SBM DEPARTMENT DAY

December 3rd 2026
Domaine du Haut-Carré
Talence



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Département de recherche
SBM | Sciences biologiques et médicales
université de BORDEAUX

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As in previous years, the annual Biological and Medical Sciences Day offers you the opportunity to create and strengthen collaborative projects and interactions between the various research laboratories, notably through selected oral presentations representative of the many lines of research developed in our department.

Two guest speakers, Christiaan van Ooij (Keele University) and François Trottein (Institut Pasteur de Lille) will present his work during the day.

The best poster, flash poster, and oral communication will be awarded prizes by the members of the jury at the end of the day.

The organisers would like to thank the members of the jury for their help in evaluating the PhD posters.

We wish you all a wonderful Biological Sciences Department Day.

Alexandra Prevot, Aline Fréville, Candice Chapouly, Chloé Rousson, Clément Dugravier, Hala Al-Adhami, Hande Sena Kandemir, Katia Boniface, Mélina Abdou, Paôline Laurent, Thierry Noël, Vanessa Desplat

WIFI

Voici une procédure à suivre :
- Se connecter au réseau wifi «UBx-invites»
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- If you encounter a connection problem, right-click on the «UBx-invites» wifi network and select «Forget», then try to reconnect.

Login :
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Programme

Morning session

8h30-9h00 **Welcome & Registration**

9h00-9h10 **Introduction**

Le comité d'organisation

9h10-9h20 **Platform presentation**

Chair: Candice Chapouly

Béatrice Turcq | *TBMCore*

9h20-9h25 **Bureau OSE (Offre Service Europe)**

Alice Recalde

9h25-10h10 **Keynote speaker**

Chairs: Aline Fréville & François Moisan

Christiaan van Ooij | *Keele University*
«All in the family: how expansion of gene families generates new functions in malaria parasites»

10h10-10h40 **First poster session & Coffee break**

10h40-12h00 **First scientific session**

Chairs: Manuel Rojo & Hala Al Adhami

Camille Evain | *IBGC, U5095*
«New transgenic mouse models to decipher pathogenic mechanisms of MFN2-related neuropathy»

Lara Josserand | *BMC, U1034*
«Role of endothelial cells in the physiopathology of portal vein thrombosis»

Camille Humeau | *BRIC, U1312*
«Mitochondrial-associated CB1: a missing piece in glioblastoma therapy?»

Gaïd Le Corre | *BRIC, U1312*
«A PDX model for evolution of adenomyoepithelioma to squamous carcinoma»

Kathyanna Arnould | *MFP, U5234*
«Dissecting conserved lipid droplet biology in Trypanosoma brucei reveals an important role for Seipin»

12h00-12h30 **Poster Flash Talks**
Chairs: Ahmad Sharanek & Candice Chapouly

Chloé Rousson | *ImmunoConcEpt, U5164*
«Study of the phenotype and functions of skin regulatory T cells in pigmentation disorders»

Clara Jollet | *BRIC, U1312*
«Mutated bêta-catenin alters the immune response and chemokine network in hepatocellular carcinoma and uncovers CXCL16 as a novel ex»

Elora Bonzon-Dubos | *BRIC, U1312*
«From oncogenic dependency to new therapeutical strategy: gene editing of CTNNB1 point mutations in hepatoblastoma»

Lesa Faith Ndayisaba | *BRIC, U1312*
«Telocyte-derived Netrin-1 targets endothelial UNC5B to drive vascular pruning during infantile hemangioma involution»

Emilien Réaud | *MRGM, U1211*
«Characterization of the mode of action of neurotoxic substances responsible for neurodevelopmental disorders using zebrafish»

Artur Jolimay-Groener | BRIC, U1312
«Thérapie génique de la protoporphyrie érythropoïétique (PPE) par édition de base»

12h30-14h00 **Lunch break & Second poster session**

Programme

Afternoon session

14h00-14h45 Keynote speaker

Chairs: Paoline Laurent & Victor Appay

François Trottein | *Institut Pasteur de Lille*
«Aging and respiratory infections: cellular senescence, gut dysbiosis, and beyond»

14h45-15h25 Second scientific session

Chairs: Vanja Sisirak & Philippe Pasdois

Sarah Huot-Marchand | *ImmunoConcEpt, U5164*
«Des cellules qui explosent pour sonner l'alarme immunitaire, parfois à tort»

Gauthier Follain | *BRIC, U1312*
«Deciphering the physical and cellular mechanisms driving cancer cell dissemination»

15h25-16h00 Coffee break

16h00-16h15 Diversité, Egalité et Parité au travail

16h15-16h55 Third scientific session

Chairs: Antonio Pagano-Zottola & Tony Sourisseau

Mathilde Pohin | *ImmunoConcEpt, U5164*
«Neutrophils contribution to severe hallmarks of IBD»

Aline Freville | *MFP, U5234*
«Identification of PV6, a non-exported Plasmepsin V substrate required for post-invasion metamorphosis in malaria parasites»

16h55 Award ceremony & closing remarks

Keynote speakers

Christiaan van Ooij | Keele University

«All in the family: how expansion of gene families generates new functions in malaria parasites»

Malaria parasites contain many different small and large gene families. Some of these gene families are present in all parasite species, others only in a few species and absent in the rest. In some cases, the family is represented by only one member in one species while other species contain many genes. In nearly all cases, the function of these families remains unknown, as does the relationship between the genes. To understand how these families function and how the function of individual members of the family changes or remains redundant as the family expands, we focused on the pir gene family. This family is present in most, but not all, Plasmodium species; 66 pir genes are present in Plasmodium knowlesi, a simian malaria parasite that can be cultured in human cells, but pir genes are absent in Plasmodium falciparum, the deadliest of the human malaria parasites. The pir family ranges in size from four family members in some species to nearly 2000 in others. Nonetheless, even in parasites with many family members, one stands out. A large, multispecies phylogenetic study revealed that the pir genes can be divided into many subfamilies, many of which are species-specific. However, the clade containing the highly conserved gene (the pirC1 clade), contains a single gene from each Plasmodium species. We focused on this pirC1 gene, with the aim to identify the function of this individual gene and potentially the entire family. This revealed that this protein is essential for exponential growth, despite the presence of many family members in the parasite, and may have an important function in nutrient uptake. This shows that large gene families may retain essential functions and serves as a template for the investigation of other gene families.

Biography:

Christiaan grew up in The Netherlands but moved to the US as a teenager, where he went to college and got his PhD at the University of California, San Francisco. His first post-doc was at Harvard University, investigating protein localization in Bacillus subtilis. It was during his second post-doc, in Kasturi Haldar's lab, that he first started studying malaria parasite, focusing on the export of parasite proteins into the host cell. He then moved to London, where he worked as editor for Nature Reviews Microbiology for 3.5 years. A Wellcome Trust Career Re-Entry Fellowship gave him the opportunity to go back to the lab, at the National Institute for Medical Research, in North London, and continue his investigations of malaria parasites. After six years at the NIMNR, he set up his own lab at the London School of Hygiene & Tropical Medicine and then in 2024 moved his lab to Keele University.

François Trottein | Institut Pasteur de Lille

«Aging and respiratory infections: cellular senescence, gut dysbiosis, and beyond»

The global population is aging rapidly, with the proportion of individuals aged 65 years and older increasing substantially worldwide. This demographic shift poses major challenges for healthcare systems and public health, as aging is associated with increased susceptibility to a broad spectrum of diseases, including cardiovascular, metabolic, neurodegenerative, and infectious disorders. Respiratory infections are of particular concern, given their high burden and severity in older individuals. Using relevant preclinical models of aging, we are exploring the contribution of two major age-associated processes, i.e., cellular senescence and gut dysbiosis, to the pathogenesis and outcomes of respiratory viral and bacterial infections. Our recent findings indicate that both processes can contribute to disease severity and/or long-term outcomes following infection. Importantly, targeting age-associated cellular senescence and/or gut dysbiosis through senolytic interventions or microbiota-derived metabolites can mitigate disease outcomes in these experimental models. How these findings may translate to human disease will also be discussed.

This work was supported in part by the ANR (AAP générique 2022), ANR-23-CE15-0014-01, GUTSY

Biography:

Dr. François Trottein's research focuses on host-pathogen interactions, innate immunity, and respiratory infections. His work explores the mechanisms by which parasites, bacteria, and viruses evade immune responses, with the aim of developing novel therapeutic approaches targeting the innate immune system. He has made major contributions to the understanding of innate immunity and the role of lipids, including eicosanoids and antigenic lipids, in immune responses. His group investigates respiratory infections, with particular emphasis on influenza, SARS-CoV-2, and Streptococcus pneumoniae, as well as the influence of the gut microbiota on immune defense. More recently, his team has expanded its research to age-related changes in immune defense mechanisms and their impact on respiratory infections.

First scientific session

Camille Evain | IBGC, U5095

«New transgenic mouse models to decipher pathogenic mechanisms of MFN2-related neuropathy»

Mitochondria form a highly dynamic network whose morphology are regulated by a constant balance between fusion and fission events. In mammals, fusion of the outer mitochondrial membrane (OMM) plays a central role in maintaining mitochondrial network architecture, promoting subcellular trafficking, and ensuring proper mixing of mitochondrial content. This process is mediating by two paralogous proteins, mitofusin 1 and mitofusin 2 (MFN1 / MFN2). Mitochondrial OMM fusion is essential for embryonic development, highlighting the critical importance of mitofusin-dependent processes for cellular homeostasis. Despite their strong structural and functional similarities and ubiquitous expression, mutations in mfn2, but not mfn1, cause Charcot–Marie–Tooth disease type 2A (CMT2A), a dominant inherited neuropathy that affects long axons of the peripheral nervous system. Notably, no disease-causing mutations have been described in mfn1. Consistently, conditional mouse models have shown that neuronal loss of MFN2 is lethal, whereas loss of MFN1 is well tolerated, highlighting a striking functional divergence between these two closely related proteins.

Recent studies further suggest that impaired OMM fusion can lead to defects in coenzyme Q metabolism and mitochondrial DNA maintenance, ultimately compromising oxidative phosphorylation and cellular energy homeostasis. However, the pathogenic mechanisms underlying the vulnerability of neurons to MFN2 dysfunction remain poorly understood., in particular how impaired OMM fusion impacts neuronal mitochondrial dynamics and bioenergetics. To address these questions, we are generating neuron-specific MFN1 or MFN2 knockout mice with mitoTAG (mitochondria-targeted GFP), a novel model established in adult animals, allowing us to study mitochondrial dynamics and metabolism specifically in neurons.

Lara Josserand | BMC, U1034

«Role of endothelial cells in the physiopathology of portal vein thrombosis»

Portal vein thrombosis (PVT) belongs to splanchnic vein thromboses, which occur in the circulation draining the digestive tract. This atypical form of thrombosis is a serious condition: severe acute forms can be life-threatening, and the long-term risk of recurrence is substantial. In this context, the endothelium, which lines the inner surface of vessels, is of particular interest. It is a heterogeneous entity, both between organs and within a single organ. Under physiological conditions, it forms an anticoagulant surface, but it can become prothrombotic. As portal blood has a distinctive composition, rich in nutrients and gut-derived pathogens, we believe it may influence portal endothelial cells (ECs) and locally shift them toward a prothrombotic phenotype, thereby contributing to an environment favoring PVT development.

We hypothesize that portal ECs differ from those of other venous territories and are shaped by their environment, which renders them prothrombotic and contributes to PVT genesis. We therefore aimed to compare portal ECs with ECs from a territory not exposed to portal blood, namely the inferior vena cava (IVC). To investigate in an unsupervised manner the changes occurring in portal ECs, and to generate the first transcriptomic atlas of this specific anatomical location, we used single-cell RNA sequencing (scRNA-seq).

We developed a surgical and enzymatic digestion protocol yielding samples of large-caliber veins from C57BL6/J mice compatible with scRNA-seq analysis. Portal and IVC ECs displayed transcriptomic differences, with 178 differentially expressed genes (DEGs) upregulated in portal ECs.
In conclusion, we provide the first characterization of portal vein and IVC from BL6 mice under physiological conditions using scRNA-seq. We also highlight transcriptional differences between portal and IVC ECs.

Camille Humeau | BRIC, U1312

«Mitochondrial-associated CB1: a missing piece in glioblastoma therapy?»

Glioblastoma (GB), an aggressive and incurable brain tumor, exhibits marked metabolic plasticity, allowing tumor cells to switch between glycolysis and oxidative phosphorylation to meet energy demands. The coexistence of multiple active metabolic pathways within the same tumor highlights the need for strategies that can simultaneously disrupt both energy production pathways. The cannabinoid receptor type 1 (CB1), a major G protein-coupled receptor in the central nervous system, is not only found on the plasma membrane (pmCB1), but is also functionally associated with mitochondrial membranes (mtCB1), where it regulates oxidative phosphorylation and glycolysis. Although cannabinoids, CB1 receptor agonists, have shown antitumor effects in GB cells, studies have mainly focused on pmCB1, overlooking the potential role of mtCB1 in tumor metabolism. Therefore, mtCB1 may be a promising candidate for impairing the bioenergetic flexibility in GB.

Preliminary findings indicate that cannabinoids reduce mitochondrial respiration and invasive potential in wild-type murine GB cells, but not in KO counterparts, suggesting a CB1 specific mechanism. High-resolution respirometry on isolated mitochondria further reveals a selective inhibition of complex I activity following treatment with cannabinoids.

These findings support a functional role for mtCB1 in controlling the energy metabolism underlying GB progression.

Gaïd Le Corre | BRIC, U1312

«A PDX model for evolution of adenomyoepithelioma to squamous carcinoma»

Adenomyoepithelioma is a rare subtype of human breast cancer in which basal (myoepithlial) and luminal (adenoid) cell types coexist. The simplest explanation is that a tumour stem cell differentiates to form the two cell types. We have established a human malignant adenomyoepthilioma as a patient-derived xenograft (PDX). This PDX shows a wide variety of phenotypes, including adenomyoepithelial cells, FOXA1-positive hormone sensing cells, and FOXC1-positive LASP/basal-like cells. At early passages, these mammary phenotypes dominate the histology, but starting at xenograft passage 3, squamous cells appear, and at passage 4 large regions within the tumour convert to squamous carcinoma accompanied by abundant desmoplastic stroma. Malignant myoepitheliomas frequently contain metaplastic cells and progress to squamous carcinoma in patients, so the evolution of our PDX in mice recapitulates the progression seen in patients. This highly plastic model offers us the opportunity to test the role of specific transcription factors and signalling pathways in the control of cell identity in the mammary lineage, and to use them to control differentiation of the cells.

Kathyanna Arnould | MFP, U5234

«Dissecting conserved lipid droplet biology in Trypanosoma brucei reveals an important role for Seipin»

Lipid droplets (LDs) are conserved organelles that regulate lipid storage and metabolic homeostasis in all eukaryotes. Although their biogenesis has been extensively studied in yeast and mammals, it remains poorly understood in protozoan parasites, whose highly divergent biology provides unique opportunities to uncover both conserved and parasite-specific mechanisms.

Here, we identified and characterized TbSeipin, the Trypanosoma brucei orthologue of the ER protein Seipin, the master regulator of LD biogenesis. Structural modelling and functional complementation in Saccharomyces cerevisiae demonstrated strong evolutionary conservation. Using an integrated approach combining CRISPR/Cas9 genome editing, quantitative microscopy and lipidomics, we investigated the role of TbSeipin in parasite physiology.

TbSeipin localized to ER subdomains at ER–LD contact sites and proved essential for proper LD biogenesis. Its depletion caused major alterations in LD morphology and abundance and was lethal in bloodstream-form parasites. Lipidomic analyses revealed extensive remodeling of neutral lipids and membrane phospholipids, indicating that TbSeipin coordinates lipid storage with membrane lipid homeostasis rather than simply controlling LD formation.

Unexpectedly, TbSeipin deficiency also impaired parasite proliferation, leading to defects in kinetoplast segregation, cytokinesis and the accumulation of multinucleated cells. These findings reveal a direct connection between lipid homeostasis and cell division in T. brucei.

Together, our work identifies TbSeipin as a conserved regulator of LD biogenesis while uncovering an unexpected essential role in coordinating lipid metabolism and cytokinesis. Beyond advancing our understanding of parasite biology, this study establishes T. brucei as a powerful model to investigate fundamental mechanisms of lipid droplet biology and illustrates how evolutionarily divergent protozoa can reveal new functions of conserved eukaryotic organelles highlighting protozoan parasites as powerful experimental systems to uncover fundamental principles of eukaryotic cell organization that remain hidden in classical model systems.

Poster Flash Talks

P1 - Study of the phenotype and functions of skin regulatory T cells in pigmentation disorders

Chloé Rousson | ImmunoConcEpt, U5164

Vitiligo is the most common depigmenting skin disorder affecting 0.36% of the global population. This chronic inflammatory disease is characterized by the appearance of white patches on the skin, due to the loss of melanocytes, the cells responsible for skin pigmentation. Genetic predisposition combined with environmental factors lead to the skin accumulation of autoreactive CD8+ memory T-cells leading to melanocyte disappearance. Our previous work showed that clinically unaffected pigmented skin from patients with vitiligo already contains a subset of autoreactive CD8+ T-cells capable of producing pro-inflammatory cytokines. In addition, we found that regulatory T-cells (Tregs) could play a key role in limiting immune activation.

The objective of my PhD is to characterize the phenotype of Tregs, investigate how they suppress the harmful activity of CD8+ T-cells in pigmented skin and to identify the mechanims underlying Treg dysfunction at sites of depigmentation.

Using scRNAseq data generated from skin samples collected from lesional (PL) and non-lesional (NL) skin of six patients with vitiligo, five Tregs clusters were identified. Further analyses will assess their transcriptomic profiles. CellChat analysis will be used to evaluate the interactions between Treg clusters and other immune and non-immune cell populations. The ultimate objective is to identify the potential role of Tregs in regulating CD8+ T-cell activity in vitiligo.

These analyses will be used to identify, at the transcriptomic level, Treg markers associated with lesion skin and their expression will be validated at the protein level using spectral flow cytometry.

Next, to assess the phenotype and functional activity of Tregs in the context of vitiligo-associated inflammation, experimental procedures are currently being established to isolate healthy Tregs and culture them in the presence of pro-inflammatory cytokines characteristic of vitiligo. Functional assays using activated CD8+ T-cells labelled with CellTrace Violet will be performed in co-culture with Tregs to assess their suppressive capacity and functional activity. Altogether, this project will provide an in-depth characterization of the phenotype and function of Tregs in vitiligo skin.

P2 - Mutated bêta-catenin alters the immune response and chemokine network in hepatocellular carcinoma and uncovers CXCL16 as a novel ex

Clara Jollet | BRIC, U1312

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and the third leading cause of cancer-related death worldwide. Despite the clinical benefits of immunotherapy for some patients, nearly two-thirds of mutated Bêta-catenin HCC do not respond to it. This resistance is notably associated with low infiltration of immune cells into the tumor, but the mechanisms responsible for this immune exclusion remain largely misunderstood. This study explores the role of oncogenic Bêta-catenin in reshaping the tumor immune microenvironment by investigating its impact on the biogenesis and chemokine content of small extracellular vesicles (EVs).

Transcriptomic and proteomic analyses performed in liver cancer cell lines revealed that Bêta catenin activation suppresses the expression of the transmembrane chemokine CXCL16 and RAB27A, a major regulator of exosome biogenesis. Consistent with these results, nanoparticle tracking and live-cell imaging analyses revealed a decrease in exosome secretion induced by mutated Bêta-catenin in liver cancer cell lines. Interestingly, characterization of small tumor derived EVs isolated by size exclusion chromatography revealed the presence of the chemokine CXCL16 on their surface using both ELISA test and HEKAT NanoSorter®. To investigate the functional role of mutated ß-catenin in immune infiltration, 3D models of spheroids were established and showed that the oncogenic ß-catenin regulates immune cell infiltration through exosome secretion. Notably, the infiltration of natural killer (NK) cells, which are recruited and activated by CXCL16, was significantly reduced. Furthermore, in patients' tumors, the expression of Rab27A and CXCL16 was positively correlated with that of NK cells markers in HCC with a Bêta-catenin mutation. These results identify a novel oncogenic Bêta-catenin-EV-CXCL16 NK axis involved in the remodeling of the tumor microenvironment. This pathway represents a potential therapeutic target for restoring antitumor immunity and overcoming resistance to immunotherapy in mutated Bêta-catenin HCCs.

P3 - From oncogenic dependency to new therapeutical strategy: gene editing of CTNNB1 point mutations in hepatoblastoma

Elora Bonzon-Dubos | BRIC, U1312

Hepatoblastoma (HB) is a rare but aggressive pediatric liver cancer. In most HBs, point mutations and deletions are found in the CTNNB1 gene that codes for the Bêta-catenin protein. These mutations lead to an aberrant but functional Bêta-catenin and a constitutive activation of the WNT/Bêta-catenin pathway that controls multiple tumoral processes.

As CTNNB1 gene point mutations are key drivers in HB progression, we hypothesized that the correction of these mutations by gene editing could lead to a reversion of the tumoral cell phenotype.

To perform point mutation correction, we use a CRISPR-based approache: the base editor system. With this strategy, we found a decrease of HB cells proliferation once the mutated base was corrected. Associated with this, we showed a decrease of the Bêta-catenin levels in the nuclei correlated with a lower expression of target genes of this protein. A transcriptomic analysis was performed and showed several differential expression genes and dysregulated pathways mainly involved in the cytoskeleton remodelling after correction. For now, we need to investigate further the underlying mechanisms involved in this phenotypical change and to evaluate its applicability in vivo.

In parallel, we are developing an original nanocarrier to deliver properly the gene editing systems into the HB cells. These new transporters are bioinspired, biocompatible and biodegradable. Our current results attest of their low cytotoxicity on cells and their capacity to encapsulate siRNA to deliver it in HB cells.

P4 - Telocyte-derived Netrin-1 targets endothelial UNC5B to drive vascular pruning during infantile hemangioma involution

Lesa Faith Ndayisaba | BRIC, U1312

Infantile hemangioma (IH) is the most common benign tumor in children, affecting 4% of newborns. It is a dermal tumor of endothelial origin, whose deleterious impact on patients depends on its location. It follows a distinctive life cycle: a first proliferative phase characterized by increased ectopic angiogenesis and aberrant endothelial cell proliferation, leading to a hyperplasic vascular network, and a second, involuting phase, driven by spontaneous vessel regression, leading to tumor disappearance between 5 and 7 years of age. Stromal telocytes may contribute to this regression: morphological changes in telocytes correlate with the decreasing number of vessels, suggesting their involvement in IH regression. We further demonstrated an anti-angiogenic effect of telocytes in vitro, using a 3D sprouting angiogenesis assay.

To elucidate the molecular basis of this anti-angiogenic effect, we performed a targeted transcriptional screen of 25 anti-angiogenic factors and identified Netrin-1 as the most overexpressed, with a 12-fold increase in IH-derived telocytes compared with control telocytes from foreskin. Netrin-1 is a potent repulsive guidance molecule acting through binding to UNC5B receptors in both the neuronal and endothelial systems. Using a coculture model of primary endothelial cells (HUVECs) with IH telocytes (IH-TCs), we observed segregation of the two cell populations, an effect that was abolished both by a Netrin-1-blocking mAb and by genetic knockdown of Netrin-1 in IH-TCs, and that was absent in cocultures with control telocytes (Ctl-TCs). Using an in vitro transendothelial transwell permeability assay, we also found that IH-TCs increased the permeability of confluent HUVEC monolayers, compared with Ctl-TCs, through disruption of inter-endothelial VE-cadherin junctions, an effect counteracted by the addition of anti-Netrin-1.

The anti-angiogenic and vascular remodeling («pruning») effects of IH-TC-derived Netrin-1 were further confirmed using i) an endothelial sprouting bead assay and ii) a fibrin hydrogel pseudo-vessel network assay, with both genetic and antibody-based Netrin-1 inhibition.

Together, these data suggest that telocyte-derived Netrin-1 acts as an endothelial repulsive factor involved in the endothelial cell «pruning» that occurs during the involution phase of infantile hemangioma.

P5 - Characterization of the mode of action of neurotoxic substances responsible for neurodevelopmental disorders using zebrafish

Emilien Réaud | MRGM, U1211

The incidence of neurodevelopmental disorders (NDDs) (e.g., attention deficit hyperactivity disorder, autism spectrum disorders, epilepsy) has been rising for several decades. Although NDDs are highly heritable, genetic factors alone cannot account for this increase, pointing to a substantial contribution from environmental factors, in particular man-made chemicals encountered during critical neurodevelopmental periods such as gestation and early childhood. Neurodevelopment (ND) is indeed a highly regulated process with a tight timeframe, in which a myriad of molecular and cellular events is precisely integrated and executed. Disruption of any of ND's main steps, such as proliferation, migration, and differentiation, can have severe and long-lasting consequences, including on behavior. The overall objective of my PhD project is to decode how real-life exposure to neurobehavioral disruptors (NBDs), i.e., emerging pollutants affecting the nervous and neuroendocrine systems during early development, alone or in mixtures, contributes to NDD pathogenesis.

To achieve this, the project uses early developmental stages of zebrafish as a model and integrates mechanistic experiments and advanced bioinformatics to uncover conserved pathways and biomarkers causally linking pollutant exposure to adverse neurobehavioral outcomes. The research team supervising this work is internationally recognized for the development of new approach methodologies, particularly within the context of European projects (e.g., OBERON, PARC), such as the Electrical Stimulation Locomotor Test (ESLT), which generates behavioral fingerprints specific to exposure conditions. In an ESLT screening of 92 selected compounds under acute exposure, hierarchical clustering grouped several fingerprints of uncharacterized mode of action (MoA) compounds with reference NBDs, suggesting shared MoA, which were confirmed by biochemical assays. Extending this approach to developmental exposure, the PhD project will distinguish neurodevelopmental effects from general developmental toxicity by integrating molecular, cellular, morphological and behavioral analyses. This will consolidate zebrafish-based approaches for developmental neurotoxicity assessment, supporting safer chemical regulation and helping prevent neurodevelopmental disorders.

P6 - Thérapie génique de la protoporphyrie érythropoïétique (PPE) par édition de base

Artur Jolimay-Groener | BRIC, U1312

La protoporphyrie érythropoïétique (PPE) est une maladie métabolique rare de la voie de biosynthèse de l'hème due à un déficit d'activité de la ferrochelatase (FECH). Ce déficit entraîne l'accumulation de protoporphyrine IX (PPIX), une molécule phototoxique responsable d'une photosensibilité cutanée sévère qui, dans les formes les plus graves, peut s'accompagner d'une atteinte hépatique pouvant évoluer vers l'insuffisance hépatocellulaire. Les options thérapeutiques actuelles, comme la photoprotection stricte ou les analogues de l'α-MSH, sont essentiellement symptomatiques. La greffe allogénique de cellules souches hématopoïétiques (CSH) représente aujourd'hui la seule approche curative, mais elle est réservée aux formes sévères en raison des risques importants de morbidité et de mortalité, et de la disponibilité limitée des greffons.

Cette maladie est caractérisée, chez environ 95% des patients, par la co ségrégation d'un variant délétère du gène FECH, en trans avec un allèle hypomorphe commun (c.315 48T>C). Ce variant favorise l'utilisation d'un site d'épissage cryptique et la production d'un transcrit aberrant, faisant chuter l'activité globale de la FECH et aboutissant à l'accumulation de PPIX. Les stratégies de thérapie génique développées pour la PPE reposent principalement sur des stratégies de thérapie additive utilisant des vecteurs rétroviraux ou lentiviraux avec des risques d'insertion oncogénique aléatoire du transgène, ou sur l'utilisation transitoire d'oligonucléotides antisens (ASO) ciblant l'anomalie.

Ce projet vise à développer une stratégie de thérapie génique innovante et transposable en clinique fondée sur la correction ciblée de l'allèle hypomorphe du gène FECH par des éditeurs de bases de type cytidine (CBE) couplés à une nucléase Cas9 à spécificité de PAM élargie (SpRY).

Nous avons montré que l'utilisation des CBE avec la désaminase TadCBEd permet une correction ciblée du génome dans des fibroblastes immortalisés issus de patients, restaurant partiellement l'activité de la FECH, et diminuant l'accumulation de PPIX dans ces cellules, validant la preuve de concept de cette approche.

Sarah Huot-Marchand | ImmunoConcEpt, U5164

«Des cellules qui explosent pour sonner l'alarme immunitaire, parfois à tort»

Toutes les cellules ne disparaissent pas en silence pour céder la place à la réparation tissulaire, face au danger, certaines déclenchent une véritable autodestruction inflammatoire. Lors de ma thèse, j'ai exploré l'une de ces morts explosives au niveau pulmonaire : la pyroptose, face aux agressions de la fumée de cigarette et de l'ozone. Nos travaux ont mis en évidence que la protéine Gasdermine D agit comme une véritable perforatrice cellulaire au sein des macrophages et des neutrophiles, mais aussi et surtout directement dans les pneumocytes de type 1 qui tapissent nos alvéoles et permettent les échanges gazeux. Activée par des récepteurs de l'immunité innée, NLRP3 et NLRP6, cette mort cellulaire pro-inflammatoire conduit à la destruction du tissu pulmonaire.

L'étude de ces morts cellulaires m'a ensuite conduite vers des atteintes rénales durant mon post-doctorat, au cœur de pathologies auto-immunes comme la vascularite à ANCA. Dans cette maladie, les neutrophiles activés par des auto-anticorps infiltrent les reins et meurent de manière pro-inflammatoire dans le tissu rénal : c'est la NETose. En projetant leur ADN tel un filet toxique ainsi que leur contenu enzymatique, ils entraînent des lésions rénales. Décrypter ce mécanisme offre de nouvelles clés pour freiner la dégradation de l'organe.

Demain, c'est du côté de la peau que mes futurs projets poursuivront cette enquête, à travers les réactions allergiques médicamenteuses graves. J'explorerai comment la mort inflammatoire des kératinocytes s'allie à la NETose des neutrophiles pour provoquer le décollement cutané dans les syndromes de Stevens-Johnson et de Lyell (TEN). En parallèle, j'étudierai l'EETose, son équivalent chez les éosinophiles, dans le syndrome DRESS. Du poumon au rein jusqu'à la peau, traquer ces morts cellulaires ouvre la voie à des thérapies ciblées transversales.

Gauthier Follain | BRIC, U1312

«Deciphering the physical and cellular mechanisms driving cancer cell dissemination»

Metastatic dissemination is a multistep process in which circulating cancer cells must survive in the bloodstream, arrest within the microvasculature and ultimately cross the vascular barrier to colonize distant tissues. Although these steps represent major bottlenecks of metastatic progression, the mechanisms by which cancer cells adapt to, and physically interact with, the vascular microenvironment remain incompletely understood. My research projects aim to understand how cancer cell properties and vascular microenvironmental cues cooperate to determine metastatic dissemination.

During my PhD, I investigated flow-dependent mechanisms regulating cancer cell interactions with the endothelium, and during my postdoctoral research I extended this work to dissect the cellular mechanisms underlying cancer cell arrest and extravasation. These studies combined advanced live-cell imaging, quantitative cell biology and biophysics to reveal how both cancer cells and endothelial cells dynamically adapt during vascular dissemination.

In our emerging laboratory in Bordeaux, I will build on this expertise with a particular focus on renal cell carcinoma (RCC), using patient-derived tumor cells accessible through Prof. Bernhard's medical team and the UroCCR national network. We will investigate the mechanisms governing vascular arrest and extravasation, work at identifying kidney cancer biomarkers and develop the use of live cell functional biology tests for clinical predictions. This program will combine advanced imaging and quantitative approaches with in vivo models to resolve the heterogeneity of cancer cell behavior during metastatic dissemination. Ultimately, our multidisciplinary approach seeks to bridge fundamental cancer cell biology and clinical oncology, providing a mechanistic framework to understand and predict how individual tumor cells successfully initiate metastatic dissemination.

Third scientific session

Mathilde Pohin | ImmunoConcEpt, U5164

«Neutrophils contribution to severe hallmarks of IBD»

Inflammatory bowel diseases (IBD) are marked by chronic intestinal inflammation and impaired mucosal healing, resulting in persistent tissue damage. We study how immune cells, particularly neutrophils, interact with the unique microenvironment of the inflamed IBD gut to determine whether injured tissue repairs successfully or progresses to acute severe lesions carrying additional risks. By identifying the signals that govern inflammation and tissue repair, we aim to propose new strategies to promote mucosal healing in patients with IBD.

Aline Freville | MFP, U5234

«Identification of PV6, a non-exported Plasmepsin V substrate required for post-invasion metamorphosis in malaria parasites»

Malaria parasites extensively remodel their host erythrocytes through the export of parasite proteins. Many of these proteins contain a five-amino-acid motif known as the Plasmodium export element (PEXEL), which is cleaved by the parasite protease Plasmepsin V (PM V) and is generally considered a hallmark of protein export. Although PM V-mediated processing has traditionally been associated with protein export, we identified an unexpected class of PM V substrates through the characterisation of PV6, a PEXEL-containing protein whose deletion causes an immediate developmental arrest following erythrocyte invasion. We demonstrated that, despite being processed by PM V, PV6 is not exported into the host erythrocyte but instead remains within the parasitophorous vacuole. PV6 is the first identified native PM V substrate to remain within this compartment, challenging the established view that PEXEL processing necessarily directs proteins for export.

Interestingly, the essential function of PV6 is exerted during the very first minutes following erythrocyte invasion, when the parasite undergoes a rapid and extensive metamorphosis, transforming from an invasive merozoite into an amoeboid-shaped cell. We demonstrated that PV6 is required for this transformation, as parasites lacking PV6 fail to acquire the amoeboid morphology and instead remain spherical, with a significantly smaller surface area. This early morphological remodelling is crucial for parasite adaptation to its new intracellular environment and contributes to the preservation of infected erythrocytes during splenic passage. Together, these findings uncover an unexpected role for a non-exported PM V substrate in regulating the rapid post-invasion metamorphosis of *Plasmodium falciparum*.

***Poster in competition**

P7* - AXL Intracellular Domain nuclear interactome controls spliceosome in FLT3-ITD Acute Myeloid Leukemia

Yanxiao Han | BRIC

Acute myeloid leukemia (AML) is an aggressive hematological malignancy whose incidence has doubled over the past two decades. FLT3 internal tandem duplication (FLT3-ITD) is one of the most frequent alterations in AML, occurring in approximately one third of patients and associated with poor prognosis. A decade ago, AXL has been involved in cooperating mechanism in the hematopoietic niche condition. Clinically, the use of the dual FLT3/AXL inhibition with Gilteritinib, allows a remission rate near 85% in elderly patients although five-year survival and cumulative relapse rates remain largely unchanged. This suggests that leukemia-initiating cells (LICs) persist within the hematopoietic niche and show intrinsic resistance to current therapies regardless of the targeted kinase.

Our work aims to investigate why dual inhibition of FLT3 and AXL is not efficient in preventing the persistence of AML LICs. To decipher the underlying molecular mechanisms, we modeled the bone marrow niche by co-culturing AML cells with stromal cells under low oxygen concentrations.

In these conditions, AXL is overexpressed and undergoes sequential proteolytic cleavage by -secretase and -secretase, generating an intracellular domain (ICD). Using cytoplasmic and nuclear fractionation, we demonstrated that AXL-ICD translocates into the nucleus which is confirmed by confocal microscopy. Affinity purification of a 10xHis-tagged AXL-ICD followed by proteomic analysis of cytoplasmic and nuclear fractions identified the AXL-ICD nuclear interactome for which 310 proteins are detected in two different FLT3-ITD AML cell lines. Surprisingly, 80% of the nuclear interactome is accounted for proteins involved in RNA splicing regulation. Meanwhile, the pathway analysis of the top interactants reveals enrichment in RNA splicing, transcription regulation, chromatin remodeling and epigenetic pathways.

These findings suggest AXL-ICD as a key driver of leukemic resistance in the bone marrow niche and suggest a mechanism involving transcriptional regulation. Ongoing studies integrating transcriptomic and splicing regulation analyses aim to elucidate the mechanisms by which AXL-ICD drives leukemic persistence.

P8* - Roles of histone isoforms in triple negative breast cancer

Maïlys Baché | BRIC

Triple negative breast cancer (TNBC) accounts for 15-20% of breast cancer cases. It is the most aggressive subtype, with nearly half of patients developing metastases within the first years after diagnosis. This poor prognosis directly stems from the lack of estrogen and progesterone receptor expression, and HER2 amplification, which leaves TNBC without any targeted therapy. This makes the discovery of novel targets a priority.
We previously identified the embryonic isoform of RNA Polymerase III (ePol III), defined by its POLR3G subunit. This isoform is overexpressed in TNBC where it drives tumorigenesis and metastasis. Indeed, its knockout (KO) is sufficient to blunt tumor aggressiveness. However, molecular effectors downstream of ePol III remain unknown to this day.

Strikingly, POLR3G KO, despite RNA Pol III's canonical role in transcribing non coding RNAs, collapses the expression of several mRNAs, including an interesting set of histone variants that are essential for germline and stem cell functioning. Given their established role in stemness, these variants ought to emerge as relevant candidate downstream effectors of ePol III-driven carcinogenesis in this stem-like and aggressive cancer. We hypothesize that the loss of these histones variants will phenocopy POLR3G loss and blunt tumor aggressiveness. To test this hypothesis, we combine functional assays, with genome-wide mapping of histone variants binding sites, and interactome profiling in MDA-MB-231 cells. Single and combinatorial histone KO clones are being isolated for functional characterization. In the established POLR3G KO model, loss of ePol III cripples colony formation and 3D growth, consistent with an impaired tumorigenic potential.
Together, these findings uncover a previously undescribed ePol III–histone axis driving TNBC aggressiveness. As functional and molecular characterization of the histone KO cell lines advances, this axis emerges as a promising new therapeutic entry point into a cancer subtype that currently has none.

P9* - Proximity proteomics deciphers autophagy-linked host factors at the site of AdV-induced membrane damage

Mathilde Lartigau | *MFP*

Adenoviruses (AdV) are weakly pathogenic in humans and widely used in therapy, particularly for vaccine development. They replicate by hijacking cellular mechanisms. During infection, the viral capsid undergoes partial disassembly within the endosome, leading to the release of viral protein VI (pVI). pVI then interacts with the endosomal membrane and induces its rupture, allowing the virus to escape into the cytoplasm — a key step of the viral cycle. However, membrane rupture constitutes a danger signal for the cell. It is notably detected through cytoplasmic galectins, which activate autophagy. The interactions between viral factors and the cellular mechanisms that detect and repair membrane damage remain poorly characterized.
To identify the cellular proteins recruited to the site of membrane rupture, we developed an antibody-mediated proximity biotinylation approach coupled with mass spectrometry (AMPL-MS), in collaboration with Dr. Axel Imhof (LMU, Munich, Germany). This method relies on the specific targeting of protein VI using an antibody, allowing recruitment of a biotinylation enzyme (Protein A-APEX2) to the site of endosomal damage. Proteins in immediate proximity are thereby labeled and can be purified and identified by LC-MS/MS, with specificity validated using appropriate controls.
Among approximately 4,000 cellular proteins, 10 candidates were selected based on their statistical enrichment and biological relevance. These proteins are involved in endosomal trafficking, membrane repair, ubiquitin-mediated signaling, antiviral immunity, and stress-induced apoptosis. These results highlight a coordinated involvement of distinct cellular pathways during infection.
Functional validation of these candidates by siRNA depletion is currently underway. Characterizing these virus–host cell interactions will help us better understand adenoviral evasion strategies as well as membrane damage surveillance mechanisms, with perspectives for the development of new antiviral and vaccine approaches.

P10* - When skin tolerance falters : Decoding the collapse of dendritic tolerance and activation of resident memory T cells in vitiligo

Chloé Avril | *ImmunoConcEpT*

Vitiligo is a chronic autoimmune depigmenting skin disorder affecting 0.36% of the population and associated with a major psychological burden. Despite the development of topical JAK inhibitors, therapeutic options remain limited, highlighting the critical need to decode underlying immunological mechanisms to identify novel targets.

Skin immune homeostasis relies on tightly regulated interactions between dendritic cells (DCs) and resident memory T cells (TRM). In vitiligo, autoreactive CD8+ TRM already infiltrate the clinically non-lesional (NL) skin, raising the question of how local tolerance is maintained and ultimately lost. However, the specific tolerance mechanisms preserving this fragile balance, and how a stressed microenvironment disrupts it, remain largely unknown. Previous work from our laboratory revealed higher expression of immune checkpoint molecules, specifically PD-1/PD-L1 axis, respectively expressed on CD8+ T cells and DCs in the NL skin of vitiligo patients compared to affected peri-lesional (PL) skin, suggesting a role of these regulatory mechanisms in restricting T cell activation. Furthermore, single-cell RNA sequencing (scRNA-seq) analyses of NL and PL skin identified different regulatory DC subsets enriched in patient NL skin, whereas gene ontology analysis revealed an enrichment of T cell activation pathways in PL skin.

To investigate how a stressed microenvironment disrupts this fragile balance and drives lesion formation we modeled an environmental trigger using high-dose, non-toxic UVB irradiation, mimicking severe sunburn. scRNA-seq of NL skin treated with or without high-dose UVB revealed a transcriptional downregulation of immune checkpoint ligands across the myeloid compartment. Specifically, PD-L1 gene expression decreased in regulatory DC subpopulations. Concurrently, mature DCs and Langerhans cells (LCs) significantly upregulated the expression of genes related to antigen presentation and pro-inflammatory cytokines (IL-1β, TNF-β). Furthermore, we observed an upregulation of genes associated with T cell activation (e.g., IL2RA, CD28, and CD44), pointing to the reactivation of skin T cells. In addition, flow cytometry showed a significant decrease in PD-L1 and PD-L2 expression on CD14+ myeloid cells and cDC2s, alongside a tendency to decrease in PD-1 on CD8+ TRM.

In summary, these findings demonstrate that an environmental stress may trigger vitiligo progression by collapsing DC-mediated immune checkpoint expression, thereby licensing the activation of pathogenic skin TRM.

P11* - Characterizing CMV-Specific Immune Signatures to Predict Post-Transplant Infection Risk

Anaïs Schneller | *ImmunoConcEpT*

Cytomegalovirus (CMV) remains a major cause of opportunistic infection in solid organ transplant recipients despite preventive strategies relying on donor(D)/recipient(R) serostatus. However, clinical studies have shown that combining serology with assays evaluating CMV-specific conventional cellular immunity (CMV-CMI, measuring IFNβ via ELISA or ELISPOT upon PBMC stimulation) reduces unnecessary antiviral use in ELISPOT-positive patients. ,Yet, this approach remains imperfect. Approximately 20% of CMV-seropositive recipients (Rβ) with positive CMV-CMI still develop infection, suggesting cellular immune dysfunction.

Conversely, 80% of R+ patients with negative CMV-CMI do not develop CMV disease, suggesting the involvement of other cellular actors, such as nonV2V9 T cells and CD57NKG2C+ NK cells. This study aims to comprehensively characterize CMV-specific immune components by combining spectral flow cytometry and ELISPOT.

PBMCs from 40 R kidney transplant recipients were analysed at three time points: pre-transplant baseline, an intermediate follow-up, and at CMV infection onset or a matched time point. Four dedicated spectral flow cytometry panels were used to profile immune cell populations including T cells, NK cells, and T cells, and to assess dysfunction, activation markers together with transcription factors, cytokines and cytotoxicity. In parallel, ELISPOT assays were performed on the same samples to evaluate CMV-CMI.

To characterize the cellular immune response associated with CMV control, we analyzed the profiles of nonV2V9 T cells and CD57NKG2C+ NK cells prior to infection onset. Infection-free patients showed higher nonV2V9 T cell frequencies, whereas infected patients exhibited upregulated exhaustion marker LAG-3 on these cells. Interestingly, although these infection-free patients seem to possess fewer CD57NKG2C+ NK cells, this subset exhibited enhanced activation, evidenced by elevated CX3CR1 and TIGIT expression. Together, these results indicate that nonV2V9 T cell abundance is potentially protective against CMV, while CD57NKG2C+ NK cells exert their protective effects primarily through qualitative functional features rather than quantitative expansion.

P12* - Investigating the interplay between intracellular biophysics, physiology and aging

Marc Naccour | *IBGC*

Proliferating cells can reversibly exit the cell cycle in response to external cues and enter a non-dividing state known as quiescence. Importantly, quiescent cells remain metabolically active, retaining the ability to resume growth if conditions become permissive. However, their capacity to return to proliferation decreases with time, a process referred to as chronological aging. Chronological aging is a widespread phenomenon, as the majority of cells in nature are in such a non-dividing state. Interestingly, it has been proposed that aging and cell physical properties may be interlinked. First, entry into quiescence is accompanied by a drastic rigidification of the cytoplasm and an increase in macromolecular crowding. Furthermore, unpublished data from our team showed that fission yeast cells with a larger volume coupled to a lower DNA copy number, with potential implications for protein concentration, have a different aging profile than wild-type cells. However, it remains unclear whether the changes in intracellular physics that we observe as cells enter quiescence contribute to define cellular lifespan, and how this may be brought about at the physiological level. My PhD project will first focus on establishing state-of-the-art imaging tools for generating the first quantitative maps of cytoplasmic and nuclear crowding throughout aging (e.g. single-particle tracking, quantitative phase imaging). I will then explore potential correlations between these measurements and critical physiological processes, in particular gene expression noise, mRNA export and protein production. This will also take advantage of mutants with altered crowding that have been isolated in the team. Altogether, my work will bridge unprecedented characterizations of intracellular biophysics with cell physiology and aging, providing novel insight into the regulation of this essential phenomenon.

P13* - TP-mediated chromatin anchoring drives adenoviral chromatin remodeling and shields viral genomes from DNA damage sensing

Juliette Villagomez | *MFP*

The adenoviral genome consists of double-stranded DNA organized in a chromatin-like structure, in which viral DNA associates with the pVII protein to form nucleosome-like complexes known as adenosomes. In addition, the terminal protein (TP) is covalently bound to each 5′ end of the viral genome. This structure remains highly compacted within the viral capsid. Upon nuclear entry, adenoviral chromatin becomes anchored to host chromatin through TP, followed by dynamic chromatin remodeling that coordinates early and late viral gene expression as well as viral DNA replication. However, the molecular mechanisms underlying TP-mediated chromatin anchoring remain poorly understood.

Here, we show that TP anchoring occurs through the interaction of a TP RPRE motif with the H2A–H2B acidic patch of cellular nucleosomes. A TP AAAA mutant is no longer able to bind cellular nucleosomes. Loss of TP anchoring strongly impairs adenoviral chromatin remodeling, early viral gene expression, and viral DNA replication.

Quantitative mass spectrometry analyses revealed that TP interacts with the NuRD (histone deacetylase) and FACT chromatin remodeling complexes. Functional analyses further demonstrated that these remodelers are required for TP anchoring-dependent adenoviral chromatin remodelingand replication compartment formation. In addition, mass spectrometry analyses identified several TP-associated factors involved in the DNA damage response (DDR). Immunostaining experiments showed increased *g*-H2AX accumulation on TP AAAA mutant viral genomes compared with wild-type viral DNA, indicating that TP anchoring shields adenoviral genomes from DDR sensing.

Together, these results identify TP anchoring as a key regulator of adenoviral chromatin remodeling and viral genome protection, coordinating efficient viral replication while limiting host DDR sensing.

P14* - Receptor tyrosine kinase-mediated regulation of glioblastoma stem cell maintenance, therapy resistance, and tumor progression

Malak Senouci | *BRIC*

Glioblastoma (GB) is the most aggressive primary brain tumor, with a median survival of less than 15 months despite maximal surgical resection, temozolomide chemotherapy, and radiotherapy. Treatment failure is largely driven by tumor heterogeneity and intrinsic resistance mechanisms. Glioblastoma stem cells (GSCs) are a self-renewing population capable of regenerating all tumor subpopulations and driving recurrence, representing a major therapeutic challenge. Identifying essential regulators of GSCs is therefore critical for the development of novel treatment strategies. GSCs rely on multiple context-specific pathways to survive under diverse microenvironmental conditions and therapeutic pressures. Cell-surface proteins, particularly receptor tyrosine kinases (RTKs), play central roles in transmitting extracellular signals and mediating interactions with the tumor microenvironment, making them attractive therapeutic targets. Through surface protein profiling, we identified an RTK that is highly expressed in GSCs compared with non-oncogenic neural stem cells. Analysis of patient datasets revealed that this RTK is overexpressed in GB relative to normal brain tissue, and higher expression correlates with poorer patient survival.

However, its functional role in GB had not been defined. Functional assays demonstrated that genetic deletion or pharmacological inhibition of this RTK reduces GSC proliferation and self-renewal, with variable sensitivities observed across patient-derived GSCs. Activation of the RTK reinforced GSC dependency and increased their vulnerability to inhibition. Notably, RTK depletion or inhibition impaired mitochondrial morphology and reduced oxidative phosphorylation, suggesting a critical role in GSC metabolism. Combination studies further showed that targeting this RTK sensitizes GSCs to radio- and chemotherapy. In vivo intracranial tumor assays revealed that RTK knockdown reduces tumor growth and extends survival. Together, these findings establish this RTK as a central regulator of GSC biology and underscore its potential as a therapeutic target in GB.

P15* - SARS-CoV-2 and GCN2, a strange relationship

Pauline Marchal | *MFP*

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a highly transmissible pathogen responsible for a global health crisis. A deeper understanding of its replication strategies and interactions with host cells remains essential, particularly in the context of long COVID and the continuous emergence of viral variants.
To counter viral infection, host cells activate multiple defence mechanisms, including the Integrated Stress Response (ISR). The ISR is a conserved cellular pathway that temporarily halts protein synthesis in response to stimuli such as nutrient deprivation, viral infection, or oxidative damage. The ISR promotes cellular adaptation by modulating translation and activating specific stress transcription factors.
GCN2, a key kinase in this pathway and the only one conserved through evolution (from yeast to human). It plays a role in several human diseases, including cancer, Alzheimer's disease, and obesity. Recent studies have also highlighted its role in innate immunity, where it acts as a restriction factor against retroviruses such as HIV and other RNA viruses [1, 2]. However, several RNA viruses, including HIV and SARS-CoV, have evolved strategies to manipulate the ISR to favour their own replication under stress conditions [3, 4].
Our data suggest that GCN2 is also a restriction factor against SARS-CoV-2. At the opposite, this virus may also escape ISR. In fact, after 48 hours of infection, we observe a decrease in GCN2 protein level, a potential cleavage in the Nter of GCN2 by the viral protease Mpro and an important modulation of ISR transcriptional effect. Together, these findings indicate that SARS-CoV-2 actively modulates host cellular stress responses. Elucidating the interplay between the ISR and viral infection may therefore reveal novel therapeutic targets.

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P16* - Development of aptamers for the diagnosis of trypanosome infections with a view to developing a rapid detection test : proof of

Clément Dugravier | *MFP*

Trypanosomes are parasites responsible for several animal diseases, such as Nagana, dourine, and surra, which have a major economic impact, particularly in Africa. Current treatments remain limited by their toxicity, cost, and the emergence of drug resistance, while no effective vaccine is currently available. In this context, early diagnosis represents an important challenge. The APTATryp project aims to develop a rapid, sensitive, and field-deployable diagnostic test based on the identification of specific biomarkers and the development of aptamers capable of recognizing these targets.

P17* - Exploring the oncogenic potential of large-scale copy number gains induced by CRISPR-Cas9

Camille Bergès | *BRIC*

Despite their high prevalence in cancer, the origins and functional roles of aneuploidies, in particular copy number gains (CNGs), remain poorly understood. It is still debated whether these chromosomal abnormalities are a cause or a consequence of oncogenic transformation. Emerging evidence suggests that gains may act as drivers in tumorigenesis. This “gain addiction,” recently highlighted in key studies, underscores the need for understanding their mechanisms and consequences.

Aberrations involving chromosome 1 are among the most common anomalies reported among human neoplasms and have been observed in both solid tumors and hematological malignancies. Modeling these alterations in normal cells is crucial for elucidating their mechanisms of emergence and oncogenic potential.

During previous genome editing experiments by CRISPR-Cas9, we observed genotoxic side effects, including extra-large deletions, copy-neutral loss of heterozygosity, but also events such as CNGs, and chromoplexy. These observations led us to hypothesize that double-strand breaks (DSBs) could initiate chromosomal rearrangements involving copy number gains.

Using CRISPR-Cas9, we performed double-strand breaks in chromosome 1 in a human fibroblast model. With this approach, we were able to generate complex chromosomal rearrangements, including CNGs regarding the targeted chromosome. By longitudinal genomic and cytogenetic approaches such as CGH-arrays, FISH and Optical Genome Mapping, we could track the emergence and evolution of CNGs. Single-cell RNA sequencing and transcriptome-based copy number inference complement these approaches by resolving population heterogeneity and examining the transcriptional states associated with rearranged profiles.

Interestingly, some selected profiles persisted and increased in representation during prolonged culture, suggesting a potential selective advantage. Their transcriptional profile revealed dysregulation in key processes involved in cell proliferation and differentiation.

These profiles have been subcloned, and functional assays are ongoing to determine how these genomic alterations contribute to cellular fitness and to assess their putative role in early oncogenesis.

This work establishes an experimental framework to investigate the emergence, persistence, and cellular consequences of copy number gains before overt malignant transformation. It may help clarify how structural genome alterations, in particular CNGs, contribute to early oncogenic evolution, while also informing the assessment of long-term genomic consequences following CRISPR-Cas9 editing.

P18* - Selective targeting of a mutated FLT3 isoform in AML : from structural modelling to hit optimisation

Lindita Lari | *BRIC*

Acute myeloblastic leukaemia (AML) is a heterogeneous haematological malignancy. Patients under 60 years old generally respond well to induction chemotherapy (~80%), but frequent relapse limits five-year survival to ~40%, falling to 10% for those beyond 60 years old. FLT3 is the most frequently mutated gene in AML and a key driver of leukaemogenesis: ~30% of patients carry an internal tandem duplication (ITD) in its juxta-membrane domain, causing constitutive downstream signalling and poor prognosis. FLT3 tyrosine kinase inhibitors (TKI) are currently used in clinically, but resistance often appears.

Within the CSHNL team, V.Desplat's group has identified a new isoform with alternative splicing of an exon in the FLT3 receptor that generates oncogenic signalling in AML cells and contributes to anti-FLT3 TKIs treatment resistance. Moreover, a translational study revealed that this new variant induced a poor prognosis in patients. Therefore, it is necessary to develop new and more effective therapeutic strategies for AML patients presenting this molecular alteration.

Here we report a structure-based drug discovery pipeline targeting this mutated FLT3 isoform, combining molecular modelling, chemical synthesis and biological evaluation.

A three-dimensional model of the mutated FLT3 protein was generated using MODELLER10.6 and validated by PROCHECK (97.9% of residues in favoured Ramachandran regions), confirming a stereochemical quality suitable for structure-based drug design. This model served as receptor for virtual screening of 455 compounds (20 in-house, 435 from a MedChemExpress macrocyclic library). Of 8 candidates selected for in vitro testing, 6 assessed to date, 2 showed activity against the mutated isoform, including the approved FLT3-inhibitor Pacritinib (IC_{50} = 0.46µM), confirming the robustness of our docking strategy. To establish the structure-activity relationship underlying FLT3 inhibition, seven compounds were synthesised with the chemistry team (J.Guillon) and evaluated on commercial AML cell lines and on novel AML cell lines generated by the biology team (V.Desplat), specifically expressing this mutated FLT3 isoform. Proliferation and selectivity assays identified three lead compounds with IC_{50} values ranging from 0.63-5µM against the mutated isoform, and selectivity indices exceeding 3 relative to FLT3-WT, FLT3-ITD and/or hFF-1 (a healthy human foreskin fibroblast cell line) indicating a favourable therapeutic window. Functional studies are ongoing to confirm target engagement, as apoptosis assays and analysis of downstream FLT3 signalling pathways.

Altogether, this multidisciplinary strategy, has identified three selective hit compounds and supports the continued development of selective FLT3-targeted therapies for AML patients.

P19* - Understanding the phosphorylation-dependent regulation of the cohesin complex and its functional implications

Pauline Legrand | *IBGC*

Cohesin is a highly conserved protein complex having the ability to capture DNA molecules. Its best-known function is to ensure sister chromatid cohesion by capturing in trans sister DNA molecules. This process is essential for DNA double strand break repair and for correct chromosome segregation. Cohesin also has the ability to capture DNA in cis leading to the formation of large DNA loops that define the functional architecture of the chromatin during interphase. By modulating 3D genome organization, Cohesin affects gene expression

and increasing evidence indicates that Cohesin is particularly important in transcriptional induction of developmental or differentiation programs. How is Cohesin regulated and targeted in its different DNA-related functions remains largely unknown. We aim at understanding how cohesin functions are coordinated in space and time and how signals are conveyed to cohesin?

Previous work, including our studies in S. pombe, indicates that phosphorylation of cohesin constitutes a key mechanism for modulating its activity. Our team identified two kinases, Pef1 (human CDK5 homolog) and TORC1 (nutrient sensor complex), that modulate Cohesin phosphorylation and functions and adjust cell behavior, depending on internal (cell cycle phase, DNA damage) and external signals (trophic). My project aims to understand how cohesin function and cell adaptation are regulated by phosphorylation of the Cohesin complex and its partners. We performed a large mass spectrometry analysis on Cohesin, and its regulators Mis4 (cohesin loader) and Pds5 throughout the cell cycle. In addition to the 40 phosphorylation sites reported by the community, we identified 13 new phosphorylated residues with several sites showing cell-cycle specificity. Interestingly, 10 are also phosphorylated in Human and some are located at key interfaces involved in capture or released of the DNA by the Cohesin complex. To investigate the functional significance of these modifications, we are generating a systematic library of phospho-mimetic and phospho-null mutants. These mutants are screened across a wide range of conditions to assess both sister chromatid cohesion and the ability to adapt to environmental stresses. This latter approach tests whether cohesin phosphorylation influences transcriptional programs that enable cells to survive and respond to changing conditions. I will present our strategy in detail, along with my current experiments and the preliminary data we have already obtained.

P20* - Developing new approaches to better understand the tissue specificity of mitochondrial diseases

Guillaume Duranthon | *IBGC*

The heart is a strictly aerobic organ relying on mitochondrial function to generate the ATP required for its continuous mechanical activity. Mitochondria play a central role in energy metabolism. They contain their own genome (mtDNA), which encodes key proteins required for oxidative phosphorylation (OXPHOS) and ATP production. In the mouse heart, disruption of mitochondrial dynamics, specifically outer membrane fusion through constitutive knockout of mitofusins during cardiomyocytes maturation, is lethal and promotes dilated cardiomyopathy accompanied by impaired mtDNA maintenance and reduced OXPHOS efficiency. Clinical observations indicate that defects in mtDNA replication precede the development of right ventricular heart failure in patients.
Our objective is to use multimodal approaches to characterize how loss of mitochondrial outer membrane fusion affects mitochondrial genome maintenance, energy metabolism, and heart failure progression. To address this, we use adeno-associated viruses to knockout Mitofusins 1 and 2 (Mfn1 and Mfn2) specifically in the heart and skeletal muscles of transgenic adult mice. Thanks to confocal microscopy, combined with bioenergetic measurements and assessments of cardiac mechanics, we aim to clarify the consequences of MFN1/2 loss and help define the relationship between mitochondrial dynamics, mtDNA loss, and heart failure progression in the mature adult heart.

P21* - Investigating the role of Gut Microbiota Modulation in Glioblastoma development

Sarah Lavielle | *IBGC*

Glioblastoma is the most common and aggressive brain tumour in adults and is associated with a poor prognosis, with a median survival of approximately 14–15 months. Despite the current standard of care, the Stupp protocol, which combines surgical resection, temozolomide chemotherapy, and radiotherapy, glioblastoma remains associated with frequent treatment failure. Identifying the factors contributing to tumour initiation, progression, and therapeutic resistance is therefore essential to improve patient survival and quality of life. Here, we investigate the gut–brain axis, focusing on the potential role of the gut bacterial microbiota in glioblastoma progression. This diverse microbial community has been shown to play a crucial role in several neurological disorders, including Parkinson's and Alzheimer's diseases. Emerging evidence suggests that the gut microbiota may also influence glioblastoma, although the underlying mechanisms remain poorly understood.

As our preliminary results showed that glioblastoma-bearing mice exhibit altered gut microbiota composition, we investigated the impact of gut microbiota modulation on glioblastoma aggressiveness and outcome. First, gut microbiota depletion using broad-spectrum antibiotics resulted in smaller tumours and reduced immune cell infiltration within the tumour, suggesting that the gut microbiota may contribute to glioblastoma progression, potentially through the recruitment of immune cells. We also performed faecal microbiota transplantation (FMT) from healthy donors into glioblastoma-bearing mice. FMT resulted in smaller tumours and prolonged survival, further supporting a role for the gut microbiota in glioblastoma progression and outcome and represent potential novel strategies to modulate glioblastoma aggressiveness.

P22* - ROLE OF THE IMMUNE SYSTEM AND THE METABOLIC EXCHANGES RELATED TO THE MICROBIOTA-GUT-BRAIN AXIS IN THE GLIOBLASTOMA CONTEXT

Cédric Pape | *IBGC*

This thesis project aims to study the role of the immune system and the metabolic exchanges between the three compartments being: the intestinal microbiota, the gut, and the brain; within GB context. To do so, the research work will be divided into three axes:

-First, a characterization of the immune populations presents within the GB tumor microenvironment, and the gut; coupled to a characterization of the metabolites implicated in the microbiota, gut and brain exchanges, this at the faeces, blood and organs levels.

-Then, a modulation of the immune response and the metabolic exchanges, to better understand their own impacts on GB growth and therapeutic resistance.

-Finally, a last part will be dedicated to treatments (combined or not), with the Stupp protocol (actual and unique treatment against GB), immune therapies, and/or gut microbiota modulations.

Together, these axes will hopefully help to understand how the immune system interacts with the gut microbiota, and which metabolic exchanges exists between these compartments, impacting GB growth and therapeutic resistance. This research will also allow an opening to potential new treatments, for this bad prognosis cancer.mice. Phagocytosis tests have been made by culturing BMDMs with beads. Both the proportion of BMDMs performing phagocytosis and the number of beads per BMDMs were similar between the WT and the MCT1Δmye conditions. qPCR has also been performed on enzymes of different metabolic pathway, displaying a change only for the G6PDX, involved in the pentose phosphate pathway. Finally, invasion assays showed similar invasive index of GB cells co-cultured with BMDMs, whether their genotype.

Together, these findings demonstrate a potential impact of the lactate on the MC, and therefore the impact of these cells on the GB progression.

P23* - Targeting lipid release by lipases in glioblastoma

Nahia Espie Basurco | *BRIC*

Glioblastoma (GB) is the most frequent and aggressive brain tumour in adults. With its high intratumoral heterogeneity and plasticity, resistance mechanisms are frequent, leading to patient relapse. Targeting the metabolic plasticity in GB is an interesting approach to improve treatment response and limit cancer progression.

Lipid droplets (LD) are organelles specialized in lipid storage; they participate in the metabolic plasticity that drives adaptation and resistance of GB cells. LDs are degraded by lipases, such as hormone sensitive lipase (HSL), that regulate lipid content in the cell. We aim to determine the interest of targeting lipid release to limit the metabolic plasticity of GB cells.

We show that pharmacological inhibition of HSL impedes LD degradation and decreases free fatty acid release, thereby reducing mitochondrial metabolism. It reduces cell proliferation and improves the response to chemotherapy in vitro. Regarding in vivo models, HSL KO in GB cells reduces tumour growth in mice and improves their survival. However, the current inhibitor is not appropriate to target the brain. Therefore, we aim to identify new HSL inhibitors among molecules able to cross the blood-brain barrier. We perform a virtual screening on a chemical library followed by in vitro validation on HSL activity and LD number. Based on the virtual docking of the HSL catalytic pocket, we selected 16 molecules and 7 were effectively able to decrease lipid droplet degradation.

The discovery of new HSL inhibitors able to target the brain could limit GB adaptation and improve the response to treatment.

P24* -Competition between the dehydrogenases for electron transfer in the respiratory chain of Saccharomyces cerevisiae

Corinne Pellon | *IBGC*

Cell homeostasis and proliferation require chemical energy in the form of ATP by different pathways of the cellular energy metabolism. Redox reactions of those pathways also lead to the reduction of NAD+ into NADH. The cell therefore needs to maintain ATP/ADP and NADH/NAD+ ratios within a sustainable range. Mitochondria are essential in this regard as they ensure most of the ATP synthesis and NADH reoxydation in aerobic cells through the oxidative phosphorylation (OXPHOS) system within the mitochondrial inner membrane. Cytosolic NADH is not the only substrate of the OXPHOS system as it includes various external and internal dehydrogenases with different substrates and there are electron competition processes between those dehydrogenases (Pahlman et al. 2002, Bunoust et al. 2005) for the electron transfer towards quinones, central electron carriers of the system. Understanding how the cellular NADH/NAD+ ratio is maintained at an adequate level then proves to be a major but complex issue of energy metabolism.

To address this issue, we studied the electron competition processes on isolated mitochondria from S. cerevisiae. We used an electrochemical method previously developed in our team for mitochondrial metabolism study (Martins Pinto et al. 2024). This method allows real-time measurement of the mitochondrial respiration and the quinones redox state, two complementary parameters to help understanding the mitochondrial metabolism and OXPHOS functioning. We interestingly demonstrated on our model a strong correlation between the two parameters. Our study allowed us to reveal a system favoring cytosolic NADH oxidation over other mitochondrial substrates. We demonstrated that competition processes are however not that straightforward as our results showed that they are substrate and respiration rate dependent. These results altogether give us a better understanding of how mitochondria can favor a metabolic path over another in a simplified model.

P25* - Deciphering and targeting cancer stem cell dormancy in gastric cancer

Maria Nisenboym | *BRIC*

Gastric cancer (GC), predominantly gastric adenocarcinoma, remains a major cause of cancer-related mortality worldwide, with a poor prognosis in metastatic disease[1]. Despite curative-intent treatment, many patients experience relapse months or years after apparent remission[2]. This late recurrence may be driven by cancer stem cells (CSCs), a highly plastic subpopulation capable of entering a reversible quiescent state known as dormancy. Unlike proliferating cancer cells, dormant CSCs may evade conventional chemotherapy and persist in distant organs within specialized niches, where they can later resume proliferation and initiate metastatic growth. The detection of disseminated cancer cells in patients with non-metastatic GC[3] supports the existence of such residual cell reservoirs and suggests that early dissemination and dormancy may contribute to late metastatic relapse.

We hypothesize that CSCs disseminate early and colonize dormant reservoirs in distant organs, where microenvironmental cues such as hypoxia promote and maintain their quiescent state. Alterations in these signals may subsequently trigger CSC reactivation, promoting metastatic outgrowth. The nuclear receptor NR2F1, a key regulator of tumor dormancy in several cancers, may control this process in gastric CSCs[4][5].

Our objectives are to (1) decipher the molecular mechanisms governing gastric CSC dormancy and reactivation, and (2) explore the therapeutic potential of inducing and maintaining CSC dormancy to prevent recurrence and metastatic progression.

Various GC cell lines were exposed to dormancy-inducing conditions, including hypoxia and combined ATRA/5-azacytidine (5'AZA), based on the literature and previous work from our laboratory[6]. Our preliminary results reveal a potential role for hypoxia (1% O_2) in GC dormancy. Both hypoxia and ATRA+5'AZA reduced proliferation and induced G0/G1 cell-cycle arrest without increasing cell death or senescence. Hypoxic cells displayed a dormancy-associated NR2F1⁄/Ki67⁄/p27⁄ phenotype, supporting a dormant state.

Similarly, ATRA+5'AZA reduced proliferation and increased the G0/G1 population, accompanied by a NR2F1⁄/Ki67⁄/PCNA⁄/p27⁄ signature. In vivo, four sequential cycles of 5'AZA and ATRA in NSG mice significantly reduced tumor growth and weight compared with controls. Molecular characterization of residual tumors is ongoing.

This study aims to uncover the mechanisms underlying gastric CSC dormancy and metastatic relapse. Identifying determinants of dormancy and reactivation may provide biomarkers of residual disease and reveal therapeutic strategies to prevent late metastatic recurrence.

P26* - Sharp elbows or stealthy moves? Exploring the extravasation strategies of renal cell carcinoma

Helene Helo | *BRIC*

Renal cell carcinoma (RCC) is the most common type of kidney cancer, and a significant portion of patients have metastatic disease or suffer tumour relapse. These conditions lack curative treatment, prompting research into the mechanisms by which tumour cells survive and spread through circulation. Extravasation, the process of cells exiting blood vessels, represents a major bottleneck in metastasis and a potential therapeutic target. The mechanisms by which circulating RCC cells arrest in the blood flow, adhere to the inner wall of vessels (endothelium) and escape circulation are currently unknown.

Tumour cells are a motley crew and employ a variety of strategies for crossing the endothelial barrier. Possible modes include mechanical or biochemical disruption of the endothelium or subtle remodelling of it. How paths of extravasation are reflected in the biochemical properties and extravasation efficiencies of the cells is an open question.

This project will quantify the efficiency of arrest, adhesion and extravasation of cell lines and patient-derived RCC cells, and, most importantly, carefully describe and compare the mechanisms by which the cells find their way out of the circulation. Once the phenotypes are identified, the project aims to link extravasation behaviours to the responsible molecules by screening for differences in the transcriptomes and proteomes of the cells. The project draws both on in vitro approaches, including video analysis of a microfluidic setup, and on zebrafish and mouse models for live imaging and quantification of extravasation properties in vivo and ex vivo. Patient cells increase the translatability and clinical relevance of the results, providing a valuable addition to the cell line-based data. I am pleased to invite you to my poster, in which I will present preliminary results from the first in vitro experiments with RCC cell lines and discuss their implications as well as the next steps of the project.

P27* - Unravelling the mechanisms of action of N-acetyl-L-aspartate in Acute Myeloid Leukaemia: focus on metabolism

Blandine Vignau | *BRIC*

Introduction: Acute myeloid leukaemia (AML) is a malignant haematological disorder characterised by genetic and chromosomal abnormalities leading to the uncontrolled proliferation and differentiation arrest of myeloid progenitor cells, thereby impairing normal haematopoiesis. Despite current treatments, relapses and therapeutic resistances remain frequent, underlining the need to find new therapies. Cancer metabolism has emerged as important area of research to identify potential therapeutic targets. Our metabolomic analyses have revealed a significant accumulation of N-acetyl-L-aspartate (NAA) in leukemic cells compared to its normal counterpart. Furthermore, analysis of clinical data showed that high expression of NAT8L gene (which encodes the AspNat enzyme responsible for NAA production) correlate with a poor prognosis in patients with AML. Moreover, the team has shown that mice transplanted with murine or human leukemic cells lacking NAA have a better overall survival than those receiving wild-type (WT) cells. However, the role of NAA in the hematopoietic system remains unknown. This research project aims to unravel the cellular mechanisms by which NAA promotes the progression of AML.
Methods: We are combining gene silencing approaches targeting NAT8L in human leukemic cell models. Our investigations focused at first on mitochondrial metabolism, measuring membrane potential by flow cytometry, quantifying mitochondrial mass by qPCR and assessing mitochondrial respiration. We also investigated if NAA was involved in hypoxia adaptation.
Results: Our investigations on mitochondria metabolism revealed that reduction in NAA levels induced only a slight decrease in mitochondrial activity and mitochondrial mass. We are currently measuring the impact of NAA depletion on mitochondrial respiration. We also showed that NAA is not required for cellular adaptation to hypoxia whatever the severity (3, 1 and 0.1% of O2).
Conclusion: Since mitochondrial metabolism seems to be minimally impacted by lack of NAA, we will next carry out a broader untargeted metabolomics analysis in order to identify the metabolic mechanisms driving the phenotype associated with NAA depletion and as such potentially identify additional actionable targets in order to improve survival in patients with AML.

P28* - Study of mitochondrial protein complexes involved in mitochondrial architecture and the life cycle of trypanosomes

Alexis Bourdarie | *MFP*

Trypanosoma brucei, parasite responsable de la maladie du sommeil et du Nagana, ne possède qu'une seule mitochondrie. Sa forme varie au cours du cycle de vie : ramifiée chez la forme procyclique (mouche tsétsé), elle est tubulaire chez la forme sanguine (hôte mammifère). Ce remodelage suggère l'existence d'une dynamique mitochondriale impliquant des mécanismes de fusion et de fission.

Nous avons caractérisé TbMfnL, une mitofusine atypique localisée dans les membranes mitochondriales et appartenant à la famille des dynamines. Une séquence d'adressage mitochondrial (MTS) N-terminale, absente chez la Mfn humaine, ainsi que deux domaines transmembranaires sont essentiels à sa localisation et à sa fonction.

Sa surexpression dans les formes procycliques provoque une hyperréticulation mitochondriale, avec une forte augmentation des branchements mitochondriaux. À l'inverse, son inactivation semble entraîner une diminution de ces branchements.

De manière à identifier les partenaires potentiels de TbMfnL, une approche BioID a été réalisée, ce qui a permis d'identifier une douzaine de partenaires potentiels.

Ces résultats décrivent l'étude et la caractérisation des potentiels partenaires en interaction avec TbMfnL, la première protéine impliquée dans la fusion mitochondiale chez T. brucei.

P29* - Expression, activity, and role of NMDA receptors in glioblastoma cancer cells

Emmanuelle Georget | *BRIC*

Glioblastoma (GB) is the most aggressive primary brain tumor in adults, with a median survival of 15 months. Despite a stringent treatment regimen (the Stupp protocol), GB inevitably relapse with enhanced infiltrative capacity and develops within a neuron-rich microenvironment, insights in neuron–tumor interactions is essential. Recent studies revealed functional synapses between neurons and GB cells, suggesting a role for neurotransmitter receptors such as N-méthyl D aspartate receptors (NMDARs). NMDAR signaling might exert a pro-tumoral effect by hijaccking glutamate from neurons. We aim at deciphering NMDAR signaling role in GB cell lines:

(1) by evaluating the NMDAR expression levels
(2) by modulating the NMDAR's subunit 1 expression
(3) by validating the surface expression and functionnalities of the NMDAR's subunit 1
(4) by investigating the impact of NMDAR's subunit 1 modulation on the proliferation and invasion capacities

We used patients' derived GB cell lines and assessed their proliferative and invasive capacities in 2D and 3D models following NMDAR's subunit 1 (GRIN1) modulation. NMDAR functionality was evaluated using calcium imaging with selectiv agonist and antagonist.
The NMDAR is expressed at low levels in patient derived GB cells at both level RNA and protein, but 54 % of GB cells displayed functional NMDAR activity, evidenced by calcium influx upon NMDA/Glycine stimulation at 10µM. An acute activation of the NMDAR did not significantly modify the proliferation or 3D invasion for 48h. Additionnaly a co-culture neuron-enriched revealed a higher expression of NMDAR for some GB cells.

Our findings indicate that although NMDAR expression is low in GB cell lines, a neuron-responsive subpopulation exhibits more NMDAR and supporting a potential role of invasion at the tumor edge. Understanding the NMDAR role in GB cell lines alone or in co-culture may clarify how neuron-derived signals influence GB aggressiveness through NMDAR and identify new mecanisms for therapeutics.

P30* - Gene Editing Meets EV Sorting: A Novel Strategy to Explore EV Subpopulations

Rémi Darracq | BRIC

Introduction and Aims
Extracellular vesicles (EV) are released by all cell types in the human body and have emerged over the past decade as key mediators of intercellular communication through their ability to modulate recipient cell behavior. However, the intrinsic heterogeneity of EV in terms of size, cellular origin and molecular cargo remains a major challenge for the study of specific EV subpopulations. Current approaches for tracking EV rely on the overexpression of EV marker fused to a reporter. However, this strategy induces ectopic expression and does not reflect the endogenous distribution of the marker in EV. To overcome this limitation, we propose a novel strategy to investigate EV subpopulations by combining CRISPR-based gene editing with EV sorting using Hekat NanoSorter®, a new technology based on microfluidic that enables detection, counting and sorting of fluorescent nanoparticles.
Materials and Methods
CD63, a tetraspanin widely recognized as a marker of small EV (sEV) was endogenously tagged with GFP in liver cancer cells using CRISPR-based gene editing. The edition was genetically validated by DNA sequencing. The subcellular localization of GFP-CD63 fusion protein was assessed by confocal microscopy. sEV were isolated by size exclusion chromatography and their presence was confirmed by transmission electron microscopy. The concentration of GFP+-sEV was quantified using both NanoSorter® and NanoFCM technologies. GFP+-sEV were subsequently sorted using the NanoSorter®. Sorted sEV were characterized morphologically by cryo-electron microscopy coupled with CD63-immunogold labelling and their uptake by recipient cells was evaluated using confocal microscopy and flow-cytometry.
Results and Conclusion
In the edited-cells, the fusion protein GFP-CD63 was localized to endosomal compartments. The genome editing did not affect sEV production and morphology, and enabled the detection of GFP+-sEV using NanoSorter® and NanoFCM technologies. Furthermore, GFP+-sEV sorting and recovery did not alter sEV morphology or size distribution. Importantly, sorted sEVs retained their ability to be internalized by recipient cells. Overall, this approach enables the isolation of highly pure CD63+ sEV subpopulation while preserving their morphology and uptake capacity. This strategy provides a physiologically relevant model for investigating molecularly defined EV subpopulations and their biological functions.

P31* - Propranolol targets the ADRB2-AQP1 axis to regulate tumor cell migration and multicellular organization in cutaneous angiosarcom

Faiza Laanani | *BRIC*

Cutaneous angiosarcoma is a rare and highly aggressive vascular malignancy characterized by marked heterogeneity, high metastatic potential, and poor response to systemic therapies. Propranolol, a non-selective β-adrenergic receptor antagonist successfully used to treat infantile hemangioma, has shown promising clinical activity in a subset of angiosarcoma patients [1], but the mechanisms underlying its antitumor effects and the variability in patient response remain poorly understood, limiting the identification of biomarkers for patient stratification. We hypothesize that β-adrenergic signaling, through the ADRB2-AQP1 axis previously identified as a mediator of propranolol response in vascular tumors [2], regulates angiosarcoma progression primarily by modulating tumor cell migration and multicellular tissue organization rather than cell proliferation, and that these effects can be captured quantitatively through combined live imaging and mathematical modeling. At the cellular level, live imaging of wound-healing assays is coupled with automated single-cell tracking and quantitative mathematical analysis to characterize migration dynamics, including cell trajectories, velocity, and wound closure kinetics, following propranolol treatment or genetic modulation of ADRB2 and AQP1. At the tissue level, three-dimensional angiosarcoma spheroids are used to investigate changes in tumor morphology and organization. Preliminary results show that propranolol inhibits 2D migration but increases spheroid diameter without affecting proliferation or cell viability, consistent with an effect on tissue organization rather than on cell growth. Quantitative image analysis and mathematical modeling are used to extract robust descriptors of spheroid architecture and structural heterogeneity. These findings will be further studied in vivo using our validated bioluminescent angiosarcoma xenograft models. By integrating vascular biology, quantitative imaging, and mathematical modeling across complementary experimental models, this work provides a multiscale understanding of how β-adrenergic signaling regulates tumor behavior. Beyond elucidating the mechanisms underlying propranolol response, this interdisciplinary framework may identify quantitative biomarkers of tumor organization and migration to improve patient stratification and support the development of more effective therapeutic strategies for angiosarcoma.

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P32 - A novel chronic phase model of chronic myeloid leukemia reveals early expansion of BCR::ABL1+ stem cells and progressive suppres

Elodie Richard | *BRIC*

To establish a physiologically relevant, chronic phase model of chronic myeloid leukemia (CML), we established a transgenic model that permits inducible expression of a tetracycline-regulated BCR::ABL1 transgene within a fraction of hematopoietic stem cells (HSCs). In this model, induction of Cre activity results in differential fluorescent labeling of, and thus the distinction between, normal hematopoietic cells (Tomato+ GFP-) and those that express BCR::ABL1 (Tomato+ GFP+). Longitudinal analysis of transgenic animals upon induction of BCR::ABL1 expression revealed the development of disease that included increased numbers of platelets and white blood cells, expansion of granulocytes, appearance of blast-like cells, and splenomegaly characterized by infiltration of neutrophils, all key features of chronic phase human CML. Short-term and single-cell transcriptomic analyses revealed the significant impact of BCR::ABL1 expression on both the timing and patterns of differentiation, including the rapid expansion of aberrant stem cells, attenuation of normal hematopoiesis, and perturbations in signaling networks of both normal and BCR::ABL1+ stem and progenitor cells. Our transgenic model thus enables simultaneous tracing of BCR::ABL1+ and normal hematopoietic cells within the same animal, providing insight into not only the kinetics but also the cellular and molecular players driving disease. This model represents a powerful platform for investigating leukemic stem cell biology in chronic phase CML and may ultimately facilitate studies aimed at understanding disease persistence and treatment-free remission.

P33 - A novel FKS1 mutation in Candida parapsilosis reveals a critical role for MKC1 in caspofungin resistance

Maxime Lefranc | *MFP*

Background: Caspofungin is an echinocandin antifungal that inhibits β-1,3-glucan synthesis in the fungal cell wall. An echinocandin-resistant Candida parapsilosis bloodstream isolate was recovered from a patient who had undergone allogeneic hematopoietic stem cell transplantation. The FKS1 gene, encoding the catalytic subunit of glucan synthase, harbored a heterozygous mutation resulting in I1380T substitution in addition to the naturally occurring P660A polymorphism.
Methods and Results: When introduced at the corresponding positions in the Fks1p protein of C. lusitaniae, P642A and I1359T, alone or in combination, it resulted in 6-, 12-, and ≥256-fold increases in the caspofungin minimum inhibitory concentration (MIC), respectively. The mutant strains also showed increased susceptibility to cell wall stressors, including calcofluor white and Congo red. Analysis of the Cell Wall Integrity (CWI) pathway by RT-qPCR and Western blotting revealed increased expression of MKC1 and constitutive Mkc1p activation in I1359T-containing strains, even in the absence of caspofungin. Deletion of MKC1 restored caspofungin susceptibility in C. lusitaniae, demonstrating that CWI pathway activation is a key determinant of caspofungin resistance in these mutants. Confirmation was obtained in the clinical C. parapsilosis isolate carrying the Fks1 P660A/I1380T substitutions: CRISPR-Cas9-mediated deletion of MKC1 restored caspofungin susceptibility to a level comparable to that of the FKS1 wild-type strain.
Conclusions: These findings suggest that FKS1 mutations associated with echinocandin resistance may have effects beyond altering drug–target affinity. In addition to reducing echinocandin susceptibility, these mutations may trigger constitutive activation of the CWI pathway, potentially acting as a stress signal that promotes cellular adaptation and contributes to caspofungin resistance. Mkc1p therefore emerges as a critical component of the resistance mechanism and as a potential target for further investigation.

P34 - Influence of membrane permeability on chronological lifespan

Larisa Venkova | *IBGC*

Quiescence is one of the most common states in nature. It is characterized by a reversible exit from the cell cycle and a drastic reduction of a large panel of cellular functions, from metabolic activity to gene expression. Yeast cells enter quiescence in response to environmental cues, and their ability to resume growth when re-exposed to favorable conditions decreases with time, a phenomenon referred to as chronological aging. Interestingly, recent studies show that cells experience dramatic changes in their physical properties upon quiescence entry and exit. Using fission yeast as a model, my project investigates whether this massive alteration of cell biophysics critically impacts cell physiology and chronological lifespan. Remarkably, we found that the expression of the single aquaporin water channel (Aqp1)-encoding gene is strongly increased in quiescent S. pombe cells, suggesting that modulation of membrane permeability to water may be intimately linked to aging. Consistent with this idea, I then demonstrated that aqp1 overexpression improves chronological lifespan. Combining yeast genetics, live-cell imaging and aging assays, I next showed that modulation of Aqp1 levels alters the fraction of aging cells that display autophagosomes. Moreover, my results revealed that quiescent cells with autophagosomes re-enter the cell cycle faster and at a higher rate than cells in which autophagosomes cannot be detected, and this correlates with the aging profile of these populations. Interestingly, autophagosome formation has been shown to rely on phase separation, which is altered by macromolecular crowding. Therefore, my working hypothesis is that increasing membrane permeability through increasing Aqp1 levels changes intracellular density, thereby promoting autophagosome formation and aging. Taken together, my data provide new insights into the way modulation of cell physical properties may impact chronological aging.

P35 - Understanding the role of mitophagy in glioblastoma

Maxime Toujas | *BRIC*

Glioblastomas (GB) are highly aggressive and resistant tumors with intra-tumor heterogeneity and a high rate of adaptation that ultimately cause relapse.
As GBs are known to be highly dependent on oxidative phosphorylation (OxPhos), our work focuses on understanding the implication of mitochondrial degradation through autophagy (mitophagy) in GB by finding common and distinct roles of each major pathways (NIX-, BNIP3-, Parkin/PINK1-dependent mitophagy). Using 3D and in vivo models we show that mitophagy activation differs depending on tumor area. Moreover, using the Drp1 inhibitor Mdivi-1 and the autophagy inhibitor chloroquine (CQ) we show that mitophagy is implicated in GB aggressive features such as proliferation and invasion while fine tuning cellular respiration. Using a combination of transcriptomics and metabolomics, we highlight common roles of macro-mitophagy such as mesenchymal state maintenance, deregulation of the OxPhos, Myc and hypoxia pathways as well as deregulation of the purine metabolism. Besides, we also found that some pathways are strictly restricted to each form of mitophagy: NIX is a regulator of cell cycle checkpoints while Parkin is a key regulator of cellular motility and migration.
This work allow to propose that mitophagy activation in different tumor areas commonly promotes GB aggressive properties but can also regulate specific signaling pathways, suggesting that the targeting of both activation pathways of mitophagy can reduce GB progression.

P36 - The gut talks to the tumor: peripheral serotonin as a brake on glioblastoma progression

Maria Haykal | *IBGC*

Glioblastoma is the most lethal primary brain tumor in adults. Despite a standard-of-care combining surgical resection, radiotherapy, and chemotherapy, median survival remains below 15 months, and the 5-year survival rate does not exceed 5%, highlighting the need for novel therapeutic strategies. While the gut-brain axis has emerged as a regulator of systemic physiology, its role in brain tumor progression remains largely unexplored. Peripheral serotonin – produced at ~95% by intestinal enterochromaffin cells via tryptophan hydroxylase 1 (TPH1) – is a major gut-derived signal that does not cross the blood-brain barrier yet exerts systemic effects on immunity, tryptophan metabolism, and gut microbiota composition. Importantly, microbiota regulation of enterochromaffin cell activity and serotonin biosynthesis establishes a bidirectional crosstalk that may influence the brain.
Using an orthotopic glioblastoma model in TPH1 knockout mice, we show that the absence of peripheral serotonin accelerates intracranial tumor growth as early as day 7 post-implantation. Complementary ex vivo analyses reveal that enterochromaffin cells are depleted of serotonin at baseline in KO mice. Strikingly, both EC cell serotonin content and circulating serotonin are partially restored upon tumor implantation in KO mice, suggesting a tumor-driven, TPH1-independent compensatory mechanism. Metabolomics identified alterations in the tryptophan/kynurenine pathway and microbiota-derived metabolites in KO mice. Immunofluorescence analyses of the brain reveal alterations in cholinergic and nitrergic neuronal populations, pointing to a central nervous system response downstream of peripheral serotonin depletion. Together, these data support a model in which gut-derived serotonin modulates glioblastoma progression through the gut-brain axis, opening new therapeutic perspectives centered on serotonergic targets.

P37 -Targeting mitochondrial complex I to reshape pro-tumoral macrophage function in glioblastoma

Annamaria Regina | *BRIC*

Glioblastoma (GB) remains one of the most lethal malignancies, largely owing to therapy resistance and inevitable recurrence driven by glioblastoma stem cells (GSCs). Tumor-associated macrophages (TAMs), including “M2-like” pro-tumoral and immunosuppressive macrophages, are major components of the GB tumor microenvironment and contribute to tumor progression, immune suppression, and therapeutic resistance. Although mitochondrial metabolism is increasingly recognized as an important regulator of macrophage activation and function, the contribution of mitochondrial complex I to pro-tumoral macrophage states in GB remains poorly understood.
We recently demonstrated that targeting mitochondrial complex I affects the stemness and therapeutic response of GB CSCs. We are now investigating its effects on the GB tumor microenvironment, with a particular focus on the metabolic and functional properties of “M2-like” macrophages. Specifically, we are assessing whether pharmacological inhibition of mitochondrial complex I with mubritinib alters macrophage bioenergetics, polarization-associated markers, and functional properties. Bone marrow-derived macrophages (BMDMs) were polarized toward an “M2-like” phenotype and treated with mubritinib, followed by assessment of mitochondrial respiration and macrophage functional markers.

Preliminary observations suggest that complex I inhibition modifies macrophage bioenergetics and may alter their polarization state, supporting mitochondrial metabolism as a potential vulnerability of pro-tumoral myeloid cells. Ongoing studies will determine how macrophage metabolic reprogramming influences their crosstalk with GB cells and reshapes the immune landscape of the tumor microenvironment. Ultimately, this work may provide a rationale for combining mitochondrial complex I inhibition with standard-of-care treatments and immune-directed therapeutic strategies in GB.

P38 - Deciphering PI3K inhibitor resistance mechanism to guide rational combination therapies in metastatic gastric cancer

Joaquim Javary | *BRIC*

Gastric cancer (GC) is a major global health burden, ranking 5th in incidence and mortality, with most patients diagnosed at advanced/metastatic stages, where treatment options are limited. Metastasis, driven by cancer stem cells (CSCs), is the main cause of GC mortality. PI3K signaling is frequently dysregulated in GC and mainly in metastatic forms. Although PI3K inhibitors such as Alpelisib show promise, resistance is likely to emerge, as seen with most monotherapies, through poorly understood mechanisms in CSCs. This project aims to uncover PI3K inhibitor resistance mechanisms in metastatic GC and identify rational combination therapies to overcome them. We first validated in vitro that Alpelisib reduces viability of GC cells MKN45, YTN16, AGS and MKN1, either mutated for PIK3CA or not, with an IC50 around 1µM. Moreover, Alpelisib reduces the expression of EMT and CSCs markers in GC cells. More importantly, Alpelisib fonctionnally impairs CSCs capacities of GC cells by reducing the number and the size in tumorspheres assay, even after curative treatment of already established tumorspheres. However, long-term follow-up of Alpelisib-treated tumorspheres revealed the emergence of resistance, as expected. Using predictive orthotopic GC mouse models, cell barcoding, scRNAseq, and CRISPR-Cas9 screening, we will identify the genes, pathways, and CSC populations involved in resistance. Candidate mechanisms will be functionally validated and compared with patient-derived metastatic samples to ensure clinical relevance. Rationnal combination strategies will then be assessed in preclinical models. This integrative approach should reveal biomarkers and therapeutic targets to improve treatment and survival in metastatic GC patients.

P39 - From astrocytes to tumor cells: the role of the mtCB1 receptor in glioblastoma

Hind Ibork | *BRIC*

The cannabinoid receptors type-1 (CB1), one of the most abundant G protein-coupled receptors in the central nervous system. CB1 is functionally associated with mitochondrial membranes (mtCB1) in multiple types of brain cells, thereby governing their energy fluxes. In astrocytes, mtCB1 stimulation impairs mitochondrial activity by decreasing Complex I-dependent respiration and lactate production. This last process occurs through destabilization of the N-module of Complex I, reduction of ROS production, and consequent degradation of hypoxia inducible transcription factor (HIF-1α), ultimately leading to downregulation of glycolytic enzymes. Furthermore, CB1 is expressed within glioblastoma (GBM), an aggressive and incurable form of brain malignancy characterized by robust metabolic adaptability, which makes targeting a single pathway ineffective. Extensive in vitro and in vivo investigations have demonstrated the substantial impact of cannabinoids on tumor growth and invasive properties; however, the exact mechanisms are not fully understood. Despite empirical observations highlighting the pro-apoptotic effect of CB1 agonists, their role in mitochondrial functions and in cancer cell metabolism has remained an area of limited exploration. Preliminary findings suggest the presence of mtCB1 in mouse and patient-derived GBM cells, where it can control mitochondrial oxygen consumption and lactate production in a manner similar to what has been described in astrocytes. These results underscore its potential as a compelling target for disrupting cancer cell metabolism and crucial actor in the anti-glioma effect of cannabinoids. Given its capacity to modulate both oxidative phosphorylation and glycolysis, mtCB1 emerges as an intriguing candidate for therapeutic intervention within the context of GB and its complex metabolic environment.

P40 - Deciphering Acute Myeloid Leukemia Cell Plasticity and AXL Associated Programs in the Hematopoietic Niche

Anne Berger | BRIC

Although remission rates in acute myeloid leukemia (AML) are increasing, its incidence has doubled over the past twenty years while five-year survival and relapse rates remain unimproved. Relapse is driven by the bone marrow microenvironment, where leukemic cells exploit a low O2 stromal niche to survive, evade the immune system and resist treatment. Uncovering these niche-mediated mechanisms is key to targeting microenvironment-driven persistence.
Using bone marrow modeling (1 to 3% O_2 and co-culture with HS27 stromal cells), transcriptomic analysis by RNASeq shows a large modification of expression and confirm AX Lover expression (Dumasetal,2019,2021).
In these niche conditions, we identified both invitro and ex vivo the overexpression of AXL and AXL proteolysis generating an internal cellular domain (ICD) which is localized in the nucleus. To decipher what roles AXL-ICD play in the nucleus, we express AXL-ICD with or without Histidine-Tag and perform ICD immunoprecipitation on nuclear fraction from AML cells cultured in the niche conditions.
Our results show that low O2 concentration and stromal interactions enhanced pro-survival and growth factor signaling, CAM-DR-associated adhesion and quiescence, and anti-apoptotic defenses, notably through BCL2A1 and HSPA1B. The niche also reinforced leukemic stem cell-associated programs and plasticity suggested by AXL-ICD interactome, emphasizing bone marrow microenvironment as a key driver of AML persistence and therapeutic resistance.

P41 - Disassembly of the HIV-1 integration complex: a role for TAR RNA

Carole Bertinetti | MFP

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Host chromatin invasion by retroviruses relies on their stable integration into the chromosomes of infected cells. Integration is catalyzed by the integrase protein (IN) within the Strand Transfer Complex (STC). Completion of the integration process requires then the disassembly of the STC and the DNA damage repair at the insertion site. These post-integration disassembly steps remains poorly known.
IN protein carries additional functions including binding to the genomic viral RNA, especially to the trans-activator response (TAR) region. Mutations in the IN carboxyl-terminal domain known to bind RNA affect both IN stability at the integration site and transcription of viral genes (Winans and Goff, 2020). Furthermore, recent findings demonstrate that the binding of IN to TAR RNA induces structural changes in both IN and TAR in addition to enhance Tat binding to TAR potentially optimizing the viral transactivation (Rocchi et al., 2022).
Based on these data, we proposed that the binding of TAR to IN may occur just after integration, leading to STC destabilization and promoting its dissociation from the nucleosomal site.
The in vitro dissociation assays revealed that RNA, but not DNA, efficiently promotes STC disassembly on nucleosomal templates. Among the nucleic acid structures tested, the HIV-1 TAR RNA exhibited the strongest dissociation activity, selectively releasing integrase and LEDGF/p75 from the integrated nucleosomal product without altering chromatin integrity. TAR mutants defective in integrase interaction failed to promote STC disassembly. Furthermore, we performed in cell kinetics analyses of key steps of the viral life cycle as reverse transcription, integration and transcription in K562 cells. For the first time, we monitored STC disassembly kinetics in cells by quantifying integrase–viral DNA interactions using ChIP-qPCR and with a TAR mutant virus, we observed a delay in integrase disassembly compared to the wild-type virus. Although additional conditions need to be tested to further clarify post-integration events as well as pharmacological approaches targeting this process.
Our work highlights a novel functional interplay between HIV-1 integration and transcription, which requires precise coordination to ensure the optimal invasion of host chromatin by the virus. If the disassembly of the HIV integration complex by TAR RNA proves to be critical in the viral life cycle, the pharmacological approach could lead to the discovery of a new antiviral drug.

P42 - Structure-function characterization of Gtwin endogenous retrovirus integration

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The human genome is under constant threat from invasion by mobile genetic elements, such as retroviruses and retrotransposons. The majority of eukaryotic genomes contain numerous transposable elements (TEs). If these elements are activated, they can relocate within the host genome or even multiply, significantly increasing the risk of harmful genetic changes. One might expect that natural selection would have eliminated these genomic intruders. Surprisingly, they are prevalent in eukaryotic genomes, suggesting a coexistence between host and parasite that can sometimes resemble a symbiotic relationship. Examining how a host genome responds when these parasites invade, including identifying where they insert themselves and the regions where they become active while maintaining host survival, represents a fundamental question in biology. Indeed, answering this question is vital for comprehending the true impact of TE insertions on the function of the host genome. Our RehosTE project seeks to elucidate the functional relationships between host genomes and endogenous retrovirus (ERV) integration, using Drosophila as a model system in collaboration with the Institut de Génétique Humaine (IGH) in Montpellier. Our focus is on the Gtwin ERV integrase (IN), a key viral enzyme responsible for inserting retroviral DNA into the host genome.

Through structural and functional characterization, we have uncovered critical insights into Gtwin IN's integration mechanics and chromatin-binding properties. X-ray crystallography revealed that the putative catalytic domain of Gtwin IN adopts a fold characteristic of the DDE retroviral integrase family, confirming its evolutionary and functional kinship with other retroviral INs. In vitro integration assays using reconstituted nucleosomes demonstrated that Gtwin IN efficiently catalyzes the insertion of viral sequences into both naked DNA and nucleosomal templates. This allowed us to define its chromatin structure preferences and map the functional interfaces through which Gtwin IN associates with the nucleosome surface. To further probe its chromatin engagement, we employed a direct Chromosome Binding Assay (diCBA) setup in our team, which confirmed Gtwin IN's intrinsic chromatin-binding function. Preliminary proteomic analyses led us to propose Pontin, a cellular AAA+ ATPase, as a putative chromatin-targeting factor for the Gtwin intasome complex. Its role in Gtwin chromatin targeting and integration is currently under investigation.

By comparing this new integration model with other retroviral systems studied in our team, we reinforce the concept that retroviral INs act as multifunctional chromatin binders, scanners, and potential «»readers»»—capable of interpreting chromatin cues to optimize integration. Intriguingly, our findings suggest that host cells may co-opt these viral mechanisms to regulate and balance genome invasion, ensuring a controlled integration process.

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