas for virus and RNA biology and to identify novel RNA-based therapeutic targets; a promising upcoming field of discovery.

Link to the ERC project webpage:

Keywords of the ERC project: Virus, Hepatitis, RNA, miRNA, Infection, Virus-host interaction,

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

805500

Project Acronym:

Riboinflam

Evaluation Panel:

LS6
Immunity and Infection

Principal Investigator: **Dr EMILIANO RICCI**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Assessing the role of ribosomes and mRNA translation in shaping the inflammatory response

Inflammation is a highly regulated process that acts as a first line of defense against pathogens infections. Triggered by cellular pattern recognition receptors (PRRs) that recognize specific microbial components and endogenous or exogenous non-microbial components, activation of inflammation induces a dynamic and coordinated gene expression program that leads to the production of cytokines and chemokines to attract effector cells to the site of infection. Although a robust inflammatory response is required for efficient clearance of pathogens, uncontrolled or prolonged inflammation can lead to inflammatory disorders such as septic shocks or to autoimmune diseases like lupus.

Most studies have focused so far on the transcriptional control of the inflammatory gene expression program. However, post-transcriptional regulatory mechanisms involving mRNA splicing, mRNA decay or translation have also been described to control the inflammatory response. Among these, regulation of mRNA translation allows for rapid and reversible modulation of gene expression but its precise role and control mechanisms in the inflammatory response remain poorly understood.

Using innovative technologies, our project aims at characterizing the role of ribosomes and mRNA translation in regulating the inflammatory response. In particular, we propose to identify the complete set of of ribosome accessory proteins and to determine their role in the context of “specialized ribosomes” with specific regulatory activities. We will also study the cross-talks between ribosomes and other cellular processes such as mRNA decay and uncover the role of mRNA editing in regulating translation during the inflammatory response. From this work, we expect to identify new regulatory mechanisms that orchestrate inflammation as well as cellular factors that could represent new therapeutic targets for the design of drugs modulating inflammation.

Link to the ERC project webpage:

Keywords of the ERC project: ribosome, RNA, translation, inflammation, innate immunity, macrophage, dendritic cells

Keywords that characterize the scientific profile of the potential visiting researcher/s: RNA, cell biology, innate immunity, microscopy, metabolism, mitochondria



European Research Council
Executive Agency

Established by the European Commission

Project ID:

819329

Project Acronym:

STEP 2

Evaluation Panel:

LS6

Immunity and Infection

Principal Investigator:

**Dr WOLFGANG
KASTENMÜLLER**

Host Institution:

JULIUS-MAXIMILIANS-UNIVERSITÄT WÜRZBURG - DE

Spatiotemporal regulation of T-cell Priming

The initiation of adaptive cellular immunity requires antigen-specific interactions between Dendritic cells (DC) and naive CD8 T cells in secondary lymphoid organs. We aim to understand how the dynamic migratory behavior of myeloid and lymphoid cells is coordinated to ensure that “the right cells” communicate at “the right time” in “the right place” to enable robust immune responses. Using intravital microscopy, we have recently identified a critical phase (“Step 2”) of T cell priming that follows the initial encounter of DC and CD8 T cells and is essential to develop protective immunity.

The aim of this proposal is to identify the cellular and molecular mechanisms regulating T cell differentiation during Step 2. We will employ a newly developed imaging method (“Net-Vis”) to investigate how key elements of Step 2 (XCR1 DC) receive antigenic and inflammatory “information” within a network of myeloid cells. Next, we will test a novel model of T cell priming in which stepwise relocalization to multicellular clusters within the LN orchestrates T cell differentiation. Combining deep-tissue intravital microscopy, “Niche-seq” and novel genetic approaches, we will identify the cellular players and molecules guiding these processes and test their mechanistic implications. Finally, we will investigate the identity and mechanisms of Foxp3+ T cells that co-regulate CD8 T cell activation and differentiation during Step 2.

In summary, we will exploit an array of innovative imaging, spatiotemporal transcriptomics and genetic approaches to investigate novel fundamental aspects of CD8 T cell priming during a newly discovered distinct phase of T cell activation and differentiation. Investigating the mechanisms that guide these central steps in adaptive immunity is anticipated to reveal new avenues for the therapeutic manipulation of immune responses against infection and cancer.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

677200

Project Acronym:

Immune Regulation

Evaluation Panel:

LS6
Immunity and Infection

Principal Investigator: **Dr NICOLE JOLLER**
Host Institution: **UNIVERSITAT ZURICH - CH**

How Infection History Shapes the Immune System: Pathogen-induced Changes in Regulatory T Cells

Studying host-pathogen interactions by focusing on the interaction of a single pathogen with the host has defined our understanding of these events and the insights gained form the basis for the therapeutic and vaccination strategies we use today. However, people become infected with multiple pathogens throughout their lifetime, at times even simultaneously. Still, it is largely unknown how the immune response to one pathogen alters the body's ability to respond to a second infectious agent or the susceptibility to autoimmunity or cancer. This project will address this question by focusing on infection-induced changes in regulatory T cells (Tregs) as they may lead to biased suppression and changes in the nature of subsequent immune responses. Our efforts will focus on two areas: In a first part, we will use single cell RNA-Seq to address how infections shape the Treg compartment by defining the specialized Treg subsets generated during polarized infectious settings and analyzing how they interact with effector T cells. Based on the depth of information we expect to obtain from this approach, we envisage finding thus far unappreciated interactions and functions of Tregs in the course of an immune response. The second part will investigate how an altered Treg compartment, either through genetic modifications or infection-induced, affects disease susceptibility. In this context, we will also address stability and persistence of pathogen-induced changes in the Treg compartment. Collectively the proposed experiments will allow us to start addressing how preceding infections affect disease susceptibility. Deciphering how infection history shapes the Treg compartment and how this affects susceptibility to future challenges will lay the groundwork for addressing this question more broadly in the future and as such will likely have a transformative impact on the field.

[Link to the ERC project webpage:](#)

[Keywords of the ERC project:](#) immune regulation, infection history, regulatory T cells

[Keywords that characterize the scientific profile of the potential visiting researcher/s:](#) immunology, T cell biology, animal work, computational



European Research Council
Executive Agency

Established by the European Commission

Project ID:

681829

Project Acronym:

Invadis

Evaluation Panel:

LS6

Immunity and Infection

Principal Investigator: **Dr MARC LECUIT**

Host Institution: **INSTITUT PASTEUR - FR**

Microbial invasion and dissemination within the host, mechanisms and effects

An infection is defined by the deleterious consequences of the interactions between a pathogen and a host. Thus, studying the biology of infection reveals critical properties of hosts and pathogens, and is a way forward to address basic biological questions and improve health.

We study listeriosis, a systemic infection caused by *Listeria monocytogenes* (Lm). Lm is a human foodborne pathogen that crosses the intestinal barrier, disseminates systemically, replicates in liver and spleen and reaches the central nervous system (CNS) and fetoplacental unit. Given the remarkable journey Lm makes in its host, studying listeriosis offers unprecedented opportunities to understand host cell biology, physiology and immune responses, guided by Lm. The mucosal, CNS and fetoplacental tropisms of Lm are shared by other microbes which pathogenesis is far less understood. Lm therefore stands as a unique model microorganism of general biological and medical significance.

The major challenge of this project is to go beyond reductionist approaches and embrace the complexity of actual infections.

We will use stem cell-derived organoids, live imaging, genetically engineered mouse models, the clinical and biological data from a unique cohort of 900 patients and the corresponding causative Lm strains, to investigate the molecular mechanisms of Lm tissue invasion, dissemination and host responses.

Specifically, we will (i) decipher the cell biology of microbial translocation across the intestinal epithelium; (ii) study the impact of microbial portal of entry on microbial fate, dissemination and host responses; (iii) harness Lm biodiversity to identify novel virulence factors and (iv) discover new host factors predisposing to invasive infections.

Building on the unique combination of advanced experimental systems and exclusive clinical data, this integrative and innovative project will reveal novel, physiologically relevant mechanisms of infection, with scientific and biomedical implications.

Link to the ERC project webpage: <https://research.pasteur.fr/en/team/biology-of-infection/>

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

694992

Project Acronym:

Autonomous CLL-BCRs

Evaluation Panel:

LS6
Immunity and Infection

Principal Investigator: **Dr HASSAN JUMAA**
Host Institution: **UNIVERSITAET ULM - DE**

Role of autonomous B cell receptor signalling and external antigen in the pathogenesis of chronic lymphocytic leukaemia (CLL)

The proposed project aims at investigating the molecular mechanisms that activate B cell antigen receptor (BCR) signalling in chronic lymphocytic leukaemia (CLL). While it is widely accepted that the unbroken BCR expression in CLL cells is indicative for a key role in disease development, the mechanisms that induce BCR activation and survival of malignant cells are still elusive. Using a unique reconstitution system, we have recently shown that CLL-derived BCRs possess the exceptional capacity for cell-autonomous signalling independent of external antigen. Crystallographic analyses confirmed our model that CLL-BCRs bind to intrinsic motifs in nearby BCRs on the very same cell. In addition to the BCR, several pathogenic factors influence the biological behaviour of CLL cells, but the functional hierarchy and the effect on BCR signalling are insufficiently understood. Here, we aim at investigating the structural cause of autonomous signalling as well as the characterization of important signalling pathways and their mechanistic action in CLL pathogenesis.

By combining crystallography with the measurement of autonomous signalling of wild type and mutated receptors in our unique reconstitution system, we will generate a structure-function relationship for CLL-BCRs. By generating new animal models and by employing classical as well as cutting-edge approaches of biochemistry and molecular/cellular immunology, we will comprehensively characterize the signalling pathways that are activated by autonomous signalling and might be important for CLL pathogenesis.

These systematic efforts are necessary to understand how various biological mechanisms operate and ultimately activate downstream pathways that result in a lymphoproliferative disease. In addition, a cohesive model of CLL pathogenesis, which elucidates the hierarchical order of pathogenic factors and their interaction with BCR signalling, may well lead to novel disease-specific preventive or therapeutic intervention.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

786602

Project Acronym:

ENVISION

Evaluation Panel:

LS6

Immunity and Infection

Principal Investigator: **Dr SOREN PALUDAN**

Host Institution: **AARHUS UNIVERSITET - DK**

Novel mechanisms of early defense against virus infections

Virus-induced type I interferons (IFN) have classically been considered to constitute the first line of defense against virus infections. However, recent work by us and others has identified early antiviral actions that occur independently of inducible type I and III IFN expression and sometimes even prior to IFN action (e.g. Iversen, ..., Paludan. *Nature Immunology*, 2016; Paludan. *Trends in Immunology*, 2016). These discoveries challenge the current thinking in the field that IFNs constitute the first line of defense. Hence, there is an urgent need for more detailed understanding of the immediate antiviral defense mechanisms. Most importantly, we remain to identify key players in IFN-independent antiviral responses, we completely lack insight into the mechanisms that govern these responses, and we also lack information on the importance of this layer of defense in mice and humans. In accord with this, my proposal follows four aims: (i) Identification of mechanisms of virus detection at epithelial surfaces, (ii) elucidation of the role of tonic IFN signaling in antiviral defense, (iii) identification and characterization of novel restriction factors, and (iv) deciphering the mechanisms that govern induction of the first wave of IFNs at epithelial surfaces. In addition, I will also explore the interactions between the early antiviral actions. To achieve the goals, I will combine unbiased genome-wide screens with hypothesis-driven approaches, and will integrate molecular biology/genetics/biochemistry with advanced cell culture systems, animal science and analysis of patient material. Strong preliminary data have been generated for all four aims, and world-leading collaborations are in place, hence minimizing the risks, and allowing fast progress. Our findings will (i) change the thinking in innate immunology by uncovering a novel layer of antiviral defense and (ii) provide new avenues for therapeutic modulation of immune responses.

Link to the ERC project webpage:

Keywords of the ERC project: Innate immunology

Keywords that characterize the scientific profile of the potential visiting researcher/s: Self-motivated, hard-working, collaborative, positive, curiosity-driven, ambitious



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802878

Project Acronym:

FunDiT

Evaluation Panel:

LS6
Immunity and Infection

Principal Investigator: **Dr ONDREJ STEPANEK**

Host Institution: USTAV MOLEKULARNI GENETIKY AKADEMIE VED CESKE REPUBLIKY
VEREJNA VYZKUMNA INSTITUTE - CZ

Functional Diversity of T cells

T cells have a central role in most adaptive immune responses, including immunity to infection, cancer, and autoimmunity. Increasing evidence shows that even resting steady-state T cells form many different subsets with unique functions. Variable level of self-reactivity and previous antigenic exposure are most likely two major determinants of the T-cell diversity. However, the number, identity, and biological function of steady-state T-cell subsets are still very incompletely understood. Receptors to ligands from TNF and B7 families exhibit variable expression among T-cell subsets and are important regulators of T-cell fate decisions. We hypothesize that pathways triggered by these receptors substantially contribute to the functional diversity of T cells. The FunDiT project uses a set of novel tools to systematically identify steady-state CD8+ T cell subsets and characterize their biological roles. The project has three complementary objectives.

(1) Identification of CD8+ T cell subsets. We will identify subsets based on single cell gene expression profiling. We will determine the role of self and foreign antigens in the formation of these subsets and match corresponding subsets between mice and humans.

(2) Role of particular subsets in the immune response. We will compare antigenic responses of particular subsets using our novel model allowing inducible expression of a defined TCR. The activity of T-cell subsets in three disease models (infection, cancer, autoimmunity) will be characterized.

(3) Characterization of key costimulatory/inhibitory pathways. We will use our novel mass spectrometry-based approach to identify receptors and signaling molecules involved in the signaling by ligands from TNF and B7 families in T cells.

The results will provide understanding of the adaptive immunity in particular disease context and resolve long-standing questions concerning the roles of T-cell diversity in protective immunity and tolerance to healthy tissues and tumors.

Link to the ERC project webpage: <https://adaptiveimmunity.img.cas.cz/>

Keywords of the ERC project: T cells, diversity, single cell, disease models, signaling

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

834302

Project Acronym:

ImmUne

Evaluation Panel:

LS6

Immunity and Infection

Principal Investigator: **Dr THOMAS BOEHM**

Host Institution: MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN EV
- DE

Towards identification of the unifying principles of vertebrate adaptive immunity

About 500 million years ago, the two sister groups of vertebrates independently evolved alternative forms of adaptive immunity, representing a striking example of convergent evolution. Whereas the components and functions of the immune system in jawed vertebrates (ranging from sharks to humans) are well characterized, much remains to be learned about adaptive immunity in jawless vertebrates (lampreys and hagfishes). Up to now, progress in understanding immunity in jawless fishes was hampered by their complex life-cycle, long generation time, and the difficulty of raising fish in the laboratory for extended periods, particularly after in vitro fertilization. Based on our recent methodological advances in aquatic husbandry and successful CRISPR/Cas9-mediated genetic modification, we propose to conduct a large-scale analysis of cellular immunity in lampreys laying the foundations for the identification of the unifying principles of vertebrate immunity. Our experiments will address the development and characteristics of different T cell subsets, the molecular basis of antigen receptor assembly, and the function of the two principal T cell lineages during the immune response. We will also examine the structure and function of the stromal microenvironment in the lamprey thymus equivalent, which is considered to be the site of T cell development. A particular focus will be on the functional analysis of a recently discovered MHC-like locus in the context of T cell development, and in the essential self/nonself discrimination mechanism(s) at play during the immune response. We expect that the identification of common design principles of adaptive immunity in vertebrates will provide us with an unprecedented view on immune functions in humans, potentially guiding the development of novel strategies for the treatment of failing immunity in patients with immunodeficiency and/or autoimmunity.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

677943

Project Acronym:

DynaOmics

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr LAURA ELO**

Host Institution: **TURUN YLIOPISTO - FI**

From longitudinal proteomics to dynamic individualized diagnostics

Longitudinal omics data hold great promise to improve biomarker detection and enable dynamic individualized predictions. Recent technological advances have made proteomics an increasingly attractive option but clinical longitudinal proteomic datasets are still rare and computational tools for their analysis underdeveloped. The objective of this proposal is to create a roadmap to detect clinically feasible protein markers using longitudinal data and effective computational tools. A biomedical focus is on early detection of Type 1 diabetes (T1D). Specific objectives are:

- 1) Novel biomarker detector using longitudinal data. DynaOmics introduces novel types of multi-level dynamic markers that are undetectable in conventional single-time cross-sectional studies (e.g. within-individual changes in abundance or associations), develops optimization methods for their robust and reproducible detection within and across individuals, and validates their utility in well-defined samples.
- 2) Individualized disease risk prediction dynamically. DynaOmics develops dynamic individualized predictive models using the multi-level longitudinal proteome features and novel statistical and machine learning methods that have previously not been used in this context, including joint models of longitudinal and time-to-event data, and one-class classification type techniques.
- 3) Dynamic prediction of T1D. DynaOmics builds a predictive model of dynamic T1D risk to assist early detection of the disease, which is crucial for developing future therapeutic and preventive strategies. T1D typically involves a relatively long symptom-free period before clinical diagnosis but current tools to predict early T1D risk have restricted power.

The objectives involve innovative and unconventional approaches and address major unmet challenges in the field, having high potential to open new avenues for diagnosis and treatment of complex diseases and fundamentally novel insights towards precision medicine.

Link to the ERC project webpage: <https://elolab.utu.fi>

Keywords of the ERC project: computational biomedicine, longitudinal data analysis, biomarker, machine learning, type 1 diabetes

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational biomedicine, longitudinal data analysis, machine learning



European Research Council
Executive Agency

Established by the European Commission

Project ID:

681742

Project Acronym:

NASCENT

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr PAUL FRANKS**

Host Institution: **LUNDS UNIVERSITET - SE**

Novel Approach to Systematically Characterize Exercise- and Nutrient- responsive genes in Type 2 diabetes and cardiovascular disease

Proposal summary

Type 2 diabetes and cardiovascular disease are devastating and costly morbidities whose prevalences are increasing rapidly around the world. As such, there is an urgent need to develop innovative and effective prevention and treatment strategies. As numerous clinical trials have shown, lifestyle modification is by far the best way to prevent these diseases, with lifestyle being twice as effective as the best drugs, less costly and free from side effects. Yet, human biology is complex, causing some people to respond well and others poorly to the same lifestyle interventions. Thus, a huge, as yet unrealised opportunity exists to optimize the prevention and treatment of cardiometabolic diseases by tailoring lifestyle interventions to the patient's unique biology.

NASCENT is an integrated programme of research through which I will functionally annotate and later translate discoveries of gene-lifestyle interactions made through the interrogation of large epidemiological (N>100,000) datasets at my disposal. The functional annotation of these discoveries will be done using state-of-the-art epigenomic and targeted gene editing tools, whereas the translation of those findings will be achieved using a innovative and powerful clinical trial design that focuses on treatments that are tailored to the participant's genotype (genotype-based recall).

NASCENT capitalizes on a solid foundation of cohorts, methods, and expertise that I have built-up over the past fifteen years, but also exploits state-of-the-art epigenomic and gene-editing technologies that have not previously been used in studies of gene-lifestyle interactions. I expect the integration of these established and new approaches in NASCENT to propel major advances in understanding gene-lifestyle interactions in cardiometabolic disease that help optimise disease prevention.

Link to the ERC project webpage:

Keywords of the ERC project: Genetics, Omics, Lifestyle, Diet, Exercise, Precision Medicine

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

682540

Project Acronym:

TRANSMID

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr NIEL HENS**

Host Institution: **UNIVERSITEIT HASSELT - BE**

Translational and Transdisciplinary research in Modeling Infectious Diseases

TransMID focuses on the development of novel methods to estimate key epidemiological parameters from both serological and social contact data, with the aim to significantly expand the range of public health questions that can be adequately addressed using such data. Using new statistical and mathematical theory and newly collected as well as readily available serological and social contact data (mainly from Europe), fundamental mathematical and epidemiological challenges as outlined in the following work packages will be addressed: (a) frequency and density dependent mass action relating potential effective contacts to transmission dynamics in (sub)populations of different sizes with an empirical assessment using readily available contact data, (b) behavioural and temporal variations in contact patterns and their impact on the dynamics of infectious diseases, (c) close contact household networks and the assumption of homogeneous mixing within households, (d) estimating parameters from multivariate and serial cross-sectional serological data taking temporal effects and heterogeneity in acquisition into account in combination with the use of social contact data, and (e) finally the design of sero- and social contact surveys with specific focus on serial cross-sectional surveys. TransMID is transdisciplinary in nature with applications on diseases of major public health interest, such as pertussis, cytomegalovirus and measles. Translational methodology is placed at the heart of TransMID resulting in the development of a unifying methodology for other diseases and settings. The development of a toolbox and accompanying software allow easy and effective application of these fundamentally improved techniques on many infectious diseases and in different geographic contexts, which should maximize TransMID's impact on public health in Europe and beyond.

Link to the ERC project webpage:

Keywords of the ERC project: Mathematical epidemiology

Keywords that characterize the scientific profile of the potential visiting researcher/s: Biostatistics, Epidemiologist



European Research Council
Executive Agency

Established by the European Commission

Project ID:

715732

Project Acronym:

STOP-HF

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr PETER VAN DER MEER**

Host Institution: **ACADEMISCH ZIEKENHUIS GRONINGEN - NL**

STEM CELL MODELS TO UNRAVEL THE SUSCEPTIBILITY AND RESILIENCE TO DEVELOP HEART FAILURE

The overarching objective of STOP-HF is to generate human induced pluripotent stem cells (hiPSC) derived cardiomyocytes from two specific forms of heart failure (HF) with a clear trigger to unravel common pathophysiological mechanisms involved in the early development of HF. The project is focused on two specific forms of HF, both with a clear trigger: pregnancy and anthracyclines. Better understanding of early molecular pathways leading to HF and knowledge about inter-individual susceptibility is needed. For detection of early changes on a molecular level cardiac tissue is needed. Generation of patient specific cardiac cells from skin fibroblasts (hiPSC technology) is a novel and innovative approach.

SPECIFIC OBJECTIVES

1. Fabrication and maturation of 3D cardiac tissue from hiPS derived cardiomyocytes.
2. Generate and characterize hiPS derived cardiomyocytes and endothelial cells from females with pregnancy induced HF and unravel differences on transcriptome level.
3. Generate and characterize hiPSC derived cardiomyocytes from patients with high susceptibility and resilience to develop anthracycline-induced HF and compare them on transcriptome level.
4. Integrate the results for coding and non-coding RNAs from objective 1+2 and identify overlapping pathways.
5. Validate discoveries on transcriptome level in vitro, in vivo and apply for the development of HF in the general population.

WORKPACKAGES

WP1: Optimize fabrication and maturation of 3D cardiac tissue from hiPS derived cardiomyocytes

WP 2A: Validate the model and compare hiPS derived cardiomyocytes and endothelial cells from PPCM and healthy sisters on transcriptome level;

WP 2B: Validate the model and compare hiPS derived cardiomyocytes from both patients with high susceptibility and resilience to develop HF after anthracyclins on transcriptome level;

WP 3: Integration of transcriptome data from WP 2A+2B;

WP 4: Validation of novel pathways in vitro, in vivo and new onset HF in the general population.

Link to the ERC project webpage:

Keywords of the ERC project: human induced pluripotent stemcells; heart failure; cardiomyopathy; tissue engineering; cardiology

Keywords that characterize the scientific profile of the potential visiting researcher/s: tissue engineering; induced pluripotent stem cells; MD; cardiology; heart failure



European Research Council
Executive Agency

Established by the European Commission

Project ID:

715737

Project Acronym:

QuantSURG

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr SYLVAIN GIOUX**

Host Institution: **UNIVERSITE DE STRASBOURG - FR**

Quantitative Surgical Guidance for Colorectal Surgery using Endogenous Molecular Contrast

Despite significant advances in medical imaging technologies, there currently exist no tools to effectively assist healthcare professionals during colorectal surgery. Surgeons mainly rely on their own senses, vision and touch to identify diseased tissue that should be removed or healthy tissue that should be avoided. In turn, surgery remains subjective and dependent on the experience of the surgeon, resulting in unacceptable failure, recurrence and morbidity rates, as well as in significant quality of care disparities across hospitals.

The hypothesis underlying our study is that near-infrared light travels deeply into living tissues and interacts with endogenous molecular constituents, namely oxy- and deoxy-hemoglobin, water and lipids, providing key information regarding tissue perfusion, oxygenation, hydration and metabolism. In turn, such information can be used to differentiate diseased from healthy tissue. We recently introduced a novel concept that enables the quantitative imaging of endogenous molecular information over large fields-of-view. Because this concept can be implemented in real-time, it is amenable to provide video-rate endogenous information during colorectal surgery.

In this study, we propose to push the limits of this concept by developing ground-breaking theory & technology, and creating a novel surgical guidance device capable of real-time imaging of key endogenous information for colorectal surgery. Correlation between endogenous contrast measurements and histological tissue status will be investigated onto bowel ischemia and colorectal cancer animal models. Finally, a clinically-compatible imaging device will be fabricated and translated into a first-in-human study in patients undergoing colorectal surgery. If successful, this study has the potential to solve a longstanding clinical problem by providing real-time objective feedback during colorectal surgery.

Link to the ERC project webpage: <https://healthphotonics.org/>

Keywords of the ERC project: Image-Guided Surgery; Optical Imaging

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

716063

Project Acronym:

DrugComb

Evaluation Panel:

LS7
Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr JING TANG**

Host Institution: **HELSINGIN YLIOPISTO - FI**

Informatics approaches for the rational selection of personalized cancer drug combinations

Making cancer treatment more personalized and effective is one of the grand challenges in our health care system. However, many drugs have entered clinical trials but so far showed limited efficacy or induced rapid development of resistance. We critically need multi-targeted drug combinations, which shall selectively inhibit the cancer cells and block the emergence of drug resistance. This project will develop mathematical and computational tools to identify drug combinations that can be used to provide personalized and more effective therapeutic strategies that may prevent acquired resistance. Utilizing molecular profiling and pharmacological screening data from patient-derived leukaemia and ovarian cancer samples, I will develop model-based clustering methods for identification of patient subgroups that are differentially responsive to first-line chemotherapy. For patients resistant to chemotherapy, I will develop network modelling approaches to predict the most potential drug combinations by understanding the underlying drug target interactions. The drug combination prediction will be made for each patient and will be validated using a preclinical drug testing platform on patient samples. I will explore the drug combination screen data to identify significant synergy at the therapeutically relevant doses. The drug combination hits will be mapped into signalling networks to infer their mechanisms. Drug combinations with selective efficacy in individual patient samples or in sample subgroups will be further translated into treatment options by clinical collaborators. This will lead to novel and personalized strategies to treat cancer patients.

Link to the ERC project webpage: <https://cordis.europa.eu/project/rcn/210127/factsheet/en>

Keywords of the ERC project: Bioinformatic approaches, personalized medicine, network pharmacology modelling

Keywords that characterize the scientific profile of the potential visiting researcher/s: drug target discovery, network models, text mining, artificial intelligence, statistical models



European Research Council
Executive Agency

Established by the European Commission

Project ID:

724469

Project Acronym:

VascArbor

Evaluation Panel:

LS7
Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr JEROEN ROUWKEMA**

Host Institution: **UNIVERSITEIT TWENTE - NL**

Vascular Tree Formation in Multi-Structural Tissue Engineering

Engineered tissues offer a great promise to the field of medicine as an alternative for donor tissues, for which the supply is not meeting the demands. However, the clinical application of engineered tissues is hampered. The integration of engineered tissues after implantation is limited due to the lack of a vascular network. Currently, strategies to include vascular networks rely on the spontaneous organization of vascular cells, or on the patterning of these cells. However, this results in either vascular networks that are not organized, or networks that lose their initial organization fast. This project will use a unique and novel approach to control vascular development and will therefore result in a vascular network with a controllable long-term organization. By allowing for anastomosis, and increasing nutrient delivery, this project will tackle an essential problem and will greatly enhance the clinical applicability of engineered tissues.

Within VascArbor, fluid flows through engineered tissues will be designed and controlled to guide vascular organization. Apart from that, growth factors will be patterned in space and time to further direct the formation of a vascular network with a controlled organization. In parallel, computational models will be developed that can predict vascular organization and development based on processing parameters. This will be a breakthrough in vascularized tissue engineering by enabling a direct link between a desired vascular organization, and the tissue construct geometry and processing conditions that are needed to acquire this organization.

To maximize the impact of VascArbor on the field of tissue engineering and medicine, the principles that will guide vascular organization are compatible with multiple current and future tissue fabrication technologies. Within VascArbor, tissue building blocks and bio-printing will be used to engineer vascularized cardiac muscle tissue based on the principles developed in this project.

Link to the ERC project webpage: <https://cordis.europa.eu/project/rcn/207889/factsheet/en>

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

757398

Project Acronym:

NanOnc

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr STEFAAN SOENEN**

Host Institution: **KATHOLIEKE UNIVERSITEIT LEUVEN - BE**

Nanomaterials in Oncology: Exploiting the Intrinsic Cancer-Specific Toxicity of Nanoparticles.

In our current society, therapeutic strategies against cancer suffer from dose-limiting toxicity, lack of specificity and high morbidity. To overcome this, the use of nanomaterials (NMs) is rising, where several NM formulations are undergoing clinical trials or are used in clinics where the NMs are used as drug delivery vehicles or as mediators in physical anticancer methods (e.g. hyperthermia), where to date, the success rate is limited due to low tumor targeting efficacy, lack of specificity and frequent re-use of classical toxicity mechanisms.

To overcome these issues, this research program aims to exploit the intrinsic toxicity of certain types of metal-based, degradation-prone NMs (Fe-doped ZnO, Fe-doped CuO and Ag of different sizes and coatings) towards only cancer cells as a novel and generic anti-cancer tool with 1) improved efficacy against difficult to treat cancers such as multidrug-resistant cancer cells, 2) enhanced specificity and selectivity of the treatment by the intrinsic cancer cell-specific toxicity of NMs towards cancer cells. To overcome the issues related to selective delivery of the NMs, tumor-homing cells will be used that have been shown to efficiently home to primary tumors and their metastases. In practice, the NMs used show distinct degradation kinetics that primarily induce cancer-selective toxicity. To obtain efficient tumor targeting, suicide gene-expressing tumor-homing cells will be loaded with the NMs in their cytoplasm, hereby impeding premature NM degradation. The tumor homing efficacy of these cells will be monitored via optical imaging and once at the target site these cells will be chemically destroyed using the suicide gene strategy. This will release the NMs into the tumor site, where they can selectively destroy the cancer cells. This research program will be the first to explore the full potential of cancer-specific toxicity of NMs and the use of cytoplasmic loading of cells as biological carriers for efficient delivery.

Link to the ERC project webpage: <https://www.kulnanobmi.com/erc-nanonc>

Keywords of the ERC project: nanomedicine

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

758151

Project Acronym:

CHIPS

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr MARIE PEDERSEN**

Host Institution: **KOBENHAVNS UNIVERSITET - DK**

Effects of Prenatal Exposure to Acrylamide on Health: Prospective Biomarker-Based Studies

Background: Acrylamide is a chemical formed in many commonly consumed foods and beverages. It is neurotoxic, crosses the placenta and has been associated with restriction of fetal growth in humans. In animals, acrylamide causes heritable mutations, tumors, developmental toxicity, reduced fertility and impaired growth. Therefore, the discovery of acrylamide in food in 2002 raised concern about human health effects worldwide. Still, epidemiological studies are limited and effects on health of prenatal exposure have never been evaluated. Research gaps: Epidemiological studies have mostly addressed exposure during adulthood, focused on cancer risk in adults, and relied on questionnaires entailing a high degree of exposure misclassification. Biomarker studies on prenatal exposure to acrylamide from diet are critically needed to improve exposure assessment and to determine whether acrylamide leads to major diseases later in life.

Own results: I have first authored a prospective European study showing that prenatal exposure to acrylamide, estimated by measuring hemoglobin adducts in cord blood, was associated with fetal growth restriction, for the first time.

Objectives: To determine the effects of prenatal exposure to acrylamide alone and in combination with other potentially toxic adduct-forming exposures on the health of children and young adults.

Methods: Both well-established and innovative biomarker methods will be used for characterization of prenatal exposure to acrylamide and related toxicants in blood from pregnant women and their offspring in prospective cohort studies with long-term follow-up. Risk of neurological disorders, impaired cognition, disturbed reproductive function and metabolic outcomes such as obesity and diabetes will be evaluated.

Perspectives: CHIPS project will provide a better understanding of the impact of prenatal exposure to acrylamide from diet on human health urgently needed for targeted strategies for the protection of the health.

Link to the ERC project webpage:

Keywords of the ERC project: Acrylamide, Biomarker, Diet, Epidemiological, haemoglobin adducts, Prenatal

Keywords that characterize the scientific profile of the potential visiting researcher/s: Dietary/Nutrient epidemiology, Analytical chemistry



European Research Council
Executive Agency

Established by the European Commission

Project ID:

758657

Project Acronym:

ImPRESS

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr KYRRE EMBLEM**

Host Institution: **OSLO UNIVERSITETSSYKEHUS HF - NO**

Imaging Perfusion Restrictions from Extracellular Solid Stress

Even the perfect cancer drug must reach its target to have an effect. The ImPRESS project main objective is to develop a novel imaging paradigm coined Restricted Perfusion Imaging (RPI) to reveal - for the first time in humans - vascular restrictions in solid cancers caused by mechanical solid stress, and use RPI to demonstrate that alleviating this force will repair the cancerous microenvironment and improve therapeutic response. Delivery of anti-cancer drugs to the tumor is critically dependent on a functional vascular bed. Developing biomarkers that can measure how mechanical forces in a solid tumor impair perfusion and promotes therapy resistance is essential for treatment of disease.

The ImPRESS project is based on the following observations; (I) pre-clinical work suggests that therapies targeting the tumor microenvironment and extracellular matrix may enhance drug delivery by decompressing tumor vessels; (II) results from animal models may not be transferable because compressive forces in human tumors in vivo can be many times higher; and (III) there are no available imaging technologies for medical diagnostics of solid stress in human cancers. Using RPI, ImPRESS will conduct a comprehensive series of innovative studies in brain cancer patients to answer three key questions: (Q1) Can we image vascular restrictions in human cancers and map how the vasculature changes with tumor growth or treatment? (Q2) Can we use medical engineering to image solid stress in vivo? (Q3) Can RPI show that matrix-depleting drugs improve patient response to conventional chemo- and radiation therapy as well as new targeted therapies?

The ImPRESS project holds a unique position to answer these questions by our unrivaled experience with advanced imaging of cancer patients. With successful delivery, ImPRESS will have a direct impact on patient treatment and establish an imaging paradigm that will pave the way for new scientific knowledge on how to revitalize cancer therapies.

Link to the ERC project webpage: <https://www.ous-research.no/emblem/>

Keywords of the ERC project: MRI, glioblastoma, perfusion, physical forces, extracellular matrix, cancer therapy, clinical trial, artificial intelligence, deep learning

Keywords that characterize the scientific profile of the potential visiting researcher/s: Senior researcher, imaging specialist, computer specialist, postdoctoral researcher



European Research Council
Executive Agency

Established by the European Commission

Project ID:

758813

Project Acronym:

MHINT

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr REBECCA PEARSON**

Host Institution: **UNIVERSITY OF BRISTOL - UK**

Genetic, behavioural and cognitive mechanisms underpinning the association between mother and offspring mental health problems: mental (M) health (H) intergenerational transmission (INT) - (MHINT)

Despite decades of research, and the introduction of parenting interventions, children of mentally ill mothers remain substantially more likely to have mental health problems themselves. I propose to shed new light on why mental health problems in a mother are passed on to her child, and help break this reinforcing cycle of mental health risk across generations. In order to harness the potential of modifying parenting for the prevention of child mental health risk, I will study parenting using more detailed, ecologically valid and genetically sensitive designs than have been done before.

Objectives:

- 1: To investigate the respective role of genetic and environmental (chiefly parenting) mechanisms in explaining associations between mother and child mental health. HOW: using a consortium of international cohorts with intergenerational genetic and phenotypic data (n>10,000) and, for the first time, modeling genetic risk which is and is not transmitted from mother to child to test alternative hypotheses.
- 2: To identify behavioural manifestation of maternal mental health, in observed mother-infant interaction, in an ecologically valid way. HOW: recording 300 mother- child dyads at home, using novel wearable cameras, in the next generation of a key cohort (ALSPAC-G2).
- 3: To identify cognitive underpinnings of maternal behaviour. HOW: including cognitive tasks (with eye tracking) as new measures in ALSPAC-G2, applying computational models to cognitive and (uniquely) real life data (measured in 2).
- 4: To establish whether modification of maternal parenting (highlighted in 1-3), changes child mental health. HOW: systematic review of parenting intervention trials and new synthesis methods to extract which intervention components reduce child mental health problems.

My study will provide critical new evidence regarding the nature of parenting interventions that have potential to improve child mental health and break intergenerational transmission of mental health problems.

[Link to the ERC project webpage:](#)

[Keywords of the ERC project:](#) Depression , genetics, epidemiology , inter generational , parents, behaviour

[Keywords that characterize the scientific profile of the potential visiting researcher/s:](#)



European Research Council
Executive Agency

Established by the European Commission

Project ID:

759272

Project Acronym:

STRATO

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr HENDRIK SAGER**

Host Institution: **DEUTSCHES HERZZENTRUM MUNCHEN - DE**

**Stress as a modifier of atherosclerosis
- Novel mechanistic insights and therapeutic avenues -**

Atherosclerosis and its complications such as acute coronary syndromes (myocardial infarction and unstable angina) are leading causes of death in the EU and worldwide. Mental stress is known to be a major trigger for the onset of acute coronary syndromes, even in patients with state-of-the-art medical treatment. How acute mental stress rapidly drives plaque destabilization causing acute coronary syndromes is poorly understood and consequently specific treatment, although urgently needed, is lacking. Mental stress is known to affect the immune system. Leukocytes, the effector cells of the immune system, are main instigators not only of plaque progression, but also of plaque destabilization. We hypothesize that acute mental stress rapidly aggravates plaque inflammation, which renders plaques more vulnerable and prone to rupture.

We aim to characterize the impact of stress on plaque inflammation in a mouse model of acute mental stress. We will explore the mechanisms by which acute mental stress drives plaque inflammation. Based on these findings, we aim to provide a novel treatment approach to mitigate stress exacerbated plaque inflammation. Further, we aim to translate our findings to stressed humans.

The STRATO study will be carried out in a multidisciplinary approach including basic and clinician scientists, immunologists, and psychosomatic specialists and will provide us with an unprecedented, comprehensive picture of how acute mental stress aggravates atherosclerosis. Our study will fill a gap in mechanistic knowledge and based on this will identify novel therapeutic measures with the aim to reduce acute mental stress related cardiovascular complications.

Link to the ERC project webpage: https://www.dhm.mhn.de/de/kliniken_und_institute/klinik_fuer_herz-und_kreislauf/wissenschaftliche_arbeitsgrupp/kardiovaskulaere_inflammation.cfm

Keywords of the ERC project: inflammation, cardiovascular diseases, macrophages, innate immune system, atherosclerosis, myocardial infarction

Keywords that characterize the scientific profile of the potential visiting researcher/s: interest in immunology and cardiovascular diseases



European Research Council
Executive Agency

Established by the European Commission

Project ID:

759585

Project Acronym:

ToMeTuM

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr VOJTECH ADAM**

Host Institution: **VYSOKÉ UCENÍ TECHNICKÉ V BRNĚ - CZ**

Towards the Understanding a Metal-Tumour-Metabolism

A tumour cell uses both genetic and protein weapons in its development. Gaining a greater understanding of these lethal mechanisms is a key step towards developing novel and more effective treatments. Because the metal ion metabolism of a tumour cell is not fully understood, we will address the challenge of explaining the mechanisms of how a tumour cell copes both with essential metal ions and platinum based drugs. The metal-based mechanisms help a tumour to grow on one side and to protect itself against commonly used metal-based drugs. On the other side, the exact description of these mechanisms, which are being associated with multi-drug resistance occurrence and failure of a treatment, still remains unclear. We will reveal the mechanism of the as yet not understood biochemical and molecularly-biological relationships and correlations between metal ions and proteins in a tumour development revealing the way how to suppress the growth and development of a tumour and to markedly enhance the effectiveness of a treatment.

To achieve this goal, we will focus on metallothionein and its interactions with essential metals and metal-containing anticancer drugs (cisplatin, carboplatin, and oxaliplatin). Their actions will be monitored both in vitro and in vivo. For this purpose, we will optimize electrochemical, mass spectrometric and immune-based methods. Based on processing of data obtained, new carcinogenetic pathways will be sought on cell level and proved by genetic modifications of target genes. The discovered processes and the pathways found will then be tested on two animal experimental models mice bearing breast tumours (MCF-7 and 4T1) and MeLiM minipigs bearing melanomas.

The precise description of the tumour related pathways coping with metal ions based on metallothioneins will direct new highly effective treatment strategies. Moreover, the discovery of new carcinogenetic pathways will open a window for understanding of cancer formation and development.

Link to the ERC project webpage: <http://ucb.af.mendelu.cz/>

Keywords of the ERC project: metallothionein, metallomics, tumour diseases, bioanalytical chemistry, cytostatics, metals, resistance

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

786295

Project Acronym:

EPIC

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr ZLATKO TRAJANOSKI**

Host Institution: **MEDIZINISCHE UNIVERSITÄT INNSBRUCK - AT**

Enabling Precision Immuno-oncology in Colorectal cancer

Immunotherapy with checkpoints blockers is transforming the treatment of advanced cancers. Colorectal cancer (CRC), a cancer with 1.4 million new cases diagnosed annually worldwide, is refractory to immunotherapy (with the exception of a minority of tumors with microsatellite instability). This is somehow paradoxical as CRC is a cancer for which we have shown that it is under immunological control and that tumor infiltrating lymphocytes represent a strong independent predictor of survival. Thus, there is an urgent need to broaden the clinical benefits of immune checkpoint blockers to CRC by combining agents with synergistic mechanisms of action. An attractive approach to sensitize tumors to immunotherapy is to harness immunogenic effects induced by approved conventional or targeted agents.

Here I propose a new paradigm to identify molecular determinants of resistance to immunotherapy and develop personalized in silico and in vitro models for predicting response to combination therapy in CRC. The EPIC concept is based on three pillars: 1) emphasis on antitumor T cell activity; 2) systematic interrogation of tumor-immune cell interactions using data-driven modeling and knowledge-based mechanistic modeling, and 3) generation of key quantitative data to train and validate algorithms using perturbation experiments with patient-derived tumor organoids and cutting-edge technologies for multidimensional profiling. We will investigate three immunomodulatory processes: 1) immunostimulatory effects of chemotherapeutics, 2) rewiring of signaling networks induced by targeted drugs and their interference with immunity, and 3) metabolic reprogramming of T cells to enhance antitumor immunity.

The anticipated outcome of EPIC is a precision immuno-oncology platform that integrates tumor organoids with high-throughput and high-content data for testing drug combinations, and machine learning for making therapeutic recommendations for individual patients.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802778

Project Acronym:

ENDOMICS

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr MAD S BERGHOLT**

Host Institution: **KING'S COLLEGE LONDON - UK**

Raman Endoscopic Proteo-lipidomics of Bladder Cancer

The goal of ENDOMICS is to drive forward a new paradigm of Raman endoscopic technology that enables proteomic and lipidomic analysis for diagnosis of bladder cancers in vivo. Raman endoscopy is a label-free optical technique that can provide a point-wise vibrational molecular fingerprint of tissue “optical biopsy” for cancer diagnosis in vivo. State-of-the-art Raman endoscopy, however, does not offer specific compositional analysis or insights into molecular biology of tissue. This is because the vibrational Raman bands are overlapping and cannot be deciphered into the myriad of biomolecules in complex tissue.

We will introduce a ground-breaking new methodology to enable Raman proteomic and lipidomic analysis in vivo. To this end, heterospectral co-registered Raman and mass spectrometry imaging will be used to develop a multivariate regression model “Rosetta Stone” for translating vibrational structural information (Raman spectroscopy) into compositional information. To meet the unmet clinical needs in urology we will tailor the first fibre-optic Raman endoscopic technology that can measure depth-dependent molecular profiles to simultaneously enable detection, grading and staging of bladder cancers. We will finally conduct a clinical trial by applying the technique to measure a comprehensive molecular database of bladder pathologies in vivo. The latter will allow for the identification of proteomic and lipidomic biomarkers to develop novel algorithms for real-time diagnosis of bladder cancers.

The synergy between scientific and technological advances in ENDOMICS will break ground for shedding new light on the molecular biology of bladder cancer in vivo including new insights into clinical diversity and identification of biomarkers for diagnostics, prognostics and novel therapeutic targets.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

805057

Project Acronym:

PATER

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr OSKAR KARLSSON**

Host Institution: **STOCKHOLMS UNIVERSITET - SE**

Paternal Epigenetic Inheritance: A man's life experiences may impact health of his unborn children and grandchildren

Epigenetic inheritance may not only occur in plants and fungi but also in mammals. While the effect of maternal lifestyle and in utero exposures is well studied, paternal epigenetic inheritance is a novel research field, especially in regard to chemical exposures. Many environmental pollutants exhibit anti-androgenic function. Despite the vital role of androgens in spermatogenesis, the effects of adult anti-androgen exposure on the sperm epigenome and offspring phenotype have been scarcely studied.

The overall aim of this novel project is to increase the understanding of if, and how, male life experiences such as adult exposure to the anti-androgenic model substance and pollutant DBP (di-n-butyl phthalate) may affect offspring through paternal epigenetic inheritance. I accomplish this by integrating animal and human studies, using RNA-sequencing and mass spectrometry-based peptidomics to identify DBP-induced alterations in the sperm transcriptome and peptidome, examine noncoding RNAs and peptides role in embryogenesis, development and long-term health of the offspring in two generations. To validate the mechanistic importance of the sperm molecular alterations microinjections of selected biomolecules into zygotes will be conducted. This is the first project to investigate multigenerational effects of adult male exposure to anti-androgens in detail, and investigate the role of the sperm peptidome in paternal epigenetic inheritance. Directly linking animal experimental data about paternal transmission to human studies is unique and necessary to determine causal connection between environmentally-induced biomolecular alterations in sperm and offspring phenotype. The project can contribute to ground-breaking mechanistic understanding of how male life experiences may affect offspring through epigenetic inheritance. The findings may also have important public health implications via new regulations of anti-androgenic chemicals and male preconceptional interventions.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s: Bioinformatics, RNA-seq, noncoding RNA, DNA methylation, epigenetics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

817940

Project Acronym:

METATPTs

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr ESTEBAN GURZOV**

Host Institution: **UNIVERSITE LIBRE DE BRUXELLES - BE**

PROTEIN TYROSINE PHOSPHATASES IN METABOLIC DISEASES: OXIDATION, DYSFUNCTION AND THERAPEUTIC POTENTIAL

Diabetes mellitus is characterised by hyperglycaemia caused by an absolute or relative insulin deficiency. The global prevalence of diabetes has reached more than 410 million individuals, underscoring the need for novel therapeutic strategies targeting the pathology as a multi-organ disease. Protein tyrosine phosphatases (PTPs) constitute a superfamily of enzymes that dephosphorylate tyrosine-phosphorylated proteins and oppose the actions of protein tyrosine kinases. My previous studies and preliminary data suggest that PTPs act as molecular switches for key signalling events in the development of diabetes, i.e. insulin/glucose/cytokine signalling. Dysregulation of these pathways results in metabolic consequences that are cell-specific. Oxidative stress abrogates the nucleophilic properties of the PTP active site and induces conformational changes that inhibit PTP activity and prevent substrate-binding. I have recently developed an innovative proteomic approach to quantify PTP oxidation in vivo and demonstrated that this occurs in liver/pancreas under pathological conditions, including obesity and inflammation. In this proposal, I aim to fully characterise the activity and oxidation status of PTPs in dysfunctional metabolic relevant cells in obesity and diabetes. Importantly, the crucial role of PTPs make them promising candidates for the treatment of metabolic disorders. I hypothesise that specific antioxidants, diets and/or adenovirus will restore PTP function and ameliorate the metabolic deleterious defects in pre-clinical studies. Over the next 5 years, I aim to:

- Identify the major oxidised PTPs in metabolic relevant tissues/cells in both obesity and diabetes.
- Determine the contribution of PTP inactivation in cellular responses to metabolic signalling in human samples.
- Assess the impact of tissue-specific PTP deficiency on the development of obesity and diabetes.
- Test novel therapeutic approaches targeting PTPs to prevent/reverse metabolic disorders.

Link to the ERC project webpage: https://erc.europa.eu/projects-figures/erc-funded-projects/results?search_api_views_fulltext=gurzov+

Keywords of the ERC project: Metabolism, diabetes, protein tyrosine phosphatase, liver, pancreas

Keywords that characterize the scientific profile of the potential visiting researcher/s: Molecular biology, metabolic signalling, hiPSC, mouse models



European Research Council
Executive Agency

Established by the European Commission

Project ID:

818170

Project Acronym:

Epi4MS

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr MAJA JAGODIC**

Host Institution: **KAROLINSKA INSTITUTET - SE**

Targeting the epigenome: towards a better understanding of disease pathogenesis and novel therapeutic strategies in Multiple Sclerosis

Multiple Sclerosis (MS) is a leading cause of unpredictable and incurable progressive disability in young adults. Although the exact cause remains unknown, this immune-mediated disease is likely triggered by environmental factors in genetically predisposed individuals. I propose that epigenetic mechanisms, which regulate gene expression without affecting the genetic code, mediate the processes that cause MS and that aberrant epigenetic states can be corrected, spearheading the development of alternative therapies. We will exploit the stable and reversible nature of epigenetic marks, in particular DNA methylation, to gain insights into the novel modifiable disease mechanisms by studying the target organ in a way that has not been possible before. This highly ambitious project comprises three synergistic facets formulated in specific aims to: (i) identify epigenetic states that characterize the pathogenesis of MS, (ii) prioritize functional epigenetic states using high-throughput epigenome-screens, and (iii) develop novel approaches for precision medicine based on correcting causal epigenetic states. Our unique MS biobank combined with cutting-edge methodologies to capture pathogenic cells and measure their functional states provides a rational starting point to identify MS targets. I will complement this approach with studies of the functional impact of MS targets using innovative in vitro screens, with the added value of unbiased discovery of robust regulators of specific MS pathways. Finally, my laboratory has extensive experience with animal models of MS and I will utilize these powerful systems to dissect molecular mechanisms of MS targets and test the therapeutic potential of targeted epigenome editing in vivo. Our findings will set the stage for a paradigm-shift in studying and treating chronic inflammatory diseases based on preventing and modulating aggressive immune responses by inducing self-sustained reversal of aberrant epigenetic states.

Link to the ERC project webpage:

Keywords of the ERC project: epigenetics, multiple sclerosis, genetics, inflammation

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

818808

Project Acronym:

VesselNet

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr SHULAMIT LEVENBERG**

Host Institution: **TECHNION - ISRAEL INSTITUTE OF TECHNOLOGY - IL**

Engineering Composite Tissues for Facial Reconstruction

Facial reconstruction usually involves the use of autologous grafts or composite tissue allografts, which are highly complex tissues that pose significant challenges to tissue engineering experts. Tissue engineering of independent facial elements, e.g., bone, adipose, skin and muscle tissues, has been demonstrated. However, to date, no composite soft tissues composed of multiple facial layers have been created. Composite facial tissue engineering will require proper innervation and vascularization, essential to support generation of large thick implants. However, techniques for effective innervation of engineered tissues are currently insufficient and generation of well-vascularized large and thick engineered tissues is still one of the major obstacles limiting their translation to the clinic. Our goal is to engineer thick, composite, human-scale, facial tissues (muscle-adipose-dermis composite, and bone) of a personally adaptable shape, that will be vascularized in-vitro, and innervated upon transplantation. Our concept is to create in-vitro a functional vascular network (VesselNet), composed of both large and small vessels, within engineered constructs, which will allow for the generation of thick engineered tissues under continuous flow conditions. 3D bio-printing techniques will be applied to create the engineered tissues. These tissues will serve as a model to study mechanisms involved in vessel anastomosis, and tissue organization and stabilization. The applicability of the engineered composite soft and bone tissues will be evaluated in facial, breast and abdominal wall defect reconstruction models, and in an open fracture model. Such engineered large-scale composite tissues are expected to have a major impact on reconstructive surgery and will shed light on yet unknown tissue organization mechanisms.

Link to the ERC project webpage:

Keywords of the ERC project: Engineered thick composite tissues, Vascularization, Muscle, Bone, Adipose, Innervation, 3D bioprinting, Reconstructive surgery

Keywords that characterize the scientific profile of the potential visiting researcher/s: Tissue engineering, 3D bio-printing



European Research Council
Executive Agency

Established by the European Commission

Project ID:

820137

Project Acronym:

CANCEREVO

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr MARCO GERLINGER**

Host Institution: **THE INSTITUTE OF CANCER RESEARCH: ROYAL CANCER HOSPITAL - UK**

Deciphering and predicting the evolution of cancer cell populations

The fundamental evolutionary nature of cancer is well recognized but an understanding of the dynamic evolutionary changes occurring throughout a tumour's lifetime and their clinical implications is in its infancy. Current approaches to reveal cancer evolution by sequencing of multiple biopsies remain of limited use in the clinic due to sample access problems in multi-metastatic disease. Circulating tumour DNA (ctDNA) is thought to comprehensively sample subclones across metastatic sites. However, available technologies either have high sensitivity but are restricted to the analysis of small gene panels or they allow sequencing of large target regions such as exomes but with too limited sensitivity to detect rare subclones. We developed a novel error corrected sequencing technology that will be applied to perform deep exome sequencing on longitudinal ctDNA samples from highly heterogeneous metastatic gastro-oesophageal carcinomas. This will track the evolution of the entire cancer population over the lifetime of these tumours, from metastatic disease over drug therapy to end-stage disease and enable ground breaking insights into cancer population evolution rules and mechanisms. Specifically, we will: 1. Define the genomic landscape and drivers of metastatic and end stage disease. 2. Understand the rules of cancer evolutionary dynamics of entire cancer cell populations. 3. Predict cancer evolution and define the limits of predictability. 4. Rapidly identify drug resistance mechanisms to chemo- and immunotherapy based on signals of Darwinian selection such as parallel and convergent evolution. Our sequencing technology and analysis framework will also transform the way cancer evolution metrics can be accessed and interpreted in the clinic which will have major impacts, ranging from better biomarkers to predict cancer evolution to the identification of drug targets that drive disease progression and therapy resistance.

Link to the ERC project webpage:

Keywords of the ERC project: circulating tumor DNA, ultra-deep whole exome sequencing, sequencing error correction methods, bioinformatics

Keywords that characterize the scientific profile of the potential visiting researcher/s: bioinformatics, cancer genetics, coding, sequencing error correction



European Research Council
Executive Agency

Established by the European Commission

Project ID:

851231

Project Acronym:

THERAUTISM

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr LUCIE PELLISSIER**

Host Institution: **CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS - FR**

New molecular targets and proof-of-concept therapies for Autism Spectrum Disorders

Autism is the major neurodevelopmental health public issue, affecting 1/100 child births worldwide. These disorders are diagnosed before the age of 3, based on behavioural cues: deficits in social interaction and communication as well as stereotyped and restrained behaviours. There is no medication to improve this condition. Most recent molecular targets identified within narrow frameworks (unspecific molecule, single tissue targeted, single disease model used) have failed in clinical trials. My first objective aims at thwarting this autism research gap, unravelling the common molecular and cellular dysfunctions underlying autism-related behaviours across several preclinical models and neuronal circuits. In particular, setting up translational analyses in these paradigms will identify and validate new molecular therapeutic targets. I recently deciphered one such molecular substrate, involving the loss of oxytocin transcripts in oxytocinergic axon terminals thus demonstrating the feasibility of this global approach. The second major objective of my project is to hijack the properties of a newly identified protein function to restore this new target and rescue social deficits in different preclinical models of autism. This would yield a novel and safe gene therapy vector which has never been explored before. Altogether, my research project will deliver strategic resources to the scientific and medical communities that will spur the development of new treatment options for autistic patients.

Link to the ERC project webpage:

Keywords of the ERC project: autism, translational, new targets, new therapies

Keywords that characterize the scientific profile of the potential visiting researcher/s: neuroscience, behavior
or omic



European Research Council
Executive Agency

Established by the European Commission

Project ID:

714312

Project Acronym:

RACE

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr ANNETTE VAN DER HELM - VAN MIL**

Host Institution: **ACADEMISCH ZIEKENHUIS LEIDEN - NL**

Rheumatoid Arthritis Caught Early: investigating biological mechanisms preceding chronification of joint inflammation to identify patients prior to presentation of classic chronic arthritis

Rheumatoid Arthritis (RA) causes long lasting disability. At the time of clinically evident arthritis and diagnosis, the disease is already persisting, requiring long-term suppressive treatment. My overarching aim is to prevent chronic arthritis and RA by inhibiting the evolving auto-immune response in a pre-arthritis phase. Currently, identification of RA-patients before the classic presentation with clinically evident chronic arthritis is beyond the state of the art. I here aim to achieve this early recognition by increasing the mechanistic understanding of pre-arthritis phases.

I intend to study RA-specific auto-immune responses at the cellular and humoral level as well as markers reflecting local and systemic inflammation. These aspects are selected based on my world-wide validated rule to predict RA-development in early arthritis and on recent work on progression from Clinically Suspect Arthralgia (CSA) to clinical arthritis.

This project is now finally feasible, thanks to unique 'pre-RA' cohorts and cross-boundary preparatory work done with basic scientists, clinicians and engineers. My research concept is to integrate the products of separate trajectories in a longitudinal study and translate it to the clinic.

Patients with CSA will be studied serially in time. Using validated methods and novel techniques and insights we will: delineate molecular and predictive features of RA-specific auto-antibodies and auto-antibody secreting B-cells, identify improved markers of systemic inflammation and test and validate a computer-aided image analysis system to detect subclinical joint inflammation on MRI. Serial data will be combined to reveal interactions between markers and time relationships. Lastly a prediction model identifying imminent RA will be developed. The forefront position of my group allows national and international validation.

Together, this multidisciplinary and intersectorial project will open new horizons for preventive, targeted interventions.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

724872

Project Acronym:

Celltrack

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr BJÖRN HÖGBERG**

Host Institution: **KAROLINSKA INSTITUTET - SE**

Cellular Position Tracking Using DNA Origami Barcodes

The research I propose here will provide an enabling technology; spatially resolved transcriptomics, to address important problems in cell- and developmental-biology, in particular: How are stem cells in the skin and gut proliferating without turning into cancers? How are differentiated cells related, in their transcriptome and spatial positions, to their progenitors?

To investigate these problems on a molecular level and open up paths to find completely new spatiotemporal interdependencies in complex biological systems, I propose to use our newly developed DNA-origami strategy (Benson et al, Nature, 523 p. 441 (2015)), combined with a combinatorial cloning technique, to build a new method for deep mRNA sequencing of tissue with single-cell resolution. These new types of origami are stable in physiological salt conditions and opens up their use in in-vivo applications.

In DNA-origami we can control the exact spatial position of all nucleotides. By folding the scaffold to display sequences for hybridization of fluorophores conjugated to DNA, we can create optical nano-barcodes. By using structures made out of DNA, the patterns of the optical barcodes will be readable both by imaging and by sequencing, thus enabling the creation of a mapping between cell locations in an organ and the mRNA expression of those cells.

We will use the method to perform spatially resolved transcriptomics in small organs: the mouse hair follicle, and small intestine crypt, and also perform the procedure for multiple samples collected at different time points. This will enable a high-dimensional data analysis that most likely will expose previously unknown dependencies that would provide completely new knowledge about how these biological systems work. By studying these systems, we will uncover much more information on how stem cells contribute to regeneration, the issue of de-differentiation that is a common theme in these organs and the effect this might have on the origin of cancer.

Link to the ERC project webpage: www.hogberglab.net

Keywords of the ERC project: DNA nanostructures, sequencing, spatial transcriptomics

Keywords that characterize the scientific profile of the potential visiting researcher/s: Computer science,
bioinformatics, biophysics, directed evolution



European Research Council
Executive Agency

Established by the European Commission

Project ID:

725229

Project Acronym:

EVICARE

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr JOOST SLUIJTER**

Host Institution: **UNIVERSITAIR MEDISCH CENTRUM UTRECHT - NL**

Extracellular Vesicle-Inspired CARDiac Repair

More than 3.5 million people are newly diagnosed with heart failure every year in Europe with a long-term prognosis of 50% mortality within 4 years. There is a major need for more innovative, regenerative therapies that have the potential to change the course of disease. My hypothesis is that we can recondition heart failure by stimulating cardiac repair with extracellular vesicles that are derived from progenitor cells. In my laboratory, extracellular released vesicles containing a cocktail of stimulating factors, are amongst the most potent vectors for cardiac repair.

To achieve a sustainable and long-term therapeutic effect of these vesicles and enhance cardiac function by stimulating myocardial repair, we will 1) improve local cardiac delivery of progenitor cell-derived extracellular vesicles, 2) understand the mechanism of action of extracellular vesicles, and 3) stimulate extracellular vesicles release and/or production by progenitor cells.

These questions form the rationale for the current proposal in which we will co-inject extracellular vesicles and slow-release biomaterials into the damaged myocardium. By subsequent genetic tracing, we will determine fate mapping of injected vesicles in vivo, and perform further mechanistic understanding in in vitro culture models of targeted and identified myocardial cell types. Moreover, we will upscale the vesicles production by progenitor cells further via bioreactor culturing and medium-throughput screening on factors that stimulate vesicles release.

The use of stem cell-derived extracellular vesicles to stimulate cardiac repair will potentially allow for an off-the shelf approach, including mechanistic understanding and future clinical use. Additionally, since these vesicles act as a natural carrier system outperforming current artificial drug delivery, we might understand and mimic their characteristics to enhance local (RNA-based) drug delivery systems for cardiovascular application.

Link to the ERC project webpage: <https://www.umcutrecht.nl/en/Research/Researchers/Sluijter-Joost-P-G-JPG>

Keywords of the ERC project: cardiac repair, extracellular vesicles, regeneration,

Keywords that characterize the scientific profile of the potential visiting researcher/s: collaborative, passionate, technology driven, team-player



European Research Council
Executive Agency

Established by the European Commission

Project ID:

743077

Project Acronym:

ThermalMR

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator:

Dr THORALF NIENDORF

Host Institution:

MAX DELBRUECK CENTRUM FUER MOLEKULARE MEDIZIN IN DER
HELMHOLTZ-GEMEINSCHAFT (MDC) - DE

Thermal Magnetic Resonance: A New Instrument to Define the Role of Temperature in Biological Systems and Disease for Diagnosis and Therapy

Temperature is a physical parameter with diverse biological implications and crucial clinical relevance. With an ever increasing interest in thermal applications, non-invasive in vivo methods to modulate temperature and characterize subsequent effects are imperative. Magnetic resonance (MR) is a mainstay of diagnosis but lacks inherent means for focal thermal modulation.

Ultrahigh field (UHF) MR employs higher radio frequencies (RF) than conventional MR and has unique potential to provide focal temperature manipulation and high resolution imaging (ThermalMR). Our simulations show that we can adapt an UHF- MR device to generate heat in highly focused regions of tissue by using high-density RF transmitter arrays. This new instrument will provide a revolutionary method for precise in vivo temperature manipulations. To establish high-fidelity thermal dosimetry, we will investigate pioneering strategies that exploit electrical and heat transfer tissue properties. For thermal dosage control, novel methods of MR thermometry will be developed. The capacity of ThermalMR for thermal intervention will be demonstrated in model systems. Its efficacy for drug release will be explored using new thermo-responsive nanocarriers loaded with fluorinated probes, exquisitely quantifiable with ¹⁹F MR. The applicability and safety of ThermalMR will be demonstrated in animal models followed by a feasibility study in healthy subjects. To link thermal responses of MR contrasts with molecular signatures, gene expression profiling will be performed. The aim is to understand the thermal properties of healthy and pathological tissues and explore the use of temperature modulation as a therapeutic tool. ThermalMR will eradicate the main barriers to the study and use of temperature - a critical dimension of life that is of intense clinical interest, but so far very poorly understood. This approach opens an entirely new research field of thermal phenotyping: where physics, biology and medicine meet.

[Link to the ERC project webpage:](#)

[Keywords of the ERC project:](#) magnetic resonance imaging, radiofrequency antenna, drug release, temperature

[Keywords that characterize the scientific profile of the potential visiting researcher/s:](#) open mind unbound curiosity



European Research Council
Executive Agency

Established by the European Commission

Project ID:

754365

Project Acronym:

CuHypMech

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr SHARON RUTHSTEIN**

Host Institution: **BAR ILAN UNIVERSITY - IL**

New Nuclear Medicine Imaging Radiotracer $^{64}\text{Cu(II)}$ for diagnosing Hypoxia Conditions Based on the Cellular Copper Cycle

Imaging of hypoxia is important in many disease states in oncology, cardiology, and neurology. Hypoxia is a common condition encountered within the tumour microenvironment that drives proliferation, angiogenesis, and resistance to therapy. Despite on-going efforts to identify hypoxia, until now there is no clinically approved imaging biomarker, due to both low tumour uptake, and a low signal to background (S/B) ratio that affects the imaging quality. Nuclear Medicine is using labelled radio-isotopes for PET/CT and SPECT imaging. These radio-tracers diagnose the metabolic processes in the body. Among these tracers, ^{18}F -FDG is the most routinely used as a marker of glucose metabolism. However, not all tumours consume glucose, and glucose consumption is not specific only for malignant tumours, which limits its application. Copper is a nutritional metal, recently examined as a radiotracer for hypoxia, owing to its to the oxidising environment. Clinical and in-vivo studies on various $^{64}\text{Cu(II)}$ -PET radiotracers resulted in controversial reports on the specificity of the current tracers for hypoxia imaging due to non-selective bio-distribution & low S/B ratio. This multidisciplinary proposal focuses on the discovery of comprehensive signal pathways of the cellular copper cycle using advanced biophysical methods and a proprietary design of $^{64}\text{Cu(II)}$ radiotracer. This radiotracer will be incorporated in the cellular copper cycle, and will enable to selectively target the oxidising environment in tumours. The design of the new radiotracer is based on systematic structural & functional mapping of the copper binding sites to the various copper proteins and the visualisation of the transfer mechanism. This new copper tracer should increase the selectivity of tumour uptake, stability, and improve bio-distribution. This project assimilates cold and hot chemistry and biology, while emphasising the clinical unmet need in metal based radiotracer that form stable complexes.

Link to the ERC project webpage: www.ruthstein-lab.com

Keywords of the ERC project: copper homeostasis, EPR spectroscopy, copper based radiotracers

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

757922

Project Acronym:

BugTheDrug

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr INES THIELE**

Host Institution: **NATIONAL UNIVERSITY OF IRELAND GALWAY - IE**

Predicting the effects of gut microbiota and diet on an individual's drug response and safety

Precision medicine is an emerging paradigm that aims at maximizing the benefits and minimizing the harm of drugs. Realistic mechanistic models are needed to understand and limit heterogeneity in drug responses. Consequently, novel approaches are required that explicitly account for individual variations in response to environmental influences, in addition to genetic variation. The human gut microbiota metabolizes drugs and is modulated by diet, and it exhibits significant variation among individuals. However, the influence of the gut microbiota on drug failure or drug side effects is under-researched. In this study, I will combine whole-body, genome-scale molecular resolution modeling of human metabolism and human gut microbial metabolism, which represents a network of genes, proteins, and biochemical reactions, with physiological, clinically relevant modeling of drug responses. I will perform two pilot studies on human subjects to illustrate that this innovative, versatile computational modeling framework can be used to stratify patients prior to drug prescription and to optimize drug bioavailability through personalized dietary intervention. With these studies, BugTheDrug will advance mechanistic understanding of drug-microbiota-diet interactions and their contribution to individual drug responses. I will perform the first integration of cutting-edge approaches and novel insights from four distinct research areas: systems biology, quantitative systems pharmacology, microbiology, and nutrition. BugTheDrug conceptually and technologically addresses the demand for novel approaches to the study of individual variability, thereby providing breakthrough support for progress in precision medicine.

Link to the ERC project webpage: thielelab.eu

Keywords of the ERC project: Computational modeling, metabolism, human, microbiome, drug metabolism, physiology-based pharmacokinetic modeling, Parkinson's Disease

Keywords that characterize the scientific profile of the potential visiting researcher/s: Computational modeling, metabolism, human, microbiome, drug metabolism, physiology-based pharmacokinetic modeling, Parkinson's Disease



European Research Council
Executive Agency

Established by the European Commission

Project ID:

786462

Project Acronym:

HOPE

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr GOTTFRIED BAIER**

Host Institution: **MEDIZINISCHE UNIVERSITÄT INNSBRUCK - AT**

Host Protective Engineering of Cancer Immunity by Targeting the Intracellular Immune Checkpoint NR2F6

Because of its biological complexity, cancer is still poorly understood. Chronic inflammation has been shown, both experimentally and epidemiologically, to be a predisposition to, and also an inseparable aspect of clinically prevalent cancer entities. Therefore, a detailed understanding of both tumour and immune cell functions in cancer progression is a prerequisite for more successful therapeutic strategies. My team was the first to reveal the lymphocyte-intrinsic PKC/NR2F6 axis as an essential signalling node at the crossroads between inflammation and cancer. It is the mission of this project to identify molecular signatures that influence the risk of developing tumours employing established research tools and state-of-the-art genetic, biochemical, proteomic and transcriptomic as well as large scale CRISPR/Cas9 perturbation screening-based functional genomic technologies. Defining this as yet poorly elucidated effector pathway with its profoundly relevant role would enable development of preventive and immune-therapeutic strategies against NSCLC lung cancer and potentially also against other entities. Our three-pronged approach to achieve this goal is to: (i) delineate biological and clinical properties of the immunological PKC/NR2F6 network, (ii) validate NR2F6 as an immune-oncology combination target needed to overcome limitations to "first generation anti-PD-1 checkpoint inhibitors" rendering T cells capable of rejecting tumours and their metastases at distal organs and (iii) exploit human combinatorial T cell therapy concepts for prevention of immune-related adverse events as well as of tumour recurrence by reducing opportunities for the tumour to develop resistance in the clinic. Insight into the functions of NR2F6 pathway and involved mechanisms is a prerequisite for understanding how the microenvironment at the tumour site either supports tumour growth and spread or prevents tumour initiation and progression, the latter by host-protective cancer immunity.

Link to the ERC project webpage: <http://www.baierlab.com/>

Keywords of the ERC project: Tumor immunology T cell Signaling Immune checkpoint blockade

Keywords that characterize the scientific profile of the potential visiting researcher/s: Cancer immunotherapy
and therapy resistance



European Research Council
Executive Agency

Established by the European Commission

Project ID:

801790

Project Acronym:

MOBILIZE

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr SØREN T. SKOU**

Host Institution: SYDDANSK UNIVERSITET - DK

Improving health in people with multimorbidity: a paradigm shift in health care from disease-based curative models to personalized exercise therapy and self-management

The goal of this proposal is to support the paradigm shift in the health care of people with multiple chronic conditions in Europe from a focus on disease-based curative models to holistic person-centered self-care through personalized, supervised exercise therapy and education.

The problem: The impact of multimorbidity on the individual and society is massive and much greater than the impact of single chronic conditions alone. However, effective treatments are missing and research and health care reinforce an inefficient and burdensome single-disease framework.

The solution: Exercise has the potential to disrupt the 'vicious cycle' of systemic inflammation associated with chronic conditions and improve health in multimorbidity. A personalized exercise and education program aimed at supporting subsequent self-management by the individual will be developed in an interdisciplinary collaboration, building on evidence from biomarkers, patient involvement and methodological expertise. Self-reported, physiological and societal effects will be investigated in a randomized controlled trial comparing the personalized program with standard single-disease models of care. Scientific and public dissemination and implementation ensuring significant personal and societal benefit is fundamental to the proposal.

The proposal is associated with high risk, as the current disease-based curative models involve treatment by several highly specialized health care providers, while the new person-centered self-management model is centered on a personalized program delivered by one health care provider.

The ground-breaking nature of this proposal lies in its potential to revolutionize how health care is organized for people with multimorbidity, by giving them one primary care provider, and how we use non-surgical treatment in health care and science by bringing the concept of precision medicine into multimorbidity and utilizing it to improve treatment outcome with exercise therapy as the model.

Link to the ERC project webpage: <http://www.mobilize-project.dk/>

Keywords of the ERC project: Exercise; multimorbidity; clinical trial, implementation

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

817884

Project Acronym:

ViroPedTher

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr MARTA ALONSO**

Host Institution: **UNIVERSIDAD DE NAVARRA - ES**

Oncolytic viruses for the treatment of pediatric brain tumors: An integrated clinical and lab approach

The overarching goal of my lab is to improve the prognosis of patients with high-risk pediatric brain tumors. To this end, I propose to integrate clinical and lab-based research to develop tumor-targeted oncolytic adenoviruses with the capacity to elicit a therapeutic immune response in those tumors. Our research will use novel and relevant models to accomplish the experimental aims. We have previously worked with Delta-24-RGD (DNX-2401) a replication-competent adenovirus that has been translated to the clinical scenario. In 2017, the first clinical trial phase I with DNX-2401 for newly diagnosed Diffuse Intrinsic Pontine Gliomas (DIPG; a lethal pediatric brain tumor) opened propelled by my team. Preliminary results from the first trials revealed that the intratumoral injection of the virus instigated an initial phase of oncolysis followed by a delayed inflammatory response that ultimately resulted in complete regression in a subset of the patients without associated toxicities. I hypothesized that enhancement of the immune component of the DNX-2401-based therapy will result in the complete regression of the vast majority of pediatric brain tumors. In our specific approach, we propose to understand the immune microenvironment of DIPGs and the response to viral therapy in the context of the trial. Moreover, that knowledge will leverage the design of Delta-24-based adenoviruses to recruit lymphocytes to the tumor with the competence of different type of ligands to activate the tumor infiltrating lymphocytes. I expect that this combinatorial innovative treatment will efficiently challenge the profound and inherent tumor immunosuppression and, in turn, will elicit a robust anti-tumor immune response resulting in the significant improvement of the prognosis and quality of life of patients with pediatric brain tumors. This project has the potential to produce a vertical advance in the field of pediatric oncology.

Link to the ERC project webpage:

Keywords of the ERC project: Pediatric Brain Tumors, Oncolytic Virus, Therapy, ImmunoVirotherapy, Clinical Trial,

Keywords that characterize the scientific profile of the potential visiting researcher/s: Translational Research, Bioinformatics, immunotherapy, flow cytometry, animal models, brain tumors,



European Research Council
Executive Agency

Established by the European Commission

Project ID:

818806

Project Acronym:

TALE

Evaluation Panel:

LS7

Diagnostic Tools,
Therapies and Public
Health

Principal Investigator: **Dr LUKAS JEKER**

Host Institution: **UNIVERSITÄT BASEL - CH**

Therapeutic Allele Engineering: A novel technology for cell therapy

We are currently witnessing a revolution in cell therapies that are rooted in decades of basic research in genetics, cell biology and immunology. A deep understanding of mammalian, and in particular immune, cells is currently being translated into highly efficient cell-based therapeutics. Technologic breakthroughs in genetic and genome engineering are further fueling the generation of customized, high precision therapies that are based on cells as “smart drugs”. For instance, reprogramming immune killer cells to recognize B cell leukemias resulted in unprecedented clinical responses in treatment-resistant and relapsed patients. However, currently only very few, highly selected patients benefit from these developments. A fundamental problem of today’s cell therapies is that transferred cells cannot be distinguished from host cells. We have developed “allele engineering”, a new technology that solves this challenge. Here, we outline how allele engineering will improve the safety and efficacy of cell therapies. We will 1) generate a non-viral, DNA-free safety/shielding switch 2) develop a radically new curative approach to acute myeloid leukemia 3) rationally design a safe allele engineering solution for human therapy and 4) use allele engineering as a curative therapy of scurfy syndrome, a lethal monogenic autoimmune disease. Allele engineering enables completely new treatment strategies and can be applied to any surface protein. Therefore, I anticipate that the results will have a major impact on the field.

Link to the ERC project webpage: https://erc.europa.eu/projects-figures/erc-funded-projects/results?search_api_views_fulltext=jeker

Keywords of the ERC project: Genome Engineering, cell therapy

Keywords that characterize the scientific profile of the potential visiting researcher/s: Expert in hHSC biology and/or genome editing of hHSCs. Alternatively: Human T cell engineering expert.



European Research Council
Executive Agency

Established by the European Commission

Project ID:

694578

Project Acronym:

IsoMet

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr COLIN MURRELL**

Host Institution: UNIVERSITY OF EAST ANGLIA - UK

Bacterial isoprene metabolism: a missing link in a key global biogeochemical cycle

Isoprene is a very important climate-active biogenic volatile organic compound with both global warming and cooling effects. Globally, terrestrial plants emit huge amounts (~500-750 million tonnes) of isoprene per year. This is approximately the same quantity as methane released to the atmosphere. Isoprene emissions are predicted to rise due to global warming and increased use of isoprene-emitting trees (oil palm, poplar) for biofuel production but almost nothing is known about its biogeochemical cycle. Microbes are a sink for isoprene and through their activity in soils and on the leaves of isoprene-emitting plants, they will be important in removal of isoprene in the biosphere before it gets released to the atmosphere.

The aim of the project is to obtain a critical, fundamental understanding of the metabolism and ecological importance of biological isoprene degradation and to test the hypothesis that isoprene degrading bacteria play a crucial role in the biogeochemical isoprene cycle, thus helping to mitigate the effects of this important but neglected climate-active gas. Key objectives are to elucidate the biological mechanisms by which isoprene is metabolised, establish novel methods for the study of isoprene biodegradation and to understand at the mechanistic level how isoprene cycling by microbes is regulated in the environment. Bacteria that metabolise isoprene will be isolated from a range of terrestrial and marine environments and characterised using a multidisciplinary approach and a wide range of cutting edge techniques. We will elucidate the pathways of isoprene metabolism and their regulation by characterising genes/enzymes catalysing key steps in isoprene degradation, use innovative molecular ecology methods to determine distribution, diversity and activity of isoprene degraders and assess the contribution that microbes make in the removal of isoprene from the biosphere, thereby mitigating the effects of this climate-active compound.

Link to the ERC project webpage: www.jcmurrell.co.uk

Keywords of the ERC project: isoprene environmental microbiology microbial ecology monooxygenases

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

714804

Project Acronym:

MicroBeeOme

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr PHILIPP ENGEL**

Host Institution: **UNIVERSITE DE LAUSANNE - CH**

Evolution of the honey bee gut microbiome through bacterial diversification

Animals harbor specialized bacterial communities in their guts, typically referred to as gut microbiomes. Despite the importance of gut microbiomes for host health, surprisingly little is known about their evolution. There is evidence that the complexity of the mammalian gut microbiome has emerged through the diversification of a few founder lineages. However, how lineages have diversified into discrete species and which underlying mechanisms maintain the diversity in the gut remains elusive. The current project will address these questions by studying the gut microbiome of honey bees. We have recently found that the eight dominant bacterial lineages in the honey bee gut have substantially diversified, which is a striking parallelism to the evolution of the mammalian gut microbiome. Moreover, we have established experiments to colonize microbiota-free bees with cultured isolates of divergent bee gut bacteria. This provides us with unique opportunities to study bacterial evolution in the gut in a simple and experimentally amenable system. The project is divided into four work packages addressing interconnected research questions of current biology: We will (i) determine the population genomic landscape of divergent gut bacteria, (ii) investigate whether bacterial diversification has resulted in competition or cooperation, (iii) discover novel mechanisms of bacterial interactions, and (iv) reveal how bacterial diversification impacts the symbiosis with the host. To this end, we will use a multidisciplinary approach combining comparative metagenomics, transcriptomics, metabolomics, bee colonization experiments, microscopy, bacterial genetics, and automated bee tracking. This project situated at the forefront of microbial symbiosis will provide groundbreaking insights into microbial evolution and ecology, gut microbiology, and honey bee health and biology.

[Link to the ERC project webpage:](#)

[Keywords of the ERC project:](#)

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

714916

Project Acronym:

LEAF-FALL

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr MATTEO CAMPIOLI**

Host Institution: **UNIVERSITEIT ANTWERPEN - BE**

What makes leaves fall in autumn? A new process description for the timing of leaf senescence in temperate and boreal trees

Leaf phenology is a key component in the functioning of temperate and boreal deciduous forests. The environmental cues for bud-burst in spring are well known, but little is known about the cues controlling the timing of leaf fall in autumn. Leaf fall is the last stage of leaf senescence, a process which allows trees to recover leaf nutrients. We urgently need to understand the controls timing leaf senescence to improve our projections of forest growth and climate change. I propose a new general paradigm of the onset of leaf senescence, hypothesizing that leaf senescence is triggered by the cessation of tree growth in autumn. I expect that: (i) in the absence of growth-limiting environmental conditions, tree growth cessation directly controls leaf-senescence onset; and (ii) in the presence of growth-limiting conditions, photoperiod controls leaf-senescence onset – this prevents trees from starting to senesce too early. I will test these hypotheses with a combination of: (i) manipulative experiments on young trees - these will disentangle the impact of photoperiod from that of other factors affecting tree growth cessation, namely: temperature, drought and soil nutrient availability; (ii) monitoring leaf senescence and growth in mature forest stands; (iii) comparing the leaf senescence dynamics of four major tree species (*Fagus sylvatica*, *Quercus robur*, *Betula pendula* and *Populus tremula*) in four European locations spanning from 40° to 70° N; and (iv) integrating the new paradigm into a model of forest ecosystem dynamics and testing it for the major forested areas of Europe. The aim is to solve the conundrum of the timing of leaf senescence in temperate and boreal deciduous trees, provide a new interpretation of the relationship between leaf senescence, tree growth and environment, and deliver a modelling tool able to predict leaf senescence and tree growth, for projections of forest biomass production and climate change.

Link to the ERC project webpage: <https://www.uantwerpen.be/en/projects/leaf-fall/about-leaf-fall/>

Keywords of the ERC project: deciduous trees, forest, phenology, ecophysiology

Keywords that characterize the scientific profile of the potential visiting researcher/s: PhD or Post-doc with expertise appearing from international publications



European Research Council
Executive Agency

Established by the European Commission

Project ID:

724173

Project Acronym:

RETVOLUTION

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr TONI GABALDON**

Host Institution: **FUNDACIO CENTRE DE REGULACIO GENOMICA - ES**

Reticulate evolution: patterns and impacts of non-vertical inheritance in eukaryotic genomes.

The traditional view is that species and their genomes evolve only by vertical descent, leading to evolutionary histories that can be represented by bifurcating lineages. However, modern evolutionary thinking recognizes processes of reticulate evolution, such as horizontal gene transfer or hybridization, which involve total or partial merging of genetic material from two diverged species. Today it is widely recognized that such events are rampant in prokaryotes, but a relevant role in eukaryotes has only recently been acknowledged. Unprecedented genomic and phylogenetic information, and recent work from others and us have shown that reticulate evolution in eukaryotes is more common and have more complex outcomes than previously thought. However, we still have a very limited understanding of what are the impacts at the genomic and evolutionary levels. To address this, I propose to combine innovative computational and experimental approaches. The first goal is to infer patterns of reticulate evolution across the eukaryotic tree, and relate this to current biological knowledge. The second goal is to trace the genomic aftermath of inter-species hybridization at the i) long-term, by analysing available genomes in selected eukaryotic taxa, ii) mid-term, by sequencing lineages of natural fungal hybrids, and iii) short-term, by using re-sequencing and experimental evolution in yeast. A particular focus is placed on elucidating the role of hybridization in the origin of whole genome duplications, and in facilitating the spread of horizontally transferred genes. Finally results from this and other projects will be integrated into emerging theoretical frameworks. Outcomes of this project will profoundly improve our understanding of reticular processes as drivers of eukaryotic genome evolution, and will impact other key aspects of evolutionary theory, ranging from the concept of orthology to the eukaryotic tree of life.

Link to the ERC project webpage: www.cgenomics.org

Keywords of the ERC project: Evolution, Phylogenomics, Eukaryotes, Hybridization, Comparative Genomics

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

725848

Project Acronym:

CORALASSIST

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr JAMES GUEST**

Host Institution: **UNIVERSITY OF NEWCASTLE UPON TYNE - UK**

Assisting Coral Reef Survival in the Face of Climate Change

CORALASSIST spans the disciplines of evolutionary biology, restoration ecology and proteomics and examines the role assisted gene flow (AGF) can play in sustaining biodiversity and ecosystem services in the face of climate change. AGF involves the deliberate movement of individuals or gametes within their natural range to facilitate adaptation to environmental change. Corals reefs provide an excellent model for testing AGF as a conservation tool because reef building corals are foundation species and are highly vulnerable to thermal stress. Selective breeding and translocation of thermotolerant individuals may lead to reductions in recipient population fitness due to resource trade-offs with other fitness traits, such as growth and fecundity. The overall aim of CORALASSIST is to establish the feasibility of implementing AGF in coral reef ecosystems using a combination of selective breeding, proteomics and innovative translocation techniques. CORALASSIST will address four primary questions: 1) Are there resource trade-offs between increased thermotolerance and other fitness traits in corals? 2) Which physiological and proteomic traits correlate with increased individual thermotolerance in corals? 3) Are phenotypic traits for thermotolerance heritable? 4) Can AGF and selective breeding lead to persistent shifts in thermotolerance in recipient populations? Phenotypic traits will be measured in permanently tagged individuals within selected coral populations to examine the relationships between thermotolerance and key fitness attributes. For the first time, state of the art proteomic approaches will be used to elucidate the physiological basis for increased levels of thermotolerance in corals. Innovative translocation methods will be used in tandem with selective breeding techniques to carry out the first long term assessment of heritability of thermotolerance and to test the feasibility of large scale AGF to assist conservation of coral reef ecosystems.

Link to the ERC project webpage: www.coralassistlab.org

Keywords of the ERC project: coral reefs, assisted gene flow, selective breeding, restoration ecology, proteomics, climate change

Keywords that characterize the scientific profile of the potential visiting researcher/s: coral reefs, assisted gene flow, selective breeding, restoration ecology, proteomics, climate change



European Research Council
Executive Agency

Established by the European Commission

Project ID:

726116

Project Acronym:

ecolipid

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr YIN CHEN**

Host Institution: **THE UNIVERSITY OF WARWICK - UK**

Ecophysiology of membrane lipid remodelling in marine bacteria

Membrane lipids form the structural basis of all cells. In bacteria *Escherichia coli* uses predominantly phosphorus-containing lipids (phospholipids) in its cell envelope, including phosphatidylethanolamine and phosphatidylglycerol. However, beyond *E. coli* a range of lipids are found in bacterial membranes, including phospholipids as well as phosphorus (P)-free lipids such as betaine lipids, ornithine lipids, sulfolipids and glycolipids. In the marine environment, it is well established that P availability significantly affects lipid composition in the phytoplankton, whereby non-P sulfur-containing lipids are used to substitute phospholipids in response to P stress. This remodeling offers a significant competitive advantage for these organisms, allowing them to adapt to oligotrophic environments low in P. Until very recently, abundant marine heterotrophic bacteria were thought to lack the capacity for lipid remodelling in response to P deficiency. However, recent work by myself and others has now demonstrated that lipid remodelling occurs in many ecologically important marine heterotrophs, such as the SAR11 and *Roseobacter* clades, which are not only numerically abundant in marine waters but also crucial players in the biogeochemical cycling of key elements. However, the ecological and physiological consequences of lipid remodeling, in response to nutrient limitation, remain unknown. This is important because I hypothesize that lipid remodeling has important knock-on effects restricting the ability of marine bacteria to deal with both abiotic and biotic stresses, which has profound consequences for the functioning of major biogeochemical cycles. Here I aim to use a synthesis of molecular biology, microbial physiology, and "omics" approaches to reveal the fitness trade-offs of lipid remodelling in cosmopolitan marine heterotrophic bacteria, providing novel insights into the ecophysiology of lipid remodelling and its consequences for marine nutrient cycling.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

741298

Project Acronym:

MagneticMoth

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr ERIC WARRANT**

Host Institution: **LUNDS UNIVERSITET - SE**

Hunting for the elusive “sixth” sense: navigation and magnetic sensation in a nocturnal migratory moth

Many animals – including birds, sea turtles and insects – perform spectacular long-distance migrations across the surface of the Earth. Remarkably some, like birds, can accurately migrate between highly specific locations thousands of kilometres apart, a navigational feat that requires an external compass cue and a robust sensory system to detect it. The Earth’s magnetic field is one such compass cue. But exactly how the magnetic field is sensed, and which receptor cells are involved, remains a mystery and its discovery is one of the greatest “holy grails” in modern sensory physiology, and also the main aim of this proposal. Fortuitously, I have made a pioneering discovery that a migratory insect – the Australian Bogong moth – relies on the Earth’s magnetic field to navigate at night. Due to its tractable nervous system, this insect may thus hold the key to uncovering the identity of the enigmatic magnetosensor. By tethering flying migrating moths in a flight simulator, I will dissect for the first time how insects use magnetic cues to navigate, isolating which of the two current (contentious) hypotheses for magnetic sensation apply. The most likely of these involves the action of photoreceptor-based cryptochrome (Cry) molecules in the eyes. Having cloned genes for 4 visual opsins and 2 Cry in Bogong moths, I will use in situ hybridisation to localise putative magnetoreceptors in the eyes, targeting them with intracellular electrophysiology and magnetic stimulation in an attempt to describe the physiology of these elusive sensors for the first time. The project is ground breaking since it will elucidate how a migratory insect, despite its small eyes and brain, detects and uses the Earth’s magnetic field for navigation. The discovery of the enigmatic magnetoreceptor would be a sensation, opening the floodgates for international research on this little understood sense.

[Link to the ERC project webpage:](#)

[Keywords of the ERC project:](#) Magnetic sense, migration, navigation, insect, moth

[Keywords that characterize the scientific profile of the potential visiting researcher/s:](#) Sensory biology, entomology, sensory ecology, navigation, migration



European Research Council
Executive Agency

Established by the European Commission

Project ID:

742312

Project Acronym:

MATURATION

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr CRAIG PRIMMER**

Host Institution: **HELSINGIN YLIOPISTO - FI**

Age at maturity in Atlantic salmon: molecular and ecological dissection of an adaptive trait

Life history is the nexus of biology, because various biological questions ultimately revolve around the causes and consequences of variation in reproduction and survival, i.e. fitness. Traditionally, a major tool in life-history research has been quantitative genetics because it provides an important statistical link between phenotype and genotype. However, the mechanisms by which evolution occurs may remain unclear unless such traditional approaches are combined with molecular investigations. Another complicating factor is that the fitness of male vs female life histories do not always align, and hence life history traits may be shaped by sexual conflict. This is why life-history approaches focusing on both quantifying the conflict and understanding its resolution at the genetic level are needed.

As in many species, age at maturity in Atlantic salmon is tightly linked with size at maturity and thus represents a classic evolutionary trade-off: later maturing individuals spend more time at sea before returning to freshwater to spawn and have higher reproductive success due to their larger size but also have a higher risk of dying prior to first reproduction. Our recent cover paper in *Nature* reported a large-effect gene explaining 40% of the variation in this key life history trait. Remarkably, the locus exhibits sex-dependent dominance and this resolves a potential intra-locus sexual conflict in the species. The relatively simple genetic architecture of this trait combined with the features of Atlantic salmon as a model system offer an ideal opportunity to better understand the molecular mechanisms and ecological drivers underlying a locally adapted life history trait.

In MATURATION I will i) characterize age at maturity candidate gene functions and allelic effects on phenotypes ii) elucidate fitness effects of these phenotypes and GxE interactions iii) develop a mechanistic model for the sex-dependent dominance and validate intra-locus sexual conflict resolution

Link to the ERC project webpage: <https://www.helsinki.fi/en/researchgroups/evolution-conservation-and-genomics>

Keywords of the ERC project: ecological genomics, evolutionary genomics, Atlantic salmon, sexual conflict

Keywords that characterize the scientific profile of the potential visiting researcher/s: functional genomics, ecological genomics, evolutionary genomics, sexual conflict, animal behavior, population genomics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

754290

Project Acronym:

Mech-evo-insect

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr ALEXANDER BLANKE**
Host Institution: **UNIVERSITAET ZU KOELN - DE**

The mechanical evolution from biting-chewing to piercing-sucking in insects

Insects are extremely efficient feeders that impact on the world's ecosystems and our agriculture with their feeding capabilities. Insects evolved diverse mouthpart types during ~400 million years of evolution which allowed them to conquer many food resources. How this feeding system evolved, in particular the transition from one mouthpart type to the other, is unclear. My idea represents the first extensive assessment of insect head mechanics applying latest semi-automatic workflows and engineering approaches to unravel the factors driving insect mouthpart evolution and performance.

Specifically, I will study the mechanical evolution from early biting-chewing to piercing-sucking mouthparts and head types, considering recent as well as fossil species.

In contrast to earlier studies, I aim to quantify mechanical evolution for the whole head which has never been attempted before for insects. This will be done using engineering software to simulate insect feeding, followed by 3D shape analysis and finally evolutionary modelling using algorithms based on likelihood models of evolutionary processes. The project is therefore positioned at the interconnection between experimental biology, engineering and biological simulation.

The results will impact our understanding of insect evolution, with the project identifying which mechanical factors made insects such extraordinarily successful feeders, and why their mouthparts evolved into so many different types. To achieve an integrative understanding, my idea will furthermore take into account ecological, evolutionary and life history factors. Understanding the mechanical head evolution has never been tried before in a systematic way at this scale. However, my project idea also delivers results for industry: Since modern engineering methods are used, the results can be readily exported to the industry for the design of lighter robot arms with better lifting capabilities, thus advancing robotic techniques.

Link to the ERC project webpage:

Keywords of the ERC project: Biomechanics, geometric morphometrics, Morphology, evolution

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

757648

Project Acronym:

ModelGenomLand

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr KONRAD LOHSE**

Host Institution: **THE UNIVERSITY OF EDINBURGH - UK**

Modelling the genomic landscapes of selection and speciation

Understanding how natural selection, random genetic drift and demographic events interact to generate and maintain genetic and species diversity has been the central focus of population genetics for many decades. We now have the necessary genome sequence data to make detailed and powerful inferences about the evolutionary past of populations and species, yet our ability to meaningfully interpret such data has remained fundamentally limited.

This project will use a combination of theory, development of new inference tools and a large-scale comparative analyses of genome data and has two principal aims:

First to develop a general, statistical framework for making inferences about the joint action of past selection and demography from genome sequence data. This will be achieved using analytic calculations and approximations for the joint distribution of linked polymorphic sites. We will use these results to develop new methods to quantify the genome-wide rates of positive and background selection and to scan for genomic outliers of divergence between and positive selection within species. The new methods will be tested using simulations and data from model insects (*Drosophila* and *Heliconius*).

Second, we will apply the new inference approach to genome data for 20 species pairs of European butterflies and conduct a systematic comparison of the demographic and selective forces involved in speciation. This will reveal how repeatable speciation processes are both in terms of the demographic and selective events, and the genes and genomic architectures involved. Specifically, we will test whether selection during speciation is concentrated at chromosomal rearrangements and/or candidate gene families involved in mate recognition and host plant adaptation. This project will fundamentally improve both our understanding of speciation and selection and our ability to use sequence data to study population processes (be they selection, demography or both) in any system.

Link to the ERC project webpage:

Keywords of the ERC project: population genomics, speciation

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

758161

Project Acronym:

Multicellularity

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr LASZLO NAGY**

Host Institution: **SZEGEDI BIOLOGIAI KUTATOKOZPONT - HU**

The genetic basis of the convergent evolution of fungal multicellularity

The evolution of multicellularity (MC) has been one of the major transitions in the history of life. Despite immense interest in its evolutionary origins, the genomic changes leading to the emergence of MC, especially that of complex MC (differentiated 3-dimensional structures) are poorly known. Previous comparative genomics projects aiming to understand the genetic bases of MC in one way or another relied on gene content-based analyses. However, a pattern emerging from these studies is that gene content provides only an incomplete explanation for the evolution of MC even at ancient timescales. We hypothesize that besides gene duplications, changes to cis-regulatory elements and gene expression patterns (including protein isoforms) have significantly contributed to the evolution of MC. To test this hypothesis, we will deploy a combination of computational methods, phylogenomics, comparative transcriptomics and genome-wide assays of regulatory elements. Our research focuses on fungi as a model system, where complex MC evolved convergently and in subsequent two steps. Fungi are ideal models to tackle this question for several reasons: a) multicellularity in fungi evolved multiple times, b) there are rich genomic resources (>500 complete genomes), c) complex multicellular structures can be routinely grown in the lab and d) genetic manipulations are feasible for several cornerstone species. We set out to examine which genes participate in the building of simple and complex multicellular structures and whether the evolution of regulome complexity and gene expression patterns can explain the evolution of MC better than can traditionally assayed sources of genetic innovations (e.g. gene duplications). Ultimately, our goal is to reach a general synthesis on the genetic bases of the evolution of MC and that of organismal complexity.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

771349

Project Acronym:

DEFEAT

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr MICHAEL POULSEN**

Host Institution: **KOBENHAVNS UNIVERSITET - DK**

DiseasE-FreE social life without Antibiotics resisTance

The application of antimicrobial compounds produced by hosts or defensive symbionts to counter the effects of diseases has been identified in a number of organisms, but despite extensive studies on their presence, we know essentially nothing about why antimicrobials do not trigger rampant resistance evolution in target parasites. In stark contrast to virtually any other organism, fungus-farming termites have evolved a sophisticated agricultural symbiosis that pre-dates human farming by 30 million years without suffering from specialised diseases. I will capitalise on recent pioneering work in my group on proximate evidence for antimicrobial defences in the termites, their fungal crops, and their complex gut bacterial communities, by proposing to develop the farming symbiosis as a major model to test three novel concepts that may account for the evasion of resistance evolution. First, the antimicrobial compounds may have properties and evolve in ways that preclude resistance evolution in pathogens. Second, resistance is only possible towards individual compounds and not natural antimicrobial cocktails. Third, pathogens can only successfully invade and proliferate if they bypass several consecutive lines of defence, analogous to the six hallmarks of metazoan defence against cancer development. Addressing these concepts will allow fundamental insights into the remarkable success of complementary symbiont contributions to defence, and they will clarify the forces of multilevel natural selection that have allowed long-lived insect societies to evolve sustainability. Documenting and understanding these disease management principles is fundamentally important for several branches of evolutionary biology, and strategically important for adjusting human practices for future antimicrobial stewardship.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

772284

Project Acronym:

IceCommunities

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr GENTILE FRANCESCO FICETOLA**

Host Institution: **UNIVERSITA DEGLI STUDI DI MILANO - IT**

Reconstructing community dynamics and ecosystem functioning after glacial retreat

Glaciers show a pattern of retreat at the global scale. Increasing areas are exposed and colonized by multiple organisms, but lack of global studies hampers a complete understanding of the future of recently deglaciated terrains. What will be the fate of these areas? How do animals, plants and microorganisms colonize them? How do they interact to perform successful colonization? Which are the climatic, geological and biogeographical processes determining colonization patterns? How does ecosystem functioning evolve through time? Until now, the complete reconstruction of soil communities was hampered by the complexity of identification of organisms, thus analyses at broad geographical and taxonomic scale have been so far impossible. IceCommunities will combine innovative methods and a global approach to boost our understanding of the evolution of ecosystems in recently deglaciated areas. I will investigate chronosequences ranging from recently deglaciated terrains to late successional stages of soil pedogenesis. Through environmental DNA metabarcoding I will identify species from multiple taxonomic groups (bacteria, fungi, protists, soil invertebrates, plants), to obtain a complete reconstruction of biotic communities along glacier forelands over multiple mountain areas across the globe. This will allow measuring the rate of colonization at an unprecedented detail. Information on assemblages will be combined with analyses of soil, landscape and climate to identify the drivers of community changes. I will also identify the impact of eco-geographical factors (climate, regional pool of potential colonizers) on colonization. Analysis of functional traits will allow reconstructing how functional diversity emerges during community formation, and how it scales to the functioning of food webs. IceCommunities will help to predict the future development of these increasingly important ecosystems, providing a supported rationale for the appropriate management of these areas

Link to the ERC project webpage:

Keywords of the ERC project: environmental DNA, climate change, community ecology, global change biology, DNA metabarcoding, glaciers

Keywords that characterize the scientific profile of the potential visiting researcher/s: environmental DNA, climate change, community ecology, global change biology, DNA metabarcoding



European Research Council
Executive Agency

Established by the European Commission

Project ID:

789037

Project Acronym:

EPICLINES

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr MAGNUS NORDBORG**

Host Institution: GREGOR MENDEL INSTITUT FUR MOLEKULARE PFLANZENBIOLOGIE GMBH
- AT

**Elucidating the causes and consequences of the global pattern of epigenetic variation in
*Arabidopsis thaliana***

Epigenetics continues to fascinate, especially the notion that it blurs the line between “nature and nurture” and could make Lamarckian adaptation via the inheritance of acquired characteristics possible. That this is in principle possible is clear: in the model plant *Arabidopsis thaliana* (Thale cress), experimentally induced DNA methylation variation can be inherited and affect important traits. The question is whether this is important in nature. Recent studies of *A. thaliana* have revealed a pattern of correlation between levels of methylation and climate variables that strongly suggests that methylation is important in adaptation. However, somewhat paradoxically, the experiments also showed that much of the variation for this epigenetic trait appears to have a genetic rather than an epigenetic basis. This suggests that epigenetics may indeed be important for adaptation, but as part of a genetic mechanism that is currently not understood. The goal of this project is to determine whether the global pattern of methylation has a genetic or an epigenetic basis, and to use this information to elucidate the ultimate basis for the global pattern of variation: natural selection.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

803151

Project Acronym:

Macro-EpiK

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr LAURA EME**

Host Institution: **CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS - FR**

The macroevolutionary impact of epigenetics and lateral gene transfer on eukaryotic genomes

Multicellular organisms (e.g., animals, fungi and plants) are the best-studied eukaryotes but their ancestors and the vast majority of eukaryotic diversity correspond to microbial species ("protists"). The evolutionary history of protists is closely connected to the evolution of the eukaryotic cell itself.

However, most protist diversity is still genomically unexplored, limiting our investigation of eukaryotic evolution. For example, while the importance of lateral gene transfer (LGT) in prokaryotic evolution is well recognized, its role in eukaryotic evolution is still debated. In addition, although epigenetic mechanisms represent a hallmark of eukaryotic genome regulation, we know surprisingly little about the evolution of these mechanisms across eukaryotic diversity.

The overarching goal of my project is to understand how epigenetic mechanisms and LGT have shaped the macroevolution of eukaryotic genomes. This project has several inter-related intermediate objectives, which each in themselves will bring crucial insights into eukaryotic evolution: 1) reconstructing a robust phylogeny of eukaryotes; 2) inferring the gene content of the Last Eukaryotic Common Ancestor; 3) tracing the evolution of genes involved in epigenetic mechanisms and obtaining epigenomic maps from under-studied protists; 4) investigating the intriguing hypothesis of a possible interplay between epigenetic regulation and horizontal gene transfer and its influence on eukaryotic genome evolution: Have genes involved in epigenomic mechanisms been transferred between eukaryotes? Do epigenomic modifications affect the frequency of LGT in different lineages?

To achieve this, I will characterize the transcriptomes, genomes, methylomes and small RNAs of understudied eukaryotic microbes selected for their key phylogenetic position, and to analyse them using state-of-the-art bioinformatic methods. I will target uncultivated protists, using single-cell techniques and novel genome-scaffolding approaches.

Link to the ERC project webpage:

Keywords of the ERC project: phylogenetics, protists, epigenetics, horizontal gene transfer, genomics, single-cell, transcriptomics

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

804569

Project Acronym:

FIT2GO

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr CLAUDIA BANK**

Host Institution: **FUNDACAO CALOUSTE GULBENKIAN - PT**

A toolbox for fitness landscapes in evolution

A major challenge in evolutionary biology is to quantify the processes and mechanisms by which populations adapt to new environments. In particular, the role of epistasis, which is the genetic-background dependent effect of mutations, and the constraints it imposes on adaptation, has been contentious for decades. This question can be approached using the concept of a fitness landscape: a map of genotypes or phenotypes to fitness, which dictates the dynamics and the possible paths towards increased reproductive success. This analogy has inspired a large body of theoretical work, in which various models of fitness landscapes have been proposed and analysed. Only recently, novel experimental approaches and advances in sequencing technologies have provided us with large empirical fitness landscapes at impressive resolution, which call for the evaluation of the related theory.

The aim of this proposal is to build on the theory of fitness landscapes to quantify epistasis across levels of biological organization and across environments, and to study its impact on the population genetics of adaptation and hybridization. Each work package involves classical theoretical modelling, statistical inference and method development, and data analysis and interpretation; a combination of approaches for which my research group has strong expertise. In addition, we will perform experimental evolution in *Escherichia coli* and influenza to test hypotheses related to the change of fitness effects across environments, and to adaptation by means of highly epistatic mutations. We will specifically apply our methods to evaluate the potential for predicting routes to drug resistance in pathogens. The long-term goal lies in the development of a modeling and inference framework that utilizes fitness landscape theory to infer the ecological history of a genome, which may ultimately allow for a prediction of its future adaptive potential.

Link to the ERC project webpage:

Keywords of the ERC project: Adaptation, speciation, epistasis, evolutionary theory, eco-evolutionary dynamics

Keywords that characterize the scientific profile of the potential visiting researcher/s: Virus evolution, speciation, systems biology, deep mutational scanning



European Research Council
Executive Agency

Established by the European Commission

Project ID:

832352

Project Acronym:

EvoSexChrom

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr TATIAN GIRAUD**

Host Institution: **CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS - FR**

Testing new hypotheses on the evolution of sex-related chromosomes

The sex chromosomes of plants and animals often contain large non-recombining regions due to a stepwise cessation of recombination generating “evolutionary strata” of genetic differentiation. The reasons for the extension of recombination suppression beyond sex-determining genes remain unclear. Sexual antagonism, involving the linkage to sex-determining genes of alleles beneficial in only one sex, is the prevailing hypothesis, as this explanation is both theoretically plausible and attractive. However, decades of research have unearthed little evidence to support this hypothesis. Furthermore, I have shown that chromosomes involved in sexual compatibility in systems lacking male and female functions can nevertheless display a stepwise suppression of recombination beyond mating-compatibility genes. Thus, evolutionary strata can evolve without sexual antagonism. Alternative hypotheses, such as neutral rearrangements, epigenetic changes associated with transposable elements and the sheltering of deleterious alleles accumulating near non-recombining regions, must thus be seriously considered. I propose to use a synergic combination of different approaches and biological systems to refine and test these hypotheses, to broaden the theory of sex-related chromosome evolution, and, more generally, of the evolution of supergenes (linked allelic combinations). I will use mathematical modeling to test hypothesis plausibility and generate predictions. I will use comparative and population genomic approaches to test predictions, and an innovative experimental evolution approach with functional manipulations to assess the ability of the proposed mechanisms to generate strata. The EvoSexChrom project will challenge the current theory, opening up new avenues of research and potentially creating a paradigm shift in the dynamic research field focusing on the evolution of sex-related chromosomes and other supergenes, relevant to diverse traits and organisms.

Link to the ERC project webpage:

Keywords of the ERC project: geonmics, evolution, sex chromosomes, fungi

Keywords that characterize the scientific profile of the potential visiting researcher/s: geonmics, evolution, sex chromosomes, fungi



European Research Council
Executive Agency

Established by the European Commission

Project ID:

851040

Project Acronym:

SpeciationBehaviour

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr RICHARD MERRILL**

Host Institution: **LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN - DE**

The genetic and neural basis of reproductive isolation

Speciation is a fundamental evolutionary process, which relies on the accumulation of reproductive barriers. These barriers often act before mating, and many taxa remain separate not because they fail to produce viable offspring, but because they 'choose' not to mate in the first place. Although the significance of behavioural barriers has long been recognized, an integrated understanding remains elusive: How is behavioural isolation mediated through changes in the sensory systems? Are these changes driven by selection? And what is the genetic and developmental basis of behavioural divergence in natural populations?

My research will address these questions to understand how behavioural barriers are generated, both during development and across evolutionary time. This project will be novel in uniting genomic and neurosensory data, with ecological and behavioural studies across a single radiation. Heliconius butterflies offer an excellent opportunity to achieve this as they are a group of closely related species with well-characterised ecologies, high-quality genomic resources, and are emerging as a model of evolutionary neurobiology.

These attributes will allow me to address the enduring problem of how natural selection and genetics interact to drive divergence in behavioural preferences. I will determine how components of behavioural isolation vary with ecology, both within and between species; and then explicitly test whether changes in sensory perception and processing in the brain are driven by selection imposed by the external environment. Genetic mapping will allow me to test for a link between changes in the sensory systems and mate choice. By combining these data with expression and functional analyses I will identify genes strongly implicated in the divergence of behavioural preferences. This will lead to novel insights into the developmental and neurological bases of behavioural isolation, a process fundamental to biodiversity.

Link to the ERC project webpage:

Keywords of the ERC project: speciation, behaviour, genetics, Heliconius, neuro

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

851705

Project Acronym:

MechAnt

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr DAVID LABONTE**

Host Institution: **IMPERIAL COLLEGE OF SCIENCE TECHNOLOGY AND MEDICINE - UK**

Behavioural biomechanics of insect herbivory - a case study on leaf-cutter ants

Insect herbivores are a dominant element in terrestrial ecosystems, and pose a continuing threat to global food security. However, little is known about a key determinant of insect herbivore success: the mechanics of plant-feeding. MechAnt proposes to transform our understanding of insect-plant relations by providing a rigorous biomechanical investigation into how insects cut leaves, using the major ecosystem engineers and principal insect pest of the New World, the leaf-cutter ants, as a model system. Specifically, MechAnt will combine the traditionally separate fields of behavioural ecology, mechanical engineering, materials science, computer vision and machine learning to investigate: (1) the mechanical and energetic constraints determining the cutting ability, and ontogeny of task choice of differently-sized workers, and hence the adaptive value of physical castes in eusocial insects; (2) the relationship between plant material properties, ease of cutting, and mandibular wear, which will reveal the key mechanical determinants of plant-herbivore species interactions; (3) the division of labour, ontogeny and demography of leaf-cutter colonies foraging on leaves of different “toughness”, testing the hypothesis that leaf-cutter colonies are organised according to ergonomic criteria. By integrating insights ranging from nano-scale mechanics up to whole-colony ecology, MechAnt will quantitatively link the mechanical properties of plants with the performance of individual foragers, the organisation of foraging parties, and the demography and social organisation of leaf-cutter ant colonies. The resulting understanding of the biomechanical innovations underpinning the success of the leaf-cutter ants will yield insights into the behavioural ecology of advanced plant-feeders, highlight the role of biomechanical constraints in the behaviour and evolution of herbivorous insects, and pave the way for the development of novel crop protection strategies.

Link to the ERC project webpage: https://cordis.europa.eu/project/rcn/225400/factsheet/en?WT.mc_id=RSS-Feed&WT.rss_f=project&WT.rss_a=225400&WT.rss_ev=a

Keywords of the ERC project: Biomechanics, Behavioural Ecology, Fracture, Herbivory, Machine Learning, Insects

Keywords that characterize the scientific profile of the potential visiting researcher/s: Mechanical Engineer, Programmer, Ecologist, Entomologist, Evolutionary Biologist



European Research Council
Executive Agency

Established by the European Commission

Project ID:

852725

Project Acronym:

TerreStriAL

Evaluation Panel:

LS8
Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr JAN DE VRIES**

Host Institution: GEORG-AUGUST-UNIVERSITÄT GÖTTINGENSTIFTUNG ÖFFENTLICHEN
RECHTS - DE

Terrestrialization: Stress Signalling Dynamics in the Algal Progenitors of Land Plants

Land plants abound on Earth's surface. All of this diversity arose in a singular event. The algal progenitor of land plants was a streptophyte alga and only recent phylogenomic analyses have specified the particular algal lineage that is most closely related to land plants. But why did land plants evolve only once? And what properties did the ancestors of these terrestrial organisms possess that allowed them to conquer land? Life on land involves rapid and drastic shifts in temperature, light or water availability. Hence, a prime candidate property is the ability to deal with these terrestrial stressors by dynamically responding to shifting environmental cues. My recent data highlight that the streptophyte algae closest to land plants have the genetic makeup for land plant-like stress response signalling circuits—including genes for sensing the major stress phytohormone abscisic acid (ABA). This provides us with testable candidates. To shed light on the early evolution of one of land plants' key properties, I, here, propose to combine in-depth molecular biological analyses of these candidate stress signalling and response pathways with large-scale systems biology approaches. For this, my team and I will develop streptophyte algal model systems. We will dissect the regulatory hierarchy employed during stress signalling and the response pathways it is regulating in real-time in vivo and across evolutionary time in silico. These approaches will go beyond a view of gene evolution that is based on presence/absence to address if land plant stress dynamics have evolved from algal stress regulatory networks that became hardwired into land plant biology. The aim of this work is to infer the biology of the earliest land plants by investigating their closest algal relatives and interrogating a candidate mechanism used to deal with the challenges of life on land. Understanding this mechanism means understanding a key player that paved the way for the success of plants on land.

Link to the ERC project webpage:

Keywords of the ERC project: streptophyte algae; plant evolution; comparative genomics; evolutionary bioinformatics; multi-omics

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

682580

Project Acronym:

BEAL

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr PIERRE CARDOL**
Host Institution: **UNIVERSITE DE LIEGE - BE**

Bioenergetics in microalgae : regulation modes of mitochondrial respiration, photosynthesis, and fermentative pathways, and their interactions in secondary algae

During the course of eukaryote evolution, photosynthesis was propagated from primary eukaryotic algae to non-photosynthetic organisms through multiple secondary endosymbiotic events. Collectively referred to as “secondary algae”, these photosynthetic organisms account for only 1-2% of the total global biomass, but produce a far larger part of the global annual fixation of carbon on Earth.

ATP is the universal chemical energy carrier in living cells. In photosynthetic eukaryotes, it is produced by two major cellular processes: photosynthesis and respiration taking place in chloroplasts and mitochondria, respectively. Both processes support the production of biomass and govern gas (O₂ and CO₂) exchanges. On the other hand, anaerobic fermentative enzymes have also been identified in several primary and secondary algae. The regulation modes and interactions of respiration, photosynthesis and fermentation are fairly well understood in primary green algae. Conversely, the complex evolutionary history of secondary algae implies a great variety of original regulatory mechanisms that have been barely investigated to date.

Over the last years my laboratory has developed and optimized a range of multidisciplinary approaches that now allow us, within the frame of the BEAL (BioEnergetics in microALgae) project, to (i) characterize and compare the photosynthetic regulation modes by biophysical approaches, (ii) use genetic and biochemical approaches to gain fundamental knowledge on aerobic respiration and anaerobic fermentative pathways, and (iii) investigate and compare interconnections between respiration, photosynthesis, and fermentation in organisms resulting from distinct evolutionary scenarios. On a long term, these developments will be instrumental to unravel bioenergetics constraints on growth in microalgae, a required knowledge to exploit the microalgal diversity in a biotechnological perspective, and to understand the complexity of the marine phytoplankton.

Link to the ERC project webpage: <http://labos.ulg.ac.be/genetique-physiologie-microalgues/research/erc-beal/>

Keywords of the ERC project: photosynthesis, microalgae

Keywords that characterize the scientific profile of the potential visiting researcher/s: biochemist, spectroscopy



European Research Council
Executive Agency

Established by the European Commission

Project ID:

726176

Project Acronym:

FRAGCLIM

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr JOSE MARIA MONTOYA TERAN**

Host Institution: **CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS - FR**

The Combined Effects of Climatic Warming and Habitat Fragmentation on Biodiversity, Community Dynamics and Ecosystem Functioning

Climatic warming and habitat fragmentation are the largest threats to biodiversity and ecosystems globally. To forecast and mitigate their effects is the environmental challenge of our age. Despite substantial progress on the ecological consequences of climatic warming and habitat fragmentation individually, there is a fundamental gap in our understanding and prediction of their combined effects.

The goal of FRAGCLIM is to determine the individual and combined effects of climatic warming and habitat fragmentation on biodiversity, community dynamics, and ecosystem functioning in complex multitrophic communities. To achieve this, it uses an integrative approach that combines the development of new theory on metacommunities and temperature-dependent food web dynamics in close dialogue with a unique long-term aquatic mesocosm experiment. It is articulated around five objectives. In the first three, FRAGCLIM will determine the effects of (i) warming, (ii) fragmentation, and (iii) warming and fragmentation combined, on numerous facets of biodiversity, community structure, food web dynamics, spatial and temporal stability, and key ecosystem functions. Then, it will (iv) investigate the extent of evolutionary thermal adaptation to warming and isolation due to fragmentation, and its consequences for biodiversity dynamics. Finally, (v) it will provide creative solutions to mitigate the combined effects of warming and fragmentation.

FRAGCLIM proposes an ambitious integrative and innovative research programme that will provide a much-needed new perspective on the ecological and evolutionary consequences of warming and fragmentation. It will greatly contribute to bridging the gaps between theoretical and empirical ecology, and between ecological and evolutionary responses to global change. FRAGCLIM will foster links with environmental policy by providing new mitigation measures to climate change in fragmented systems that derive from our theoretical and empirical findings.

Link to the ERC project webpage:

Keywords of the ERC project: Climate Change, habitat fragmentation, theoretical ecology, ecosystem functioning, food webs

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

803768

Project Acronym:

Evolphysiol

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr FILIPA SOUSA**

Host Institution: **UNIVERSITAT WIEN - AT**

Evolution of Physiology: The link between Earth and Life

The history of life is a subject that attracts the interest from both researchers and the society in general - it is in the human nature to wonder about our own history. Our only sources of information about microbial evolution reside in genomic data and geological records. Major advances in sequencing techniques are overwhelming databases with rich and novel insights into microbial taxonomic diversity, in particular about new uncultured lineages. Through metagenomics we now know that they are there but we still do not understand what they are doing. The key to that understanding is not genomics, it is physiology. Our main impediment to understand environmental microbial life is our lack of insights into the physiology of newly discovered lineages, how they harness and conserve energy. While phylogenetic trees based on universal genes can be generated for thousands of lineages at a time, they do not represent the genome as a whole and, most importantly, due to lateral gene transfer, branching patterns in the tree of life have never correlated well with key physiological traits. The goal of this proposal, whose focus is physiology, is to better understand how microbes harness energy from available environmental sources, how they learned to use new ones, and how this process unfolded during microbial evolution. This will involve i) large-scale comparative phylogenetic analysis of genes involved in and genomically associated with physiology combined with ii) experimental data, using as evolutionary constraints geochemical records of available environmental energy sources. With a top-down approach this work will successively eliminate among extant biological traits ones that cannot be ancient, constraining the physiological space of older microbial solutions. This proposal will lead to testable predictions regarding the order of events in evolutionary bioenergetic transitions, the focus on biological energy harnessing will narrow the gap between geochemistry and microbiology.

Link to the ERC project webpage:

Keywords of the ERC project: evolution, bioenergetics, biochemistry, genomic analysis, geochemistry, early earth

Keywords that characterize the scientific profile of the potential visiting researcher/s: biochemist, geochemist, computational scientist



European Research Council
Executive Agency

Established by the European Commission

Project ID:

804673

Project Acronym:

sEEIngDOM

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr ANDREW TANENTZAP**

Host Institution: THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF
CAMBRIDGE - UK

Ecological and Evolutionary Importance of Molecular Diversity in Dissolved Organic Matter

Dissolved organic matter (DOM) is central to the functioning of freshwater ecosystems that support life on Earth. For example, DOM has a major role in global carbon (C) cycling by helping to bury four times more C in the bottom of lakes and rivers than across all of the world's oceans. DOM also majorly influences the growth of aquatic organisms and impedes drinking water treatment for millions of people, such as by increasing microbial growth. Yet, despite its importance, DOM remains poorly understood because it has been measured with little resolution for nearly 200 years. Recent technological advances have now shown that a handful of lake water can contain thousands of different molecules of varying origin and composition. But the role of all these different molecules in aquatic ecosystems largely remains a mystery.

This project will discover the importance of the tremendous diversity of molecules – termed chemodiversity – found in DOM for lake functioning and human wellbeing. It will do so by combining cutting-edge techniques in analytical chemistry, genomics, and statistical modelling with careful lab-based studies, proven field experiments, and large-scale observational surveys. By thinking about species of molecules as we would species of organisms, this project will draw upon rich theory and methods developed for the study of biodiversity. The work will allow us to learn how variation in chemodiversity across lakes is driven by associations with different microbes and how these microbes reciprocally adapt and evolve to different DOM. In the process, we will improve predictions of how important functions and services provided by lakes, such as C cycling and drinking water, vary with chemodiversity. An exciting application of this work is to improve emerging technologies for water purification by identifying microbial consortia that can consume chemodiversity and make water clearer.

Link to the ERC project webpage: <https://www.ecosystemchange.com/ercfunded-seeingdom>

Keywords of the ERC project: ecology, evolution, lakes, microbial, biogeochemistry, carbon cycling, diversity, genomics, mass spectrometry, water quality

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

853442

Project Acronym:

BOSADMIX

Evaluation Panel:

LS8

Evolutionary, Population
and Environmental
Biology

Principal Investigator: **Dr RASMUS HELLER**

Host Institution: **KOBENHAVNS UNIVERSITET - DK**

Genetic admixture and its impact on domestication in the Bos genus: a model for genetic improvement of livestock

Background

Genetic exchange across species boundaries is emerging as a much more common phenomenon than previously assumed. This introduces potentially adaptive genetic variation into recipient populations. Such interspecies admixture is believed to have played an important role in domestication events, particularly in members of the Bos genus, which uniquely harbours no fewer than five independently domesticated lineages. Understanding these independent, yet reticulated evolutionary events is of fundamental interest for managing the genetic resources of domestic and wild bovines.

Objectives

I propose to investigate the role of interspecies admixture in domestication through four linked topics. The first is to systematically map the interspecies admixture among seven Asian Bos species, and to determine whether introgressed elements have been beneficial to the recipient populations. The second is to identify genes that have been under strong selection in each independent domestication process. The third is to link adaptively introgressed genomic elements with phenotypic effects. The fourth will address the future of genetic resources in all Asian Bos.

Methods

The project will bring together a large set of complete genomes and use a combination of population genetic and comparative genomic methods. Phenotypic data and experiments will be performed to validate the phenotypic effects of key introgressed elements and genes under selection during the domestication process.

Expected outcome and importance

The project will improve our understanding of the evolutionary dynamics of genetic elements that cross the species barrier, in particular the interplay between admixture and the domestication process. It will also provide important insights into the domestication process itself. A joint understanding of these processes is crucial for assessing which types of foreign genetic elements that can be useful for genetic improvement of domestic species.

Link to the ERC project webpage: <https://rathmuth.wixsite.com/wildlifegenetics/projects>

Keywords of the ERC project: adaptive introgression; admixture; genetic improvement, domestication; speciation

Keywords that characterize the scientific profile of the potential visiting researcher/s: population genetics; evolutionary genetics; comparative genomics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

680040

Project Acronym:

EVOLOR

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator:

Dr ENIKO KUBINYI

Host Institution:

EOTVOS LORAND TUDOMANYEGYETEM - HU

Cognitive Ageing in Dogs

The aim of this project is to understand the causal factors contributing to the cognitive decline during senescence and to develop sensitive and standardized behaviour tests for early detection in order to increase the welfare of affected species. With the rapidly ageing population of Europe, related research is a priority in the European Union.

We will focus both on characterising the ageing phenotype and the underlying biological processes in dogs as a well-established natural animal model. We develop a reliable and valid test battery applying innovative multidisciplinary methods (e.g. eye-tracking, motion path analysis, identification of behaviour using inertial sensors, EEG, fMRI, candidate gene, and epigenetics) in both longitudinal and cross-sectional studies. We expect to reveal specific environmental risk factors which hasten ageing and also protective factors which may postpone it. We aim to provide objective criteria (behavioural, physiological and genetic biomarkers) to assess and predict the ageing trajectory for specific individual dogs. This would help veterinarians to recognise the symptoms early, and initiate necessary counter actions.

This approach establishes the framework for answering the broad question that how we can extend the healthy life of ageing dogs which indirectly also contributes to the welfare of the owner and decreases veterinary expenses. The detailed description of the ageing phenotype may also facilitate the use of dogs as a natural model for human senescence, including the development and application of pharmaceutical interventions.

We expect that our approach offers the scientific foundation to delay the onset of cognitive ageing in dog populations by 1-2 years, and also increase the proportion of dogs that enjoy healthy ageing.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

695078

Project Acronym:

noMAGIC

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr ANNA MORONI**

Host Institution: **UNIVERSITA DEGLI STUDI DI MILANO - IT**

Noninvasive Manipulation of Gating in Ion Channels

noMAGIC has the visionary goal of engineering genetically encoded ion channels, which can be remotely controlled (gated) by stimuli that penetrate deep into human tissue without negative side effects. The control over ion channel activity by deep penetrating stimuli will revolutionize research in neurobiology and physiology as it paves the way for remote and genuine non-invasive control of cell activity in vivo. Synthetic channels, which can be gated by magnetic fields (MF), near infrared (NIR) radiation or ultrasound (US) will be engineered in the frame of noMAGIC by three complementary work packages (WP1-3). Design and engineering of the channels will be performed in WP1 by reiterated steps of rational and irrational design, high throughput screening and in vitro and in vivo functional testing. We have identified two sensor modules for MF and NIR radiation, respectively, which will be functionally connected to a channel pore for a remote control of gating. For the US-gated channel we will engineer a channel pore that is maximally responding to local changes in the lipid environment induced by US. Design and engineering of channels will be complemented by a computational approach (WP2), which analyses, from elastic network models, the mechanical connections in the channel pore and which extracts information on the forces, which are required to gate a channel by the three stimuli. The outcome of WP2 will provide general design rules for synthetic channels with implications much beyond the present project. WP3 also contributes to the engineering effort in WP1 by a spectrum of avant-garde spectroscopic methods, which resolve structural changes of the channel proteins under the influence of remote stimuli. These structural insights will greatly advance our understanding of structure/function correlates in composite ion channels and it will inspire the design and engineering of channels, which respond to remote stimuli.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

695669

Project Acronym:

PicoCB

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr FLORIAN HOLLFELDER**

Host Institution: THE CHANCELLOR MASTERS AND SCHOLARSO OF THE UNIVERSITY OF
CAMBRIDGE - UK

Exploring the Chemical Biology of Sequence Space via Picoliter Droplets

Directed evolution of functional proteins has arguably emerged as an approach to protein engineering that can complement or better design-led approaches to protein function. However, as a random process, enormous numbers of variants have to be screened and selected to have a chance to identify successful catalysts. This process is costly and cumbersome: Industrial screening facilities require investment of tens to hundred millions of dollars. My group has implemented key steps towards conducting quantitative biological experiments in a much cheaper format. Screening of individual library members in monodisperse oil-in-water compartments ('microdroplets') that are generated at kHz frequencies in microfluidic devices has been shown to be possible. The droplet compartment constitutes a link between a given phenotype and its encoding genotype, by capturing reaction product, and thus providing a unique system to screen for catalysis. In this way quantitative fitness landscapes for interconversion of members of enzyme superfamilies along the lines of catalytic promiscuity, understanding the factors governing specificity and the mechanistic interpretation of the observed evolutionary pathways can be made. We now apply this screening system of unprecedented capacity for directed evolution and metagenomic screening of enzymes in in vivo and in vitro formats. We plan to apply this system to do experiments that would not be possible with conventional, lower throughput approaches: (i) screening of metagenomic libraries for rare and promiscuous activities that characterise environmental gene collections for their reactivity and potential for applied biocatalysis; (ii) developing a fundamental understanding of and strategic guidelines for enzyme evolution based on fitness landscapes that record data on multiple, promiscuous activities in response to Indel mutations; and (iii) evolution of gene networks to build up signalling networks in vitro.

Link to the ERC project webpage:

Keywords of the ERC project: microfluidics, chemical biology, protein engineering, enzymology, antibody engineering, metagenomics, enzyme mechanism, physical-organic chemistry, reaction mechanism, bioacatalysis, high-throughput screening

Keywords that characterize the scientific profile of the potential visiting researcher/s: microfluidics, chemical biology, protein engineering, enzymology, antibody engineering, metagenomics, enzyme mechanism, physical-organic chemistry, reaction mechanism, bioacatalysis, high-throughput screening



European Research Council
Executive Agency

Established by the European Commission

Project ID:

714289

Project Acronym:

Stress Imaging

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr ROMANA SCHIRHAGL**

Host Institution: **ACADEMISCH ZIEKENHUIS GRONINGEN - NL**

Nanoscale Stress Imaging with Imperfect Diamonds

My goal is to optically detect the magnetic resonance of free radicals/ROS inside cells. Radicals are suspected to play a crucial role in numerous pathogenic conditions including diseases responsible for most deaths worldwide (as arteriosclerosis, cancer, immune responses to pathogens). They are also involved in many processes in healthy cells as mitochondrial metabolism or aging of cells and part of the working mechanism of many drugs. Despite their relevance relatively little is known about where and when radicals are built, how they work or which ones play a role. Their short lifetime and reactivity poses a problem for many state of the art methods. Thus they are often a bottleneck in understanding stress responses. My goal is to develop a method, which can detect their magnetic resonance in the nanoscale. The method is based on a fluorescent defect in diamond, which changes its optical properties based on its magnetic surrounding. While this technique has been able to detect even the faint signal of a single electron spin, this technique is entirely new to biological fields. We can localize where, when and how much of a certain radical is generated with nm resolution. This is impossible with the current state of the art. Furthermore, since we obtain spectra we can also differentiate radicals to some extent. I am proposing to investigate two systems: 1) the involvement of radicals in the aging of yeast cells 2) the response of macrophages to stress. In the first project I will test the so-called free radical theory, which states that organisms age because cells accumulate free radical damage over time. In the second project I will answer the question how a macrophage reacts to the impact of a pathogen or a drug. Outcomes of this project would enable us to increase our understanding on how stress responses work on a molecular level. This will open up new possibilities to assess if and how drugs are working or how and why certain pathogens are worse than others.

Link to the ERC project webpage:

Keywords of the ERC project: diamond magnetometry; biological applications

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

725061

Project Acronym:

TEMUBLYM

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr CAROLINA TAFALLA**

Host Institution: INSTITUTO NACIONAL DE INVESTIGACION Y TECNOLOGIA AGRARIA Y
ALIMENTARIA OA MP - ES

Teleost mucosal B1-like lymphocytes at the crossroad of tolerance and immunity

B cells are one of the main players of immunity, responsible for the production of immunoglobulins (Igs). In 2011, I was granted an ERC Starting grant to undertake the phenotypical and functional characterization of teleost B lymphocytes based on the hypothesis that they do not behave as mammalian B2 cells (conventional B cells) but closely resemble mammalian innate B1 lymphocytes involved in extrafollicular T-independent (TI) responses. Since then, my laboratory has gathered considerable evidences that strengthen this hypothesis. These studies were mostly carried out in central lymphoid compartments, but did not address how teleost B1-like cells regulate the delicate balance between immunity and tolerance at mucosal interfaces, in species lacking follicular structures. In this new project, I want to pursue my studies on B lymphocyte functionality, focusing on how teleost mucosal B cells are regulated, still under the assumption that fish B lymphocytes resemble better a B1 model. We will study how fish B cells differentiate to antibody secreting cells (ASCs) and establish extrafollicular long-term memory, taking into account novel results in mammals that have challenged traditional paradigms and revealed that long-term immunological memory can be established through TI IgM B1-like responses. Furthermore, we will also study the role of IgD in the gills, as previous studies from my group suggest that this Ig plays a key role in the regulation of immunity in this specific mucosa, as it seems to do in humans in areas such as the upper respiratory tract.

Addressing how fish B cells mount a protective mucosal immune response in the absence of T cell help from organized follicles could provide new mechanistic insights into IgM and IgD responses emerging in humans. From a practical view, our work will contribute to understand why satisfactory mucosal vaccination is still an unreach goal for most diseases in both mammals and fish, despite their strong demand.

Link to the ERC project webpage:

Keywords of the ERC project: fish, B cells, Immunoglobulins, 725061

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

742654

Project Acronym:

EpiTrack

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr SAULIUS KLIMASAUSKAS**

Host Institution: **VILNIAUS UNIVERSITETAS - LT**

Single-cell temporal tracking of epigenetic DNA marks

Over the past decade, epigenetic phenomena have taken centre stage in our understanding of gene regulation, cellular differentiation and human disease. DNA methylation is a prevalent epigenetic modification in mammals, which is brought about by enzymatic transfer of methyl groups from the S-adenosylmethionine (SAM) cofactor by three known DNA methyltransferases (DNMTs). The most dramatic epigenomic reprogramming in mammalian development occurs after fertilization, whereby a global loss of DNA methylation is followed by massive reinstatement of new methylation patterns, different for each cell type. Although DNA methylation has been extensively investigated, key mechanistic aspects of these fascinating events remain obscure. The goal of this proposal is to bridge the gap in our understanding of how the genomic methylation patterns are established and how they govern cell plasticity and variability during differentiation and development. These questions could only be answered by precise determination of where and when methylation marks are deposited by the individual DNMTs, and how these methylation marks affect gene expression. To achieve this ambitious goal, we will metabolically engineer mouse cells to permit SAM analog-based chemical pulse-tagging of their methylation sites in vivo. We will then advance profiling of DNA modifications to the single cell level via innovative integration of microdroplet-based barcoding, precise genomic mapping and super-resolution imaging. Using this unique experimental system we will determine, with unprecedented detail and throughput, the dynamics and variability of DNA methylation and gene expression patterns during differentiation of mouse embryonic cells to neural and other lineages. This project will give a comprehensive, time-resolved view of the roles that the DNMTs play in mammalian development, which will open new horizons in epigenomic research and will advance our understanding of human development and disease.

Link to the ERC project webpage:

Keywords of the ERC project: Metabolic engineering, DNA methyltransferases, epigenetic regulation, S-adenosylmethionine analogs

Keywords that characterize the scientific profile of the potential visiting researcher/s: Enzyme engineering, evolution
directed



European Research Council
Executive Agency

Established by the European Commission

Project ID:

755617

Project Acronym:

SENTIFLEX

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr JOCHEM VERRELST**

Host Institution: **UNIVERSITAT DE VALENCIA - ES**

Fluorescence-based photosynthesis estimates for vegetation productivity monitoring from space

Global food security will remain a worldwide concern for the next 50 years and beyond. Agricultural production undergoes an increasing pressure by global anthropogenic changes, including rising population, increased protein demands and climatic extremes. Because of the immediate and dynamic nature of these changes, productivity monitoring measures are urgently needed to ensure both the stability and continued increase of the global food supply. Europe has expressed ambitions to keep its fingers on the pulse of its agricultural lands. In response to that, this proposal - named SENTIFLEX - is dedicated to developing a European vegetation productivity monitoring facility based on the synergy of Sentinel-3 (S3) with FLEX satellite fluorescence data. ESA's 8th Earth Explorer FLEX is the first mission specifically designed to globally measure Sun-Induced chlorophyll Fluorescence (SIF) emission from terrestrial vegetation. These two European Earth observation missions offer immense possibilities to increase our knowledge of the basic functioning of the Earth's vegetation, i.e., the photosynthetic activity of plants resulting in carbon fixation. Two complementary approaches are envisioned to realize quantification of photosynthesis through satellite SIF and S3. First, the work seeks to advance the science in establishing and consolidating relationships between canopy-leaving SIF and unbiased estimates of photosynthesis of the plants, thereby disentangling the role of dynamic vegetative and atmospheric variables. Second, consolidated relationships between SIF and photosynthesis will be used to build a FLEX-S3 data processing assimilation scheme through process-based vegetation models that will deliver spatiotemporally highly resolved information on Europe's vegetation productivity. To streamline all these datasets into a prototype vegetation productivity monitoring facility, new data processing concepts will be introduced such as the emulation of radiative transfer models.

Link to the ERC project webpage: <https://ipl.uv.es/sentiflex/>

Keywords of the ERC project: vegetation properties mapping, FLEX, Sentinel, Earth Observation, fluorescence, photosynthesis, productivity

Keywords that characterize the scientific profile of the potential visiting researcher/s: Programmer, Matlab, Python, remote sensing, data analyst, machine learning



European Research Council
Executive Agency

Established by the European Commission

Project ID:

757833

Project Acronym:

FORMICA

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr PIETER DE FRENNE**

Host Institution: **UNIVERSITEIT GENT - BE**

Microclimatic buffering of plant responses to macroclimate warming in temperate forests

Recent global warming is acting across ecosystems and threatening biodiversity. Yet, due to slow responses, many biological communities are lagging behind warming of the macroclimate (the climate of a large geographic region). The buffering of microclimates near the ground measured in localized areas, arising from terrain features such as vegetation and topography, can explain why many species are lagging behind macroclimate warming. However, almost all studies ignore the effects of microclimatic buffering and key uncertainties still exist about this mechanism. Microclimates are particularly evident in forests, where understorey habitats are buffered by overstorey trees. In temperate forests, the understorey contains the vast majority of plant diversity and plays an essential role in driving ecosystem processes.

The overall goal of FORMICA (FORest MICroclimate Assessment) is to quantify and understand the role of microclimatic buffering in modulating forest understorey plant responses to macroclimate warming. We will perform the best assessment to date of the effects of microclimates on plants by applying microtemperature loggers, experimental heating, fluorescent tubes and a large-scale transplant experiment in temperate forests across Europe. For the first time, plant data from the individual to ecosystem level will be related to microclimate along wide temperature gradients and forest management regimes. The empirical results will then be integrated in cutting-edge demographic distribution models to forecast plant diversity in temperate forests as macroclimate warms.

FORMICA will provide the first integrative study on microclimatic buffering of macroclimate warming in forests. Interdisciplinary concepts and methods will be applied, including from climatology, forestry and ecology. FORMICA will reshape our current understanding of the impacts of climate change on forests and help land managers and policy makers to develop urgently needed adaptation strategies.

Link to the ERC project webpage: www.formica.ugent.be

Keywords of the ERC project: climate change, forests, microclimate

Keywords that characterize the scientific profile of the potential visiting researcher/s: climate change, forests



European Research Council
Executive Agency

Established by the European Commission

Project ID:

770835

Project Acronym:

SynBioBrain

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr CHRIS BARNES**

Host Institution: **UNIVERSITY COLLEGE LONDON - UK**

Building biological computers from bacterial populations

Biosensors detect compounds using a biological component combined with a physio-chemical detector. Using synthetic biology, we can now engineer bacteria into whole-cell biosensors where sensing, transduction and output occur within the living cell. Applications include the detection of harmful environmental agents, bioprocess monitoring, and detecting medically relevant biomarkers. As we move towards more sophisticated applications, single channel read-out will be replaced with sensors that have multiple inputs and more complex information processing capabilities. Whilst digital logic within a single strain of bacteria can be implemented, consortia offer a powerful alternative, where information is integrated and processed in a distributed fashion. This proposal sets out a research project that will construct biological computers formed from engineered bacterial populations that communicate using quorum sensing molecules. Information from multiple biosensor inputs will be integrated and processed by the biocomputer, the output of which will be spatial patterning. The architecture will be based on cellular automata, which can perform any computation, including logic and temporal logic operations, memory and counting, all of which can be used to distinguish states in complex biological and chemical environments. Our biocomputers will be housed in microfluidic devices using hydrogel structures to create two and three dimensional regular arrangements. As a proof-of-concept, we will develop a biocomputer for the analysis and monitoring of intestinal and microbiota health through stool samples. Sensors for inflammation, pH and short chain fatty acids will be combined into a device that can indicate whether an individual has inflammatory bowel disease or irritable bowel syndrome. A low-cost device for use at home, which distinguishes between these conditions, could potentially save the global health care industry billions of dollars in unnecessary diagnostic treatments.

Link to the ERC project webpage:

Keywords of the ERC project: synthetic biology; biosensors; systems biology; biological computation

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

771820

Project Acronym:

3DPROTEINPUZZLES

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr INGEMAR ANDRÉ**

Host Institution: **LUNDS UNIVERSITET - SE**

Shape-directed protein assembly design

Large protein complexes carry out some of the most complex functions in biology. Such structures are often assembled spontaneously from individual components through the process of self-assembly. If self-assembled protein complexes could be engineered from first principle it would enable a wide range of applications in biomedicine, nanotechnology and materials science. Recently, approaches to rationally design proteins to self-assemble into predefined structures have emerged. The highlight of this work is the design of protein cages that may be engineered into protein containers. However, current approaches for self-assembly design does not result in the assemblies with the required structural complexity to encode many of the sophisticated functions found in nature. To move forward, we have to learn how to engineer protein subunits with more than one designed interface that can assemble into tightly interacting complexes. In this proposal we propose a new protein design paradigm, shape directed protein design, in order to address shortcomings of the current methodology. The proposed method combines geometric shape matching and computational protein design. Using this approach we will de novo design assemblies with a wide variety of structural states, including protein complexes with cyclic and dihedral symmetry as well as icosahedral protein capsids built from novel protein building blocks. To enable these two design challenges we also develop a high-throughput assay to measure assembly stability in vivo that builds on a three-color fluorescent assay. This method will not only facilitate the screening of orders of magnitude more design constructs, but also enable the application of directed evolution to experimentally improve stable and assembly properties of designed containers as well as other designed assemblies.

Link to the ERC project webpage:

Keywords of the ERC project: Computational protein design, protein self-assembly

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

787115

Project Acronym:

MaCChines

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr ROMAN JERALA**

Host Institution: **KEMIJSKI INSTITUT - SI**

Molecular machines based on coiled-coil protein origami

Proteins are the most versatile and complex smart nanomaterials, forming molecular machines and performing numerous functions from structure building, recognition, catalysis to locomotion. Nature however explored only a tiny fraction of possible protein sequences and structures. Design of proteins with new, in nature unseen shapes and features, offers high rewards for medicine, technology and science. In 2013 my group pioneered the design of a new type of modular coiled-coil protein origami (CCPO) folds. This type of de novo designed proteins are defined by the sequence of coiled-coil (CC) dimer-forming modules that are concatenated by flexible linkers into a single polypeptide chain that self-assembles into a polyhedral cage based on pairwise CC interactions. This is in contrast to naturally evolved proteins where their fold is defined by a compact hydrophobic core. We recently demonstrated the robustness of this strategy by the largest de novo designed single chain protein, construction of tetrahedral, pyramid, trigonal prism and bipyramid cages that self-assemble in vivo.

This proposal builds on unique advantages of CCPOs and represents a new frontier of this branch of protein design science. I propose to introduce functional domains into selected positions of CCPO cages, implement new types of building modules that will enable regulated CCPO assembly and disassembly, test new strategies of caging and release of cargo molecules for targeted delivery, design knotted and crosslinked protein cages and introduce toehold displacement for the regulated structural rearrangement of CCPOs required for designed molecular machines, which will be demonstrated on protein nanotweezers. Technology for the positional combinatorial library-based single pot assembly of CCPO genes will provide high throughput of CCPO variants. Project will result in new methodology, understanding of potentials of CCPOs for designed molecular machines and in demonstration of different applications.

Link to the ERC project webpage:

Keywords of the ERC project: protein design, synthetic biology, coiled coil protein origami, designed molecular machines, designed vaccines, cryoelectron microscopy,

Keywords that characterize the scientific profile of the potential visiting researcher/s: structural biology, molecular modeling, synthetic biology, biophysics, molecular biology, protein chemistry, bionanotechnology



European Research Council
Executive Agency

Established by the European Commission

Project ID:

787768

Project Acronym:

H-Unique

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr BRYAN WILLIAMS**

Host Institution: **UNIVERSITY OF LANCASTER - UK**

In search of uniqueness - harnessing anatomical hand variation

H-unique will be the first multimodal automated interrogation of visible hand anatomy, through analysis and interpretation of human variation. It will be an interdisciplinary project, supported by anatomists, anthropologists, geneticists, bioinformaticians, image analysts and computer scientists. We will investigate inherent and acquired variation in search of uniqueness, as the hand retains and displays a multiplicity of anatomical variants formed by different aetiologies (genetics, development, environment, accident etc).

Hard biometrics, such as fingerprints, are well understood and some soft biometrics are gaining traction within both biometric and forensic domains (e.g. superficial vein pattern, skin crease pattern, morphometry, scars, tattoos and pigmentation pattern). A combinatorial approach of soft and hard biometrics has not been previously attempted from images of the hand. We will pioneer the development of new methods that will release the full extent of variation locked within the visible anatomy of the human hand and reconstruct its discriminatory profile as a retro-engineered multimodal biometric. A significant step change is required in the science to both reliably and repeatably extract and compare anatomical information from large numbers of images especially when the hand is not in a standard position or when either the resolution or lighting in the image is not ideal.

Large datasets are vital for this work to be legally admissible. Through citizen engagement with science, this research will collect images from over 5,000 participants, creating an active, open source, ground-truth dataset. It will examine and address the effects of variable image conditions on data extraction and will design algorithms that permit auto-pattern searching across large numbers of stored images of variable quality. This will provide a major novel breakthrough in the study of anatomical variation, with wide-ranging, interdisciplinary and transdisciplinary impact.

Link to the ERC project webpage: <https://www.lancaster.ac.uk/scc/research/h-unique/>

Keywords of the ERC project: Forensic anthropology, image analysis, machine learning, biometrics, computer science, mathematics, anatomy

Keywords that characterize the scientific profile of the potential visiting researcher/s: Biometrics, machine learning, forensics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

801954

Project Acronym:

PhytoTrace

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr EVA OBURGER**

Host Institution: **UNIVERSITAET FUER BODENKULTUR WIEN - AT**

Wanted: Micronutrients! Phytosiderophore-mediated acquisition strategies in grass crops

Understanding how plants respond to micronutrient deficiency and which biogeochemical processes are induced at the root-soil interface, i.e. the rhizosphere, is crucial to improve crop yield and micronutrient grain content for high quality food and feed. Iron nutrition by grass species relies on the release and re-uptake of phytosiderophores, which are root exudates that form stable complexes with Fe but also other trace metals such as Zn and Cu. However, neither the importance of phytosiderophores under Zn and Cu deficient conditions nor the interplay of plant responses and rhizosphere processes are well understood as the majority of studies in the past was carried out under 'soil-free' hydroponic conditions. In this project, I aim to elucidate the mechanisms controlling phytosiderophore-mediated micronutrient acquisition of barley (*Hordeum vulgare*) under Zn, Cu, and as reference, Fe deficient conditions, with particular emphasis on soil environments. Barley is the fifth most produced crop worldwide and of great importance in regions that are characterized by harsh living conditions. In a holistic approach, my team and I will apply innovative soil-based and traditional hydroponic root exudation sampling approaches in combination with advanced plant molecular techniques to study the phytosiderophore release and uptake system under different experimental conditions. The chemical synthesis of otherwise commercially unavailable phytosiderophores in their natural and ¹³C-labelled form will allow us to trace their decomposition and metal solubilizing efficiency in the plant-microbe-soil system to uncover the interplay of plant genetic responses and rhizosphere processes affecting the time-window of PS-mediated MN acquisition. Moving beyond 'soil-free' experimental designs of the past, this project will generate key knowledge to improve selection of crops with highly efficient micronutrient acquisition traits to alleviate micronutrient malnutrition of people world-wide.

Link to the ERC project webpage:
https://forschung.boku.ac.at/fis/suchen.projekt_uebersicht?sprache_in=en&ansicht_in=&menue_id_in=300&id_in=12821

Keywords of the ERC project: Soil; Barley (*Hordeum vulgare*); Micronutrient (Fe, Zn, Cu) deficiency; Phytosiderophores; Root exudates;

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

802000

Project Acronym:

ribolife

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr HANNES MUTSCHLER**

Host Institution: **MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN EV
- DE**

Resurrecting LUCA - Engineering of RNA-encoded Cellular Life Using Dual Evolution and Intergenomic Transplantation

Modern cellular life strictly depends on DNA as genetic material. However, a large body of evidence infers the existence of a previous, more primitive biology in which RNA also stored information in cellular entities. Recreating a living cellular fossil representing this transition from an ancient RNA world to modern DNA-based life would fundamentally advance our understanding of our biology's history, and enable us to explore its biological properties experimentally. However, the reengineering of existing molecular systems into a viable doppelganger of the Last Universal Common Ancestor (LUCA) or one of its precursors is extremely challenging.

I propose to use a novel, combined top-down and bottom-up approach to create a modern-day doppelganger of LUCA by engineering bacterial hybrids with core cellular functions encoded on RNA. Using Darwinian Evolution as driver, my team and I will prototype and refine synthetic RNA-replicons through alternating replication in both cell-free and intracellular environments. This "dual evolution" approach will shape increasingly complex RNA networks capable of encoding complex genetic information. Following this, we will use these networks to create information-rich RNA chromosomes, enabling the transfer of essential genomic information from DNA to RNA. Finally, we will address this intergenomic transplantation by combining a novel RNA-delivery strategy with iterative rounds of genome deletion and complementation using state-of-the art CRISPR-Cas9 assisted genome editing.

The proposed research will fundamentally advance synthetic biology, and could positively answer the transformative questions: Can we create, program and evolve life-like systems that can survive in both cell-free and intracellular environments? Can we use these entities to construct an alternative biology in which central cellular activities are encoded on genomes not made of DNA?

Link to the ERC project webpage:

Keywords of the ERC project: RNA replication, directed evolution, genome engineering, RNA nanotechnology

Keywords that characterize the scientific profile of the potential visiting researcher/s: microbiology, imaging, genome engineering



European Research Council
Executive Agency

Established by the European Commission

Project ID:

805094

Project Acronym:

GRASP

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr CHARLES MELNYK**

Host Institution: **SVERIGES LANTBRUKSUNIVERSITET - SE**

Overcoming plant graft incompatibility by modifying signalling and perception

For millennia, people have cut and joined together different plants through a process known as grafting. Plants tissues from different genotypes fuse, vasculature connects and a chimeric organism forms that combines desirable characteristics from different plants such as high yields or disease resistance. However, plants can only be grafted to closely related species and in some instances, they cannot be grafted to themselves. This phenomenon is referred to as graft incompatibility and the mechanistic basis is completely unknown. Our previous work on graft formation in *Arabidopsis thaliana* has uncovered genes that rapidly activate in grafted tissues to signal the presence of adjoining tissue and initiate a vascular reconnection process. These genes activate around the cut only during graft formation and present a powerful tool to screen large numbers of chemicals and genes that could promote tissue perception and vascular formation. With these sensors and our previously established grafting tools in the model plant *Arabidopsis*, we can address fundamental questions about grafting biology that have direct relevance to improving graft formation through:

1. Identifying genes required for the recognition response using forward and reverse genetic screens.
2. Determining and characterising signals that activate vascular induction using a chemical genetics screen.
3. Characterising the transcriptional basis for compatibility and incompatibility by analysing tissues and species that graft and comparing these to tissues and species that do not graft.
4. Overcoming graft incompatibility and improving graft formation by applying the knowledge obtained from the three previous objectives.

We thus aim to broaden our fundamental understanding of the processes associated with grafting including wound healing, vascular formation and tissue regeneration, while at the same time, use this information to improve graft formation and expand the range of grafted species.

Link to the ERC project webpage:

Keywords of the ERC project: Plants, *Arabidopsis*, grafting, transcriptomics, chemical genomics, monocots

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

815379

Project Acronym:

AutoCAb

Evaluation Panel:

LS9

**Applied life Sciences and
Non-Medical
Biotechnology**

Principal Investigator: **Dr SAREL FLEISHMAN**

Host Institution: **WEIZMANN INSTITUTE OF SCIENCE - IL**

Automated computational design of site-targeted repertoires of camelid antibodies

We propose to develop the first high-throughput strategy to design, synthesize, and screen repertoires comprising millions of single-domain camelid antibodies (VHH) that target desired protein surfaces. Each VHH will be individually designed for high stability and target-site affinity. We will leverage recent methods developed by our lab for designing stable, specific, and accurate backbones at interfaces, the advent of massive and affordable custom-DNA oligo synthesis, and machine learning methods to accomplish the following aims:

Aim 1: Establish a completely automated computational pipeline that uses Rosetta to design millions of VHHs targeting desired protein surfaces. The variable regions in each design will be encoded in DNA oligo pools, which will be assembled to generate the entire site-targeted repertoire. We will then use high-throughput binding screens followed by deep sequencing to characterize the designs' target-site affinity and isolate high-affinity binders.

Aim 2: Develop an epitope-focusing strategy that designs several variants of a target antigen, each of which encodes dozens of radical surface mutations outside the target site to disrupt potential off-target site binding. The designs will be used to isolate site-targeting binders from repertoires of Aim 1.

Each high-throughput screen will provide unprecedented experimental data on target-site affinity in millions of individually designed VHHs.

Aim 3: Use machine learning methods to infer combinations of molecular features that distinguish high-affinity binders from non binders. These will be encoded in subsequent designed repertoires, leading to a continuous "learning loop" of methods for high-affinity, site-targeted binding.

AutoCAb's interdisciplinary strategy will thus lead to deeper understanding of and new general methods for designing stable, high-affinity, site-targeted antibodies, potentially revolutionizing binder and inhibitor discovery in basic and applied biomedical research.

Link to the ERC project webpage: https://erc.europa.eu/projects-figures/erc-funded-projects/results?f%5B0%5D=funding_scheme%3AConsolidator%20Grant%20%28CoG%29&page=10

Keywords of the ERC project: Antibody design; Rosetta; camelid antibodies; machine learning

Keywords that characterize the scientific profile of the potential visiting researcher/s: Experience in programming and practical methods in protein biochemistry



European Research Council
Executive Agency

Established by the European Commission

Project ID:

819934

Project Acronym:

ProMiDis

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr GEORGIOS SKRETAS**

Host Institution: **ETHNIKO IDRYMA EREVNON - EL**

A unified drug discovery platform for protein misfolding diseases

It is now widely recognized that a variety of major diseases, such as Alzheimer's disease, Huntington's disease, systemic amyloidosis, cystic fibrosis, type 2 diabetes etc., are characterized by a common molecular origin: the misfolding of specific proteins. These disorders have been termed protein misfolding diseases (PMDs) and the vast majority of them remain incurable. Here, I propose the development of a unified approach for the discovery of potential therapeutics against PMDs. I will generate engineered bacterial cells that function as a broadly applicable discovery platform for compounds that rescue the misfolding of PMD-associated proteins (MisPs). These compounds will be selected from libraries of drug-like molecules biosynthesized in engineered bacteria using a technology that allows the facile production of billions of different test molecules. These libraries will then be screened in the same bacterial cells that produce them and the rare molecules that rescue MisP misfolding effectively will be selected using an ultrahigh-throughput genetic screen. The effect of the selected compounds on MisP folding will then be evaluated by biochemical and biophysical methods, while their ability to inhibit MisP-induced pathogenicity will be tested in appropriate mammalian cell assays and in established animal models of the associated PMD. The molecules that rescue the misfolding of the target MisPs and antagonize their associated pathogenicity both in vitro and in vivo, will become drug candidates against the corresponding diseases. This procedure will be applied for different MisPs to identify potential therapeutics for four major PMDs: Huntington's disease, cardiotoxic light chain amyloidosis, dialysis-related amyloidosis and retinitis pigmentosa. Successful realization of ProMiDis will provide invaluable therapeutic leads against major diseases and a unified framework for anti-PMD drug discovery.

Link to the ERC project webpage:

Keywords of the ERC project: protein misfolding and aggregation, protein misfolding diseases, molecular evolution, combinatorial libraries, high-throughput screening, early-stage drug discovery, engineered microorganisms, synthetic biology

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

820124

Project Acronym:

DeCoCt

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr ERIC KEMEN**

Host Institution: **EBERHARD KARLS UNIVERSITAET TUEBINGEN - DE**

Knowledge based design of complex synthetic microbial communities for plant protection

Complex microbial communities ("microbiota") that populate surfaces of higher organisms critically impact health of their hosts: They contribute to vital functions such as host fitness, nutrient acquisition, stress tolerance and pathogen resistance but are, at the same time, reservoirs for facultative pathogens or can promote pathogenesis. How and why communities shift from a beneficial to a detrimental state is largely unknown and we are far from utilizing identified mechanisms.

In order to cure detrimental microbiota, that were damaged or reverted through stress factors including previous diseases, decoding the complex processes governing microbiota dynamics is a key challenge. To develop durable probiotics, communal stability or the ability of a community to return to a steady state following perturbation is a key factor.

Our lab has broad expertise in studying microbial communities through lab experiments and analyzing factors that shape the microbiota of *Arabidopsis thaliana* plants under natural conditions and common garden experiments. We have discovered a hierarchical order in microbial community networks with hub microbes as key elements. A recent breakthrough was the discovery of microbial taxa that persist throughout the life of *A. thaliana* plants and their importance in network stability.

In this project we will use our expertise to identify key stability factors and drivers of communal dynamics to reconstitute synthetic communities. How to seed microbial communities that develop into functional probiotics is a key challenge. We will use knowledge based assembly of complex communities to seeds protective microbiota. We will challenge those through pathogens and abiotic factors to refine and test the predictive power of our analyses. Therefore, DeCoCt represents a highly innovative approach that holds the potential to gain novel insights beyond the current scope of microbiota and probiotics research.

Link to the ERC project webpage: <https://uni-tuebingen.de/en/faculties/faculty-of-science/departments/interdepartmental-centres/center-for-plant-molecular-biology/res/microbial-interactions/>

Keywords of the ERC project: microbial communities, community structure, probiotics, plant, synthetic microbial communities

Keywords that characterize the scientific profile of the potential visiting researcher/s: microbiology, computational biology



European Research Council
Executive Agency

Established by the European Commission

Project ID:

850974

Project Acronym:

MABSTER

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator:

Dr ANDREAS LAUSTSEN

Host Institution:

DANMARKS TEKNISKE UNIVERSITET - DK

Monoclonal Antibodies with Binding Sensitive To Environmental Regulation

Snakebite envenoming is a Neglected Tropical Disease (NTD) that each year affects 2.5 million victims and kills >100,000, unless they are treated with antivenom. Conventional antivenoms, derived from immunized animals, inflict serum sickness and anaphylaxis in patients, and are costly to manufacture. Monoclonal human antibodies with special toxin-binding properties that are sensitive towards regulation by their microenvironment (e.g. pH), which may be discovered using phage display selection, may solve this issue, providing significant societal impact by enabling the development of cost-effective antivenoms to victims in low and middle-income countries. In this project, phage display selection, high-density peptide microarray technology, and antibody engineering techniques will in three scientific objectives be harnessed in the pursuit of developing novel methodologies for discovery of therapeutic human monoclonal antibodies that are recyclable (can neutralize more than one snake toxin per antibody), broadly cross-reactive (can neutralize different types of snake toxins), and that are both broadly cross-reactive and recyclable at the same time. This will open up for entirely new ways of designing biotherapeutics against complex indications, such as snakebite envenoming, but also cancer, infectious, and parasitic diseases, where the targets can be elusive due to hyper-mutability. The ERC Starting Grant offers a unique opportunity to consolidate me as an international key scientific researcher in this field of antibody discovery and NTDs. I have already independently led a research group in this area for 2 years, I have in-depth experience with toxin-targeted antibody discovery (my dr.tech dissertation similar to the German "habilitation" will be submitted during fall 2018), and I am already involved in high level policy in the field of snakebite envenoming via my role as a scientific advisor for the World Health Organization.

Link to the ERC project webpage: <http://tropicalpharmacology.com>

Keywords of the ERC project: Antibody discovery; phage display; biotherapeutics; toxinology; antivenom; protein engineering; synthetic biology; antibody technologies; antibodies

Keywords that characterize the scientific profile of the potential visiting researcher/s: Antibody discovery; phage display; biotherapeutics; protein engineering; synthetic biology; antibody technologies; antibodies; molecular biology; genetic engineering; structural biology; bioinformatics; high-throughput technology; microbiology; drug disco



European Research Council
Executive Agency

Established by the European Commission

Project ID:

715260

Project Acronym:

SC-EpiCode

Evaluation Panel:

LS9

**Applied life Sciences and
Non-Medical
Biotechnology**

Principal Investigator: **Dr OREN RAM**

Host Institution: **THE HEBREW UNIVERSITY OF JERUSALEM - IL**

Decoding the Epigenomic Regulatory Code by the Use of Single Cell Technologies

Chromatin regulators adjust genome functions by modifying chromatin states. Comprehensive characterization of chromatin states, associations of chromatin regulators, and expression profiles is crucial for investigating: 1. Cellular differentiation triggers. 2. The nature of the underlying chromatin regulatory mechanisms. 3. The effect of cellular heterogeneity, and 4. How chromatin affects mRNA expression. Mapping chromatin states by sequencing immunoprecipitated chromatin (ChIP-seq) provides an extraordinary resource for studying cellular states. However, a major shortcoming is that the profiles reflect a composite average over the studied cell population, concealing important information about the underlying subpopulations. To address this hurdle, I pioneered Drop-Seq, a novel drop based microfluidic technology for single cell ChIP-seq and RNA-seq. Applying the technique to thousands of embryonic stem (ES) cells, we identified a spectrum of sub-populations defined by differences in chromatin signatures of pluripotency and differentiation priming. However, despite initial progress, the extent and significance of chromatin-state heterogeneity and its relationship with mRNA expression remain largely uncharted. The central aim of this proposal is to develop a novel framework to systematically characterize cell-to-cell variability at the epigenomic level. Our approach will include the development of technology enabling ChIP-seq and RNA-seq on the same cell. We will also exploit drop-based microfluidics to develop a robust CRISPR/Cas9-based approach to assess single and multiple perturbations. Finally, we will apply these innovative technologies to questions about cellular heterogeneity and epigenomic regulation during early differentiation of ES cells. This proposal will reveal the function and interplay between chromatin regulators, histone marks and transcription events, and shed light on the underlying regulation leading to cell fate decisions.

Link to the ERC project webpage:

Keywords of the ERC project: Single cell technologies, epigenomics, chromatin, stem cells, differentiation, computational biology

Keywords that characterize the scientific profile of the potential visiting researcher/s: Multidisciplinary, cancer cellular heterogeneity



European Research Council
Executive Agency

Established by the European Commission

Project ID:

804229

Project Acronym:

LIMBo

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr CLÁUDIA NUNES DOS SANTOS**

Host Institution: **UNIVERSIDADE NOVA DE LISBOA - PT**

Zooming the link between diet and brain health: how phenolic metabolites modulate brain inflammation

Currently a big concern of our aging society is to efficiently delay the onset of neurodegenerative diseases which are progressively rising in incidence. The paradigm that a diet rich in the phenolics, prevalent e.g. in fruits, is beneficial to brain health has reached the public. However their mechanistic actions in brain functions remain to be seen, particularly since the nature of those acting in the brain remains overlooked. I wish to address this gap by identifying candidate compounds that can support development of effective strategies to delay neurodegeneration.

Specifically, I will be analysing the potential of dietary phenolics in both prevention and treatment (i.e delay) of neuroinflammation – key process shared in neurodegenerative diseases. To break down the current indeterminate status of “cause vs effect”, my vision is to focus my research on metabolites derived from dietary phenolics that reach the brain. I will be investigating their effects in both established and unknown response pathways of microglia cells - the innate immune cells of the central nervous system, either alone or when communicating with other brain cells. Ultimately, to attain an integrated view of their effects I will establish nutrition trials in mice. LIMBo considers both pro- and anti- inflammatory processes to preliminary validate the action of any promising metabolite in prevention and/or therapeutics.

LIMBo provides valuable scientific insights for future implementation of healthy brain diets. My group is in a unique position to address LIMBo objectives due to multidisciplinary expertise in organic synthesis, metabolomics and molecular and cellular biology, together with our previous data on novel neuroactive metabolites.

LIMBo also creates far-reaching opportunities by generating knowledge that impacts our fundamental understanding on the diversity of phenolic metabolites and their specific influences in neuroinflammation and potential use as prodrugs.

Link to the ERC project webpage:

Keywords of the ERC project: polyphenols metabolism, neurodegeneration, microglia. brain

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

818890

Project Acronym:

ArtHep

Evaluation Panel:

LS9

**Applied life Sciences and
Non-Medical
Biotechnology**

Principal Investigator: **Dr BRIGITTE STADLER**
Host Institution: **AARHUS UNIVERSITET - DK**

Hepatocytes-Like Microreactors for Liver Tissue Engineering

The global epidemics of obesity and diabetes type 2 lead to higher abundance of medical conditions like non-alcoholic fatty liver disease causing an increase in liver failure and demand for liver transplants. The shortage of donor organs and the insufficient success in tissue engineering to ex vivo grow complex organs like the liver is a global medical challenge.

ArtHep targets the assembly of hepatic-like tissue, consisting of biological and synthetic entities, mimicking the core structure elements and key functions of the liver. ArtHep comprises an entirely new concept in liver regeneration with multi-angled core impact: i) cell mimics are expected to reduce the pressure to obtain donor cells, ii) the integrated biocatalytic subunits are destined to take over tasks of the damaged liver slowing down the progress of liver damage, and iii) the matching micro-environment in the bioprinted tissue is anticipated to facilitate the connection between the transplant and the liver.

Success criteria of ArtHep include engineering enzyme-mimics, which can perform core biocatalytic conversions similar to the liver, the assembly of biocatalytic active subunits and their encapsulation in cell-like carriers (microreactors), which have mechanical properties that match the liver tissue and that have a camouflaging coating to mimic the surface cues of liver tissue-relevant cells. Finally, matured bioprinted liver-lobules consisting of microreactors and live cells need to connect to liver tissue when transplanted into rats.

I am convinced that the ground-breaking research in ArtHep will contribute to the excellence of science in Europe while providing the game-changing foundation to counteract the ever increasing donor liver shortage. Further, consolidating my scientific efforts and moving them forward into unexplored dimensions in biomimicry for medical purposes, is a unique opportunity to advance my career.

Link to the ERC project webpage: <https://cordis.europa.eu/project/rcn/220696/factsheet/en>

Keywords of the ERC project: polymer chemistry, liver, enzyme mimics, hydrogels, hepatocytes

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

819800

Project Acronym:

BionicBacteria

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr ROB LAVIGNE**

Host Institution: **KATHOLIEKE UNIVERSITEIT LEUVEN - BE**

Integrating a novel layer of synthetic biology tools in *Pseudomonas*, inspired by bacterial viruses

As nature's first bioengineers, bacteriophages have evolved to modify, adapt and control their bacterial hosts through billions of years of interactions. Indeed, like modern synthetic biologists aspire to do, bacteriophages already evade bacterial silencing of their xenogeneic DNA, subvert host gene expression, and co-opt both the central and peripheral metabolisms of their hosts. Studying these key insights from a molecular systems biology perspective, inspired us to develop these evolutionary fully-adapted phage mechanisms as a next-level layer of synthetic biology tools. Thus, BIONICbacteria will provide conceptual novel synthetic biology tools that allow direct manipulation of specific protein activity, post-translational modifications, RNA stability, and metabolite concentrations.

The goal of BIONICbacteria is to pioneer an unconventional way to perform synthetic biology, tapping an unlimited source of novel phage tools genetic circuits and phage modulators. To achieve these goals, we will apply and develop state-of-the-art technologies in molecular microbiology and focus on three principal aims:

- (1) To exploit new phage-encoded genetic circuits as synthetic biology parts and as intricate biotechnological chassis.
- (2) To build synthetic phage modulators (SPMs) as novel payloads to directly impact the bacterial metabolism in a targeted manner.
- (3) To create designer bacteria by integrating SPMs-containing circuits into bacterial strains as proof-of-concepts for applications in industrial fermentations and vaccine design.

This proposed "plug-in" approach of evolutionary-adapted synthetic modules, will allow us to domesticate *Pseudomonas* strains in radically new ways. By building proofs-of-concept for applications in industrial fermentations and vaccine development, we address key problem in these areas with potentially high-gain solutions for society and industry.

Link to the ERC project webpage: <https://www.biw.kuleuven.be/biosyst/a2h/LoGT/projects/>

Keywords of the ERC project: microbial synthetic biology, bacteriophage, *Pseudomonas*

Keywords that characterize the scientific profile of the potential visiting researcher/s: systems biology, molecular microbiology, biotechnology



European Research Council
Executive Agency

Established by the European Commission

Project ID:

818089

Project Acronym:

METACELL

Evaluation Panel:

LS9

Applied life Sciences and
Non-Medical
Biotechnology

Principal Investigator: **Dr FERNANDO LÓPEZ GALLEGO**

Host Institution: ASOCIACION CENTRO DE INVESTIGACION COOPERATIVA EN
BIOMATERIALES- CIC biomaGUNE - ES

Artificial metabolic cells for biomanufacturing of bio-based chiral fine chemicals

One of the major challenges of sustainable chemistry is expanding the palette of bio-based chemicals that can replace, or at least ameliorate, the exploitation of fuel-based chemicals. Cell-free metabolic engineering using soluble enzymes is an emerging and versatile approach that seeks to increase the selectivity and productivity of chemical biomanufacturing processes. However, soluble and isolated enzymes present major issues in terms of efficiency, stability and re-usability that hamper industrial applications.

To solve these problems, enzymes can be rationally immobilized on smart materials resulting in robust, efficient and self-sufficient heterogeneous biocatalysts, but immobilization is still restricted to simple enzyme cascades. METACELL mission is developing self-sufficient artificial metabolic cells (AMCs) by immobilizing complex metabolic networks on hierarchical porous materials. To this aim, the solid surfaces must play an active role in the chemical process rather than just being a mere immobilization support.

This integrative proposal will exploit protein engineering, surface chemistry, bio-organic chemistry and protein immobilization tools for the successful development of 1) a cell-free artificial metabolism, 2) innovative engineering tools to modify both enzyme and material surfaces and 3) continuous synthesis of industrially relevant fine chemicals catalyzed by AMCs packed into flow reactors. The resulting technology of METACELL will serve as a prototyping platform to test artificial biosynthetic pathways with application in combinatorial chemistry (e.g drugs discovery). METACELL may also offer long-term solutions for the on-demand production of drugs at the point-of-care.

In addition to the technological outputs, METACELL will also provide essential information to understand how spatial organization of multi-enzyme systems affect the performance of in vitro biosynthetic pathways confined into artificial chassis (solid materials).

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:



European Research Council
Executive Agency

Established by the European Commission

Project ID:

810186

Project Acronym:

BacterialCORE

Evaluation Panel:

SYG
Synergy

Principal Investigator: **Dr SIGAL BEN-YEHUDA**

Host Institution: **THE HEBREW UNIVERSITY OF JERUSALEM - IL**

Widespread Bacterial CORE Complex Executes Intra- and Inter-Kingdom Cytoplasmic Molecular Trade

The enormous versatility of bacteria enables the formation of multi-species communities that colonize nearly every niche on earth, making them the dominant life form and a major component of the biomass. Exchange of molecular information among neighboring bacteria in such communities, as well as between bacteria and proximal eukaryotic cells, is key for bacterial success. Yet, the principles controlling these multicellular interactions are poorly defined. Here we describe the identification of a bacterial protein complex, herein termed CORE, whose function is to traffic cytoplasmic molecules among different bacterial species, and between pathogenic bacteria and their human host cells. The CORE is composed of five membrane proteins, highly conserved across the entire bacterial kingdom, providing a ubiquitous platform that facilitates both intra- and inter-kingdom crosstalk. Our preliminary data support the idea that the CORE acts as a shared module for the assembly of larger apparatuses, executing this universal molecular flow among organisms. We propose to elucidate components, structure and biogenesis of the CORE machinery, operating during bacteria-bacteria and pathogen-host interactions. We further aim to provide an unbiased-global view of the extent and identity of cytoplasmic molecules traded via CORE including metabolites, proteins and RNA, and to reveal the criteria determining the specificity of the transported cargo. Furthermore, we intend to decipher the impact of CORE-mediated molecular exchange on bacterial physiology and virulence, and devise anti-CORE compounds to combat pathogenic bacteria. This study is expected to transform the way we currently view bacterial communities and host-pathogen interactions. We anticipate these findings to lead to the development of creative strategies to modulate, predict and even design bacterial communities, and lay the foundation for new and innovative approaches to fight bacterial diseases.

Link to the ERC project webpage:

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s: Bacteria, nanotubes, Bacillus, host-pathogen interactions, intercellular communication



European Research Council
Executive Agency

Established by the European Commission

Project ID:

810377

Project Acronym:

ConnectToBrain

Evaluation Panel:

SYG
Synergy

Principal Investigator: **Dr RISTO ILMONIEMI**

Host Institution: **AALTO KORKEAKOULUSAATIO SR - FI**

Connecting to the Networks of the Human Brain

ConnectToBrain will introduce whole-brain multi-locus transcranial magnetic stimulation (mTMS), in which the brain-stimulating electric-field location, direction, magnitude and timing are controlled electronically based on real-time high-density electroencephalography (hdEEG) information of activity and connectivity in brain networks. The final mTMS apparatus will consist of 50 coils. Superpositions of electric fields produced by the different overlapping coils allow spatiotemporally millimeter- and millisecond-precise stimulus sequences to arbitrary cortical sites without physical movements of the coil set. Spatial targeting of mTMS will be further improved by measuring individual brain conductivity distributions with ultra-low-field MRI. The proposed hdEEG methodology uses a brain-computer interface (BCI) and a computer-brain interface (CBI) in a closed, algorithmically-controlled loop. BCI receives real-time information about brain activity and connectivity from hdEEG, while CBI adapts mTMS to drive brain activity and connectivity into desired directions. ConnectToBrain will allow unprecedented tracking of dynamic changes and reorganization of brain networks in real-time, and network-targeted closed-loop stimulation. This radically novel technology will cause a paradigm shift from current open-loop practice that is only moderately effective in therapy. We will apply ConnectToBrain to reach new levels of efficacy of therapeutic applications. Patients after stroke and with Alzheimer's disease will be tested and treated as models of network disorders.

Our high-risk, high-gain endeavor will reach the ambitious goals only through the Synergy of the 3 PIs, world leaders in their complementary areas of expertise (instrumentation, algorithms, translation). If the project succeeds, we expect the value of societal, health and industrial benefits in Europe to exceed €1 billion annually, not to mention the immense value of alleviating human suffering from brain disorders.

Link to the ERC project webpage: connecttobrain.eu

Keywords of the ERC project: TMS, EEG, TMS-EEG, TMS therapy, coil design, power electronics, electromagnetism, brain networks

Keywords that characterize the scientific profile of the potential visiting researcher/s: hardware, software architecture, software design, user interface, electronics, control systems, neurotechnology, brain tissue modeling, machine learning, applied mathematics, physics, signal processing, brain networks



European Research Council
Executive Agency

Established by the European Commission

Project ID:

810377

Project Acronym:

ConnectToBrain

Evaluation Panel:

SYG
Synergy

Principal Investigator:	Dr GIAN LUCA ROMANI
Host Institution:	AALTO KORKEAKOULUSAATIO SR - FI

Connecting to the Networks of the Human Brain

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Link to the ERC project webpage: connecttobrain.eu

Keywords of the ERC project: TMS, EEG, TMS-EEG, MEG, electromagnetism, brain networks, real-time connectivity.

Keywords that characterize the scientific profile of the potential visiting researcher/s: software architecture, software design, user interface, machine learning, applied mathematics, physics, signal processing, brain networks, connectivity.



European Research Council
Executive Agency

Established by the European Commission

Project ID:

810172

Project Acronym:

Indigene

Evaluation Panel:

SYG
Synergy

Principal Investigator: **Dr EWAN BIRNEY**

Host Institution: **EUROPEAN MOLECULAR BIOLOGY LABORATORY - DE**

Genetics of Individuality

We propose to thoroughly investigate and characterise the sources of variation that results in varying phenotypes in a complex vertebrate. As well as characterising the genetic and environmental sources of variation, we will also investigate individual stochastic variation present even in fixed settings (both genetically and environmentally). To achieve this we will exploit the unique properties of Medaka fish, which can be fully inbred from the wild. We have already inbred and performed whole genome sequencing of a panel of 111 diverse Medaka fish from a single location; we propose to phenotype these fish in depth with high replication structure, ranging from organismal to molecular phenotypes. We will also phenotype entirely wild fish from the same source population as the panel with a subset of the phenotypes. We will analyse the data using state of the art methods to partition variation between genetic, environmental and stochastic components, and their interactions. We will integrate across both the different levels of phenotypic information across the cardiovascular system, and also across vertebrate phenotypes, in particular the extensive human phenotypes. By using genetic crosses and CRISPR-Cas9 techniques we will definitively prove specific interactions. We will host a "Research Hotel" for other phenotyping schemes to be applied to this panel, in particular from the Zebrafish community. This comprehensive and carefully replicated study will allow us to understand the opportunities and limitations of genetic stratification and personalised medicine in humans.

Link to the ERC project webpage:

Keywords of the ERC project: Medaka and human genetics

Keywords that characterize the scientific profile of the potential visiting researcher/s: Quantitative Genetics



European Research Council
Executive Agency

Established by the European Commission

Project ID:

810331

Project Acronym:

WATCH

Evaluation Panel:

SYG
Synergy

Principal Investigator: **Dr VINCENT PREVOT**

Host Institution: **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE - FR**

Well-Aging and the Tanycytic Control of Health

The survival of an organism depends on energy homeostasis, involving the control of neuroendocrine functions that integrate metabolic feedback and adapt the response of the organism to physiological demands. Tanycytes, specialized glial cells lining the floor of the third ventricle in the median eminence of the hypothalamus, act as linchpins of these processes, dynamically controlling the secretion of neuropeptides by hypothalamic neurons into the pituitary portal circulation and regulating blood-brain and blood-cerebrospinal fluid exchanges, both processes that depend on their morphological plasticity in response to the physiological state. In addition to their barrier properties, they actively shuttle circulating metabolic signals to hypothalamic neurons that control food intake. The overarching goal of WATCH is to synergistically employ state-of-the-art technologies in systems neuroscience, mouse genetics and bench-to-bedside research, to explore the role of these unique and versatile cells, providing new directions in biomarker research and new therapeutic approaches for a variety of disorders that impair well-aging. Our specific aims are:

1. Genetic dissection of the in vivo regulation, pathophysiological function and molecular markers of tanycytes classified according to their anatomical location.
 2. Identification of novel heterogeneous, molecularly distinct tanycytes and associated endothelial cells and determining how these characteristics evolve under distinct physiological and pathological conditions.
 3. Functional validation of newly classified subgroups of tanycytes and the specific modulation of the activity of these subgroups at the experimental level.
 4. Exploration of the functional consequences of pharmacologically activating pathways required for the tanycytic shuttling of metabolic signals on their CSF levels of these factors, hypothalamic activity and cognition in animal models and patients with morbid obesity or age-related cognitive deficits.
-

Link to the ERC project webpage:

Keywords of the ERC project: tanycytes, hypothalamus, brain-body communication

Keywords that characterize the scientific profile of the potential visiting researcher/s: neuroscience, Energy homeostasis, aging, hypothalamus