The young scientists symposium

1ER DÉCEMBRE 2021 | 9H00 - 17H00

Institut de Botanique, Amphi Charles Flahault
(tram : lignes 1 & 4, arrêts Albert 1er)

LIVRET DE LA JOURNÉE

PÔLE BIOLOGIE-SANTÉ
MONTPELLIER UNIVERSITY OF EXCELLENCE

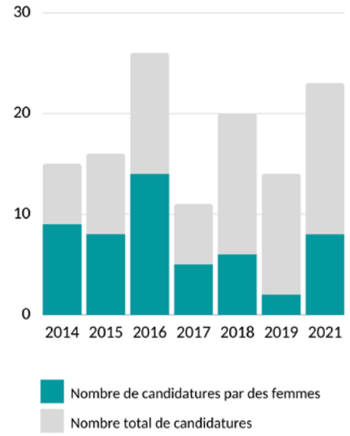
Sommaire

Avant-propos

Le Pôle de recherche Biologie-santé organise aujourd'hui la septième édition des Grandes Avancées en Biologie-Santé, rebaptisée « The young scientists symposium ». Cet évènement permet à de jeunes et talentueux chercheurs, auteurs d'avancées scientifiques majeures en Biologie-santé, de présenter leurs résultats publiés dans des revues scientifiques de très bon niveau mais également de se faire connaître de la communauté Biologie-Santé. Un prix leur sera remis en fin de symposium par le Directeur du Pôle.

Pour devenir lauréat, ces jeunes chercheurs ont dû soumettre leur article auprès de l'axe de recherche dont ils dépendent (Biologie quantitative, Cancérologie, Génétique-Epigénétique, Infectiologie & Immunologie, Médecine Expérimentale et Régénératrice, Neurosciences, Technologies pour la santé-Bioingénierie). Un jury, spécifique à chaque axe, constitué d'experts scientifiques, a sélectionné leur article. Un choix souvent difficile car les candidatures sont toutes d'un excellent niveau, attestant de la grande qualité de notre recherche.

Le nombre d'articles soumis par année est variable comme le montre le schéma ci-dessous. Pour cette édition 2021, nous avons reçu 23 candidatures tout axe confondu, dont 8 par des femmes.



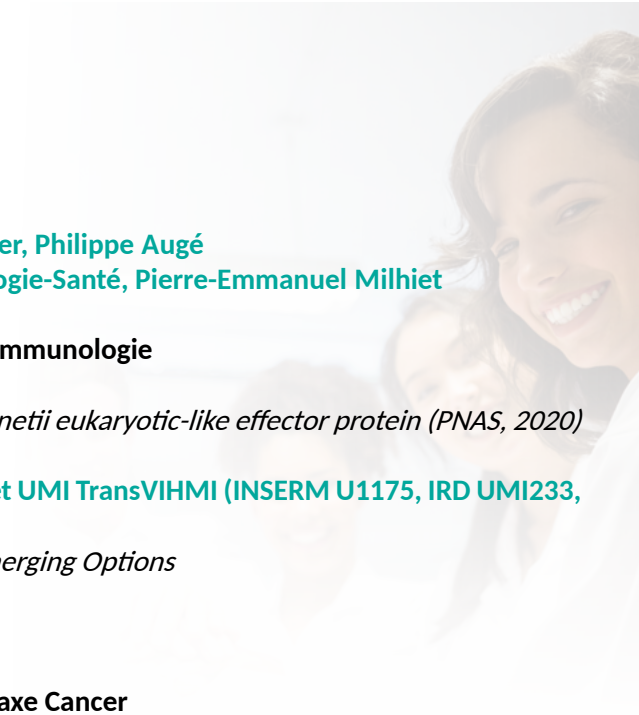
Le symposium est également l'occasion pour les jeunes chercheurs nouvellement recrutés par le CNRS, l'Inserm ou l'Université de venir se présenter et présenter le projet de recherche sur lequel ils travailleront au cours de ces prochaines années.

Enfin, cette année, nous avons l'honneur de recevoir deux conférenciers invités prestigieux :
• le Professeur Jacques Reynes du CHU de Montpellier qui nous fera une revue sur les traitements du COVID-19 (médicaments actuels et options émergentes) et
• le Dr Muriel Amblard qui nous présentera des outils chimiques à base de peptides dans le domaine de la Biologie-Santé.

Pierre-Emmanuel Milhiet
Directeur du Pôle de recherche Biologie-Santé

Brigitte Couette
Directrice opérationnelle du Pôle de recherche Biologie-Santé

Programme de la journée



8h45 Accueil café

9h00 - 9h30 **Ouverture par le Président de l'Université de Montpellier, Philippe Augé**
Introduction par le Directeur du Pôle de recherche Biologie-Santé, Pierre-Emmanuel Milhiet

9h30 - 10h00 **Mélanie Burette (IRIM), lauréate de l'Axe Infectiologie-Immunologie**
Introduction par Matteo Bonazzi
Modulation of innate immune signaling by a Coxiella burnetii eukaryotic-like effector protein (PNAS, 2020)

10h00 - 10h30 **Conférence du Pr Jacques Reynes, CHU de Montpellier et UMI TransVIHMI (INSERM U1175, IRD UMI233, Université de Montpellier) :**
COVID-19 Treatment: Current Therapeutic Drugs and Emerging Options

10h30 - 10h45 Pause

10h45 - 11h15 **Alexandra Garancher (Chaire MUSE 2021, IRCM) pour l'axe Cancer**
Introduction par Claude Sardet
Elucidating pediatric brain tumor microenvironment to improve immunotherapy

11h15 - 11h45 **Amos Fumagalli (IGF), lauréat de l'Axe Neurosciences**
Introduction par Philippe Marin
The atypical chemokine receptor 3 interacts with Connexin 43 inhibiting astrocytic gap junctional intercellular communication (Nat Commun., 2020)

11h45 - 12h15 **Présentation des projets des chercheurs recrutés en 2020 et 2021** : Julien Villeneuve (IGF, CNRS) - Antoine Besnard (IGF, INSERM) - Jakub Gruszczyk (CBS, INSERM) - Julien Faget (IRCM, INSERM) - Audrey Bernut (LPHI, CNRS)

12h15 - 13h45 Pause déjeuner

13h45 - 14h00 **Présentation des projets des chercheurs recrutés en 2020 et 2021** : Xiaojing Cong (IGF, CNRS) - Johanna Calderon (PhyMedExp, INSERM) - Isabel Chillon (IGMM, CNRS)

14h00 - 14h30 **Léo Guignard (CRBM), lauréat de l'Axe Biologie Quantitative**
Introduction par Patrick Lemaire
Contact area–dependent cell communication and the morphological invariance of ascidian embryogenesis (Science, 2020)

14h30 - 15h00 **Conférence de Muriel Amblard, Pôle Chimie et IBMM (CNRS UMR 5247, Université de Montpellier)**
Peptide-based chemical tools to address biological challenges

15h00 - 15h30 **Satish Sati (IGH), lauréat de l'Axe Génétique-épigénétique**
Introduction par Giacomo Cavalli
4D Genome Rewiring during Oncogene-Induced and Replicative Senescence (Mol Cell., 2020)

15h30 - 16h00 **Habib Belaid (IRCM, IEM), lauréat de l'Axe Technologies pour la santé -BioIngénierie**
Introduction par Vincent Cavaillès
Development of new biocompatible 3D printed graphene oxide-based scaffolds (Mater Sci Eng C Mater Biol Appl., 2020)

16h00 - 16h30 **Monia Souidi (PhyMedExp), lauréate de l'Axe Médecine Expérimentale & Régénératrice**
Introduction par Albano Meli
Oxygen Is an Ambivalent Factor for the Differentiation of Human Pluripotent Stem Cells in Cardiac 2D Monolayer and 3D Cardiac Spheroids (Int J Mol Sci., 2021)

16h30 - 17h00 **Remise des prix «Young scientist awards» aux lauréats par le Directeur du Pôle**

17h00 Clôture de la journée

Conférences

Pr JACQUES REYNES

CHU de Montpellier et UMI TransVIHMI
INSERM U1175, IRD UMI233, Université de Montpellier

COVID-19 Treatment: Current Therapeutic Drugs and Emerging Options

Jacques Reynes, MD, PhD, is professor of medicine (Infectious diseases) at the University of Montpellier and the Head of the Infectious and Tropical Diseases Department at the University Hospital of Montpellier. He is senior research clinician-scientist at the TRANSVIHMI Unit (INSERM U1175, IRD UMI 1233, University of Montpellier) and coordinator of FHU Infections and Chronicity. As a principal investigator in many international clinical trials of all phases, he has done extensive research in the field of HIV therapy. He has also published over 400 publications on a broad range of infectious diseases, including bacterial, virological and fungal infections. Recently, he conducted COVID-19 clinical trials.

MURIEL AMBLARD

Pôle Chimie et IBMM, CNRS UMR 5247, Université de Montpellier

Peptide-based chemical tools to address biological challenges

Dr Muriel AMBLARD is a CNRS Research Director at the « Institut of Biomolecules Max Mousseron » (IBMM) in Montpellier. After completing her PhD in Organic Chemistry at the University of Montpellier in the Lab of Prof Jean Martinez, she joined the group of Dr Paul Anderson at Merck Sharp & Dohm in USA as a post-doctoral fellow. In 1996, she received a position at the Laboratory of Amino Acid Peptide and Proteins in Montpellier and became a team leader at the IBMM in 2007. Her research interests are mainly at the interface of chemistry, biology and structural analysis for developing bioactive compounds and chemical tools that can mimic biological systems. She developed a number of potent receptor agonists and antagonists of several peptide hormones. Her recent work focuses on the design and synthesis of predictable and stable ribbon and helical molecular architectures that are applied to the identification of cell penetrating compounds and inhibitors of protein/protein interactions. Another part of her research interest is devoted to the development of selective protein degraders, by using Proteolysis-Targeting Chimeras (PROTACs) technology.

Lauréats du prix « Young scientist awards »

AXE INFECTIOLOGIE-IMMUNOLOGIE

Mélanie Burette (IRIM)
Directeur de recherche : Matteo Bonazzi

Modulation of innate immune signaling by a Coxiella burnetii eukaryotic-like effector protein

Melanie Burette, Julie Allombert, Karine Lambou, Ghizlane Maarifi, Sébastien Nisole, Elizabeth Di Russo Case, Fabien P. Blanchet, Cedric Hassen-Khodja, Stéphanie Cabantous, James Samuel, Eric Martinez, and Matteo Bonazzi, PNAS June 16, 2020, DOI: 10.1073/pnas.1914892117

The Q fever agent *Coxiella burnetii* uses a defect in organelle trafficking/intracellular multiplication (Dot/Icm) type 4b secretion system (T4SS) to silence the host innate immune response during infection. By investigating *C. burnetii* effector proteins containing eukaryotic-like domains, here we identify NopA (nucleolar protein A), which displays four regulator of chromosome condensation (RCC) repeats, homologous to those found in the eukaryotic Ras-related nuclear protein (Ran) guanine nucleotide exchange factor (GEF) RCC1. Accordingly, NopA is found associated with the chro-matin nuclear fraction of cells and uses the RCC-like domain to interact with Ran. Interestingly, NopA triggers an accumulation of Ran-GTP, which accumulates at nucleoli of transfected or in-fected cells, thus perturbing the nuclear import of transcription factors of the innate immune signaling pathway. Accordingly, qRT-PCR analysis on a panel of cytokines shows that cells exposed to the *C. burnetii* nopA::Tn or a Dot/Icm-defective dotA::Tn mutant strain present a functional innate immune response, as opposed to cells exposed to wild-type *C. burnetii* or the corresponding nopA complemented strain. Thus, NopA is an important regulator of the innate immune response allowing *Coxiella* to behave as a stealth pathogen.

Présentation pour l'axe CANCER

AXE CANCER

Alexandra Garancher (Chaire MUSE 2021, IRCM)
Introduction par Claude Sardet

Understanding the immune microenvironment to improve immunotherapy for pediatric brain tumors.

Medulloblastoma (MB) is the most common malignant brain tumor in children. Despite multimodal therapy, including surgical resection, craniospinal irradiation and aggressive chemotherapy, approximately 30% of patients remain incurable, due to the acquisition of resistance properties. Survivors suffer from severe long-term side effects from these therapies. The development of more effective and specific therapeutic strategies that can increase the efficacy of current treatment without additional toxicity is of a high priority. The cytotoxic effect of those therapies on tumor cells are well documented in the literature, but little is still known on their effects on immune tumor micro-environment (TME). We aim to decipher the changes induced by standard therapeutic regimen on immune TME, and to identify approaches to enhance anti-tumoral adaptive immunity at MB tumor site. The identification of biomarkers, a better characterization of the interactions of the tumor cells and its immune TME, associated to an increase of cytotoxic T-cells will lead to development of more effective therapies.

AXE NEUROSCIENCES

AMOS FUMAGALLI (IGF)
Directeur de recherche : Philippe Marin

The atypical chemokine receptor 3 interacts with Connexin 43 inhibiting astrocytic gap junctional intercellular communication

Amos Fumagalli, Joyce Heuninck, Anne Pizzoccaro, Enora Moutin, Joyce Koenen, Martial Séveno, Thierry Durroux, Marie-Pierre Junier, Géraldine Schlecht-Louf, Francoise Bachelerie, Dagmar Schütz, Ralf Stumm, Martine J. Smit, Nathalie C. Guérineau, Séverine Chaumont-Dubel & Philippe Marin, Nat Commun., 2020, DOI: 10.1038/s41467-020-18634-y

The atypical chemokine receptor 3 (ACKR3) plays a pivotal role in directing the migration of various cellular populations and its over-expression in tumors promotes cell proliferation and invasiveness. The intracellular signaling pathways transducing ACKR3-dependent effects remain poorly characterized, an issue we addressed by identifying the interactome of ACKR3. Here, we report that recombinant ACKR3 expressed in HEK293T cells recruits the gap junction protein Connexin 43 (Cx43). Cx43 and ACKR3 are co-expressed in mouse brain astrocytes and human glioblastoma cells and form a complex in embryonic mouse brain. Functional in vitro studies show enhanced ACKR3 interaction with Cx43 upon ACKR3 agonist stimulation. Furthermore, ACKR3 activation promotes β-arrestin2- and dynamin-dependent Cx43 internalization to inhibit gap junctional intercellular communication in primary astro-cytes. These results demonstrate a functional link between ACKR3 and gap junctions that might be of pathophysiological relevance.

AXE BIOLOGIE QUANTITATIVE

LÉO GUIGNARD (CRBM)
Directeur de recherche : Patrick Lemaire

Contact area–dependent cell communication and the morphological invariance of ascidian embryogenesis

Léo Guignard, Ulla-Maj Fiúza, Bruno Leggio, Julien Laussu, Emmanuel Faure, Gaël Michelin, Kilian Biasuz, Lars Hufnagel, Grégoire Malandain, Christophe Godin, Patrick Lemaire, Science, 2020, DOI: 10.1126/science.aar5663

Marine invertebrate ascidians display embryonic reproducibility: Their early embryonic cell lineages are considered invariant and are conserved between distantly related species, despite rapid genomic divergence. Here, we address the drivers of this reproducibility. We used light-sheet imaging and automated cell segmentation and tracking procedures to systematically quantify the behavior of individual cells every 2 minutes during *Phallusia mammillata* embryogenesis. Interindividual reproducibility was observed down to the area of individual cell contacts. We found tight links between the reproducibility of embryonic geometries and asymmetric cell divisions, controlled by differential sister cell inductions. We combined modeling and experimental manipulations to show that the area of contact between signaling and responding cells is a key determinant of cell communication. Our work establishes the geometric control of embryonic inductions as an alternative to classical morphogen gradients and suggests that the range of cell signaling sets the scale at which embryonic reproducibility is observed.

AXE GÉNÉTIQUE-ÉPIGÉNÉTIQUE

SATISH SATI (IGH)
Directeur de recherche : Giacomo Cavalli

4D Genome Rewiring during Oncogene-Induced and Replicative Senescence

Satish Sati, Boyan Bonev, Quentin Szabo, Daniel Jost, Paul Bensadoun, Francois Serra, Vincent Loubiere, Giorgio Lucio Papadopoulos, Juan-Carlos Rivera-Mulia, Lauriane Fritsch, Pauline Bouret, David Castillo, Josep Ll. Gelpi, Modesto Orozco, Cedric Vaillant, Franck Pellestor, Frederic Bantignies, Marc A. Marti-Renom, David M. Gilbert, Jean-Marc Lemaitre, Giacomo Cavalli, Mol Cell., 2020, DOI: 10.1016/j.molcel.2020.03.007

To understand the role of the extensive senescence-associated 3D genome reorganization, we generated genome-wide chromatin interaction maps, epigenome, replication-timing, whole-genome bisulfite sequencing and gene expression profiles from cells entering replicative senescence (RS) or upon oncogene-induced senescence (OIS). We identify senescence-associated heterochromatin domains (SAHDs). Differential intra- versus inter-SAHD interactions lead to the formation of senescence-associated heterochromatin foci (SAHFs) in OIS but not in RS. This OIS-specific configuration brings active genes located in genomic regions adjacent to SAHDs in close spatial proximity and favors their expression. We also identify DNMT1 as a factor that induces SAHFs by promoting HMGA2 expression. Upon DNMT1 depletion, OIS cells transition to a 3D genome conformation akin to that of cells in replicative senescence. These data show howmulti-omics and imaging can identify critical features of RS and OIS and discover determinants of acute senescence and SAHF formation.

AXE TECHNOLOGIES POUR LA SANTÉ -BIOINGÉNIERIE

HABIB BELAID (IRCM/ IEM)
Directeur de recherche : Vincent Cavaillès

Development of new biocompatible 3D printed graphene oxide-based scaffolds

Habib Belaid, Sakthivel Nagarajan, Catherine Teyssier, Carole Barou, Jonathan Barés, Sebastien Balme, Hélène Garay, Vincent Huon, David Cornu, Vincent Cavaillès, Mikhael Bechelany, Mater Sci Eng C Mater Biol Appl., 2020, DOI: 10.1016/j.msec.2019.110595

The aim of this work was to develop a bioresorbable, biodegradable and biocompatible synthetic polymer with good mechanical properties for bone tissue engineering applications. Polylactic acid (PLA) scaffolds were gen-erated by 3D printing using the fused deposition modelling method, and reinforced by incorporation of graphene oxide (GO). Morphological analysis by scanning electron microscopy indicated that the scaffold average pore size was between 400 and 500 µm. Topography imaging revealed a rougher surface upon GO incorporation (Sa = 5.8 µm for PLA scaffolds, and of 9.9 µm for PLA scaffolds with 0.2% GO), and contact angle measurements showed a transition from a hydrophobic surface (pure PLA scaffolds) to a hydrophilic surface after GO in-corporation. PLA thermomechanical properties were enhanced by GO incorporation, as shown by the 70 °C increase of the degradation peak (thermal gravimetric analysis). However, GO incorporation did not change significantly the melting point assessed by differential scanning calorimetry. Physicochemical analyses by X-ray diffraction and Raman spectroscopy confirmed the filler presence. Tensile testing demonstrated that the me-chanical properties were improved upon GO incorporation (30% increase of the Young's modulus with 0.3%GO). Cell viability, attachment, proliferation and differentiation assays using MG-63 osteosarcoma cells showed that PLA/GO scaffolds were biocompatible and that they promoted cell proliferation and mineralization more efficiently than pure PLA scaffolds. In conclusion, this new 3D printed nanocomposite is a promising scaffold with adequate mechanical properties and cytocompatibility which may allow bone formation.

AXE MÉDECINE EXPÉRIMENTALE & RÉGÉNÉRATRICE

MONIA SOUIDI (PhyMedExp)
Directeur de recherche : Albano Meli

Oxygen Is an Ambivalent Factor for the Differentiation of Human Pluripotent Stem Cells in Cardiac 2D Monolayer and 3D Cardiac Spheroids

Monia Souidi, Yvonne Sleiman, Ivana Acimovic, Jan Pribyl, Azzouz Charrabi, Volker Baecker, Valerie Scheuermann, Martin Pesl, Sarka Jelinkova, Petr Skladal, Petr Dvorak, Alain Lacampagne, Vladimir Rotrekl and Albano C. Meli, Int J Mol Sci., DOI: 10.3390/ijms22020662

Numerous protocols of cardiac differentiation have been established by essentially focusing on specific growth factors on human pluripotent stem cell (hPSC) differentiation efficiency. However, the optimal environmental factors to obtain cardiac myocytes in network are still unclear. The mesoderm germ layer differentiation is known to be enhanced by low oxygen exposure. Here, we hypothesized that low oxygen exposure enhances the molecular and functional maturity of the cardiomyocytes. We aimed at comparing the molecular and functional consequences of low (5%O2 or LOE) and high oxygen exposure (21% O2 or HOE) on cardiac differentiation of hPSCs in 2D-and 3D-based protocols. hPSC-CMs were differentiated through both the 2D (monolayer) and 3D (embryoid body) protocols using several lines. Cardiac marker expression and cell morphology were assessed. The mitochondrial localization and metabolic properties were evaluated. The intracellular Ca2+ handling and contractile properties were also monitored. The 2D cardiac monolayer can only be differentiated in HOE. The 3D cardiac spheroids containing hPSC-CMs in LOE further exhibited cardiac markers, hypertrophy, steadier SR Ca2+ release properties revealing a better SR Ca2+ handling, and enhanced contractile force. Preserved distribution of mitochondria and similar oxygen consumption by the mitochondrial respiratory chain complexes were also observed. Our results brought evidences that LOE is moderately beneficial for the 3D cardiac spheroids with hPSC-CMs exhibiting further maturity. In contrast, the 2D cardiac monolayers strictly require HOE.

Chercheurs CNRS et Inserm recrutés en 2020 & 2021

CNRS

JULIEN VILLENEUVE

Institut de Génomique Fonctionnelle (IGF), CNRS

Uncovering mechanisms of unconventional protein secretion – Relevance to neurodegeneration

In eukaryotic cells, cytosolic proteins can be exported out of cells even though they lack a signal sequence to enter the endoplasmic reticulum. This fundamental process that remains poorly understood is called Unconventional Protein Secretion (UPS). During aging, UPS of misfolded proteins promotes their transmission from neuron to neuron, and thus is critical in neurodegenerative diseases (NDs) progression. Within the proposed project, we will study the secretion of misfolded proteins with the objectives to uncover new UPS mechanisms and to pave the way for new strategies for therapeutic approaches of NDs. To this end, we will use a multidisciplinary approach by combining biochemical, high-throughput and *in vivo* approaches, as well as state-of-the-art imaging and genomic technologies. At the crossroad of critical challenges, the project will can make important advances into basic mechanisms that will then be exploited for biomedical applications.

AUDREY BERNUT

Laboratory of Pathogen Host Interactions (LPHI), CNRS

Infectious and inflammatory pathologies in cystic fibrosis: deciphering the role of CFTR in host innate immune response

Cystic fibrosis (CF) is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Chronic pulmonary infections accompanied by persistent inflammation result in severe progressive lung injury and are the leading causes of morbidity and mortality of CF patients. In addition to known mucociliary defects, CFTR dysfunction directly alters host innate immunity potential to both pathogens and tissue injury, leading to excessive inflammation, defective bacterial clearance, and impaired tissue repair. However, it is not known how CFTR determines innate immune functions, nor how CFTR dysfunction contributes to immunopathogenesis in CF.

In my research project, I will use CFTR-depleted zebrafish larvae as an innovative vertebrate model of inflammation and infection, combining human CF stem cell approaches, to recapitulate aspects of CF immunopathogenesis. Combined with dynamic imaging, I will i) elucidate the role of CFTR in direct regulation of inflammatory response and immunity to infection and thereby understand how alterations of CFTR are involved in CF immunopathogenesis and ii) identify new therapeutic molecules active in a CFTR-deficient context to restore innate immunity and thus identify novel therapeutic approaches for infectious and inflammatory lung damage in CF.

XIAOJING CONG

Institut de Génomique Fonctionnelle (IGF), CNRS

Transmembrane ceramidases as new drug targets

Transmembrane ceramidases are enzymes that hydrolyze ceramides and control lipid metabolism in our body. They are involved in many forms of cancer, metabolic, cardiovascular and neurodegenerative diseases. My research aims to determine whether transmembrane ceramidases could be valid drug targets for these diseases. Preclinical drug target validation is the biggest challenge in the pharmaceutical industry R&D. A poorly selected target–often due to poor probes used in target validation assays–is the main source of failure in drug development. My research incorporates molecular modeling, structural biology and functional assays to develop chemical probes that are specific and selective for transmembrane ceramidases. These probes will enable drug target validation of transmembrane ceramidases for various diseases.

ISABEL CHILLON

Institut de Génétique Moléculaire de Montpellier (IGMM), CNRS

The organization of the stress response by lncRNAs in phase-separated nuclear bodies

Cellular homeostasis is crucially regulated by long non-coding RNAs (lncRNAs). To ensure spatial compartmentalization of the stress response, some lncRNAs associate to nuclear bodies, which are membraneless ribonucleoprotein condensates that undergo liquid-liquid phase separation. Key stress-related lncRNAs include Meg3 and lincRNA-p21, which organize in speckle-like and paraspeckle nuclear bodies, respectively. However, it remains unclear how lncRNAs coordinate the different pathways of the stress response from within nuclear bodies to restore homeostasis. My goal is to elucidate the relationship between the organization of lncRNAs into phase-separated nuclear bodies and their roles in the early stress response. Using primary mouse cells as a model system, I will determine: 1) How lncRNAs organize into phase-separated nuclear bodies to respond to stress; 2) How stress affects the proteome of lncRNAs; and 3) How RNA modifications influence the proteome of lncRNAs under stress conditions. The results obtained will provide direct evidence of the specific pathways regulated by stress-related lncRNAs in nuclear bodies during the early stress response and open the door to treating diseases caused by stress maladaptation.

ANTOINE BESNARD
Institut de Génomique Fonctionnelle (IGF), INSERM

Neural mechanisms for the processing of persistent place avoidance

Persistent avoidance behavior contributes to the maintenance of anxiety and fear disorders. In strike contrast with Pavlovian defensive reactions (e.g. freezing), the neural correlates of active avoidance behavior remain poorly understood. Recent work suggests that the hippocampus constrains persistent active place avoidance. The hippocampal information flow is likely relayed to the lateral septum, which directly innervates subcortical brain regions involved in motor programs in order to prevent active avoidance of places that are no longer threatening. We will use an all-optical preparation in a rodent active place avoidance paradigm to (i) characterize a hippocamposeptal circuit controlling persistent place avoidance; (ii) decode septal neural dynamics underlying persistent place avoidance; (iii) devise a close loop system to prevent persistent place avoidance in real time. These results could establish hippocamposeptal activity as a biomarker for persistent avoidance behavior, hallmark of post-traumatic stress disorder.

JAKUB GRUSZCZYK
Centre de Biochimie Structurale (CBS), INSERM

Structure and function of the aryl hydrocarbon receptor

Each day our body comes into close contact with myriads of various chemical substances also known as xenobiotics. Understanding processes governing recognition, metabolism and removal of foreign substances is critical to fully comprehend their influence on our body. Aryl hydrocarbon receptor (AHR) is one of the crucial chemosensory proteins involved in the metabolism of many chemical pollutants. AHR binds a selection of xenobiotics and regulates expression of numerous genes involved in their detoxification. So far, we are lacking the in-depth analysis of this essential signalling pathway. Our project aims to structurally and biochemically characterise the AHR-dependent signalling pathway. We hope that we will be able to provide a detailed molecular mechanism underlying the processes of detection and detoxification of chemical pollutants and, as a result, to shed more light on this essential aspect of human physiology.

JULIEN FAGET
Institut de Recherche en Cancérologie de Montpellier (IRCM), INSERM

Understanding neutrophil homeostasis to treat lung cancer patients

Immune checkpoint inhibitors (ICIs) represent the latest revolution in the care of patients with cancer, providing long-term survival benefit in a subset (25 to 30%) of patients with lung cancer. This implies that a better identification of predictive markers and the characterization of innate and adaptive resistance mechanisms became an important challenge to further improve the clinical advantage of ICIs. Our recent work together with findings from others highlighted the critical involvement of tumor-associated neutrophils in resistance to ICIs in lung cancer. Today an increasing number of publications points to a remote programing of neutropoiesis associated with cancer development, governing the emergence of tumor promoting neutrophils.

Because identifying predictive markers of the response became critical in pathologies that receive first line ICI, we have initiated a study on a cohort of NSCLC patients (ALCINA2-03) aiming at performing a qualitative and quantitative characterisation of circulating immune cells and granulopoiesis alteration from peripheral blood samples at diagnostic. This important dataset, together with our investigations performed in mouse models of lung cancer, will be developed to 1) identify new predictive markers of the response to ICI, 2) better characterize the origin of tumor promoting neutrophils and 3) define new strategies to overcome ICI resistance mediated by tumor-promoting neutrophils.

JOHANNA CALDERON
PhyMedExp, INSERM

Neurodevelopment and Mental Health in Congenital Heart Disease

Congenital Heart Disease (CHD) is the most frequent congenital anomaly, representing 1% of live births. Advances in surgical care have significantly improved the survival rates of these patients. Patients who undergo open-heart surgery in infancy for CHD are exposed to several neurological risk factors including brain hypoxic-ischemic injury. From Harvard to INSERM, my work is focused on understanding the consequences of CHD on children and adults' neurodevelopmental and mental health outcomes. My project at INSERM is dedicated to 1) characterize the phenotypes in rare forms of heart disease including inherited cardiac arrhythmias; 2) identify the risk factors associated with neurological dysfunction and 3) develop innovative prevention and intervention strategies in public health to reduce the neurodevelopmental burden in this population.

IN PARTNERSHIP WITH