Colloque I3M 2026

PariSanté Campus
Paris 15ème

Programme et Inscriptions
i3m2026.sciencesconf.org

24 mars 2026

Inserm

Institut thématique Immunologie, inflammation, infectiologie et microbiologie

Colloque I3M 2026

PariSanté Campus

24th March 2026

Inserm

Institut thématique Immunologie, inflammation, infectiologie et microbiologie

9h15 - 9h30 — Introduction : Yazdan Yazdanpanah

Session 1 — Immunology and Inflammation

9h30 - 10h15 — Keynote : Liza Konnikova *Yale School of medicine*
Rethinking early life immunity, small but mighty

10h15 - 10h35 — Carine Meignin *Université de Strasbourg*
Evolution of STING-dependent immunity: learning from drosophila flies

10h35 - 11h00 — Coffee Break

11h00 - 11h20 — Yonatan Ganor *Institut Cochin*
Neuroimmune interactions between LCs and nociceptors in health and disease

11h20 - 11h40 — Nathalie Mielcarek *CIIL - Centre d'infection et d'immunité de Lille*
From pertussis to the next pandemic respiratory pathogen X, nasal vaccines could be the answer

11h40 - 12h00 — Sonia Elder *Institut Cochin*
Investigating macrophage-nerve crosstalk in homeostasis and post-stroke spontaneous urinary tract infection

12h00 - 12h30 — Flash Talks

12h30 - 14h30 — Lunch and Poster Session

14h10 - 14h30 — Aude Raimbault *Cellule Europe Inserm*
Opportunités de financements européens pour 2027

Session 2 — Infectious Diseases and Microbiology

14h30 - 14h50 — François Rousset *CIRI - Centre International de Recherche en Infectiologie*
What phage-bacteria interactions teach us about innate immunity

14h50 - 15h10 — Dulce Ferraz *Université de Lyon 2, RESHAPE Inserm U1290*
Social Sciences and Infectious Diseases: What Contributions to Current Challenges?

15h10 - 15h30 — Sarah Delliere *Hôpital Saint-Louis, AP-HP, Institut Pasteur*
Emerging challenges of antifungal-resistant dermatophytosis caused by Trichophyton indotineae

15h30 - 16h00 — Coffee Break

16h00 - 16h20 — Prajwal Kargal Gopalakrishna *Université Paris-Saclay, Inserm, CEA, IDMIT/UMRS1184*
An Ex Vivo Intestinal Tissue Model to Investigate Mechanisms of Sexual Transmission of Monkeypox Virus

16h20 - 17h05 — Keynote : Mohamed-Ali Hakimi *INSERM (DRCE) - Université Grenoble Alpes*
Decoding the Epigenetic Blueprint Behind Toxoplasma (Pre)sexual Commitment and Chronic Persistence

Présentations de 15 min
Sélection sur Abstract

Investigating macrophage-nerve crosstalk in homeostasis and post-stroke spontaneous urinary tract infection

Sonia Elder * [1,2,3], Laura Ramirez-Finn [1,2,3], Laura Mcculloch [4], Molly A Ingersoll [1,2,3]

[1] [Institut Cochin] Departement Infection, immunité, inflammation – Institut cochin – France
[2] Institut Pasteur – Institut Pasteur de Paris – France
[3] Université Paris Cité – Université Paris Cité, Université Paris Cité, Université Paris-Cité – France
[4] University of Edinburgh, Institute of Regeneration and Repair South – Royaume-Uni

Urinary tract infection (UTI) is one of the most common bacterial infections, affecting > 400 million individuals annually, worldwide. Unexpectedly, UTI is also the most common complication after stroke and occurs in up to 40% of patients. This suggests there may be a dysregulation between the bladder and the brain, however this connection is poorly understood. Interestingly, stroke causes striking changes to the immune compartment, including macrophages, outside the brain in peripheral organs. As a result, stroke patients experience increased susceptibility to infection, alongside systemic inflammation, which is associated with neurological decline. In other mucosal organs, neurons are in direct contact with tissue-resident macrophages and modulate their function during infection. Whether bladder macrophages are modulated by local or distal nerves during infection or stoke is unclear. Here, we use a mouse model of experimental UTI alongside a model of ischemic stroke, which gives rise to spontaneous UTI, to investigate bladder macrophages in homeostasis, infection, and during acute stroke recovery. We assess the impact of infection and stroke on bladder macrophage-nerve crosstalk, including bladder macrophage subset phenotype and subsequent susceptibility to additional UTI. Using 3D -imaging we found that bladder macrophages are associated with both nerves and blood vessels in the bladder in homeostasis and following infection. Furthermore, using bulk RNA sequencing of macrophage subsets, we saw that the expression of genes involved in bladder-nerve and bladder-blood vessel crosstalk in macrophages remain altered up to 6 weeks post-infection. Additionally, mice subjected to transient middle cerebral artery occlusion (MCAO) develop spontaneous infection characterized by presence of bacteria in the bladder and urine, which differs between the sexes. This was accompanied by the downregulation of MHCII in specific macrophage and dendritic cell subsets 48 hours after stroke, suggesting functional impairments in immune responses to bacterial infection. Taken together, we hypothesize that changes in macrophage-nerve and macrophage-blood vessel crosstalk after stroke alters macrophage response to infection.

Mots-Clés: Stroke, infection, nerves, blood vessels, macrophages

*Intervenant

An Ex Vivo Intestinal Tissue Model to Investigate Mechanisms of Sexual Transmission of Monkeypox Virus

Prajwal Kargal Gopalakrishna * [1], Sophie Luccantoni [1], Quentin Pascal [1], Audrey Ferrier [2], Cécile Herate [1], Francis Relouzat [1], Jean Nicolas Tournier [1], Roger Le Grand [1], Mariangela Cavarelli [1]

[1] Immunological diseases, microbiology and innovative therapies (IDMIT/UMRS1184); Fontenay-aux-Roses Le Kremlin-Bicêtre, France – Université Paris-Saclay, Inserm, CEA – France
[2] Microbiology and infectious diseases department, France – Institut de Recherche Biomédicale des Armées [Brétigny-sur-Orge] – France

The recent monkeypox (mpox) outbreak has highlighted the importance of sexual transmission in monkeypox virus (MPXV) dissemination, particularly through anorectal exposure. Despite strong epidemiological evidence, the early mucosal events governing viral entry, local replication, and initial host–pathogen interactions remain poorly understood. Addressing these questions requires experimental systems that preserve tissue architecture and immune complexity at sites of exposure.
We established an *ex vivo* infection model using non-human primate (NHP) tissues to investigate MPXV replication and cellular tropism along the intestinal tract. Fresh explants from anus, rectum, sigmoid colon, and jejunum were exposed to MPXV clade IIb under controlled conditions using an air–liquid interface (ALI) culture system, with skin serving as a reference tissue. This approach preserves tissue architecture and resident immune populations, enabling the analysis of viral dynamics within a physiologically relevant microenvironment.

Viral replication was quantified by infectious titration, and tissue susceptibility was assessed using RNAscope combined with immunohistochemistry to localize viral RNA within defined cellular compartments. Productive infection was detected in mucosal tissues, and spatial analyses revealed an association between MPXV-positive cells and tissue macrophages. These observations suggest a potential role for resident myeloid populations in early viral amplification and/or local persistence, warranting further mechanistic investigation.
This *ex vivo* NHP model provides a translationally relevant framework to dissect early events in MPXV sexual transmission and establishes a foundation for identifying cellular determinants of mucosal infection and targets for preventive intervention.

Mots-Clés: Monkepox (Mpox), Sexual transmission, Mucosal immunity, Ex vivo tissue explant culture, Non, human primate (NHP) model

*Intervenant

Posters
Sélection sur Abstract

# Poster	Nom	Titre de poster
1	Gauduin Maeva	A Neisseria-specific surface lipoprotein contributes to endothelial dysfunction and lethality in invasive meningococcal disease
2	Sereme Youssouf	A novel cystic fibrosis-mimetic Pseudomonas auxotrophic vaccine is protective in vivo and is associated with Th17 and IgA mucosal immunity
3	Stretcu Madalina	Characterisation of the inflammatory response and its impact on brain damage during Streptococcus agalactiae meningitis
4 Flash	Rémont Pauline	Characterization of AI-designed peptides targeting the FtsQBL complex of the cell division machinery of Escherichia coli
5	Lippens Léa	Characterization of gamma delta T cells in Autoimmune Myasthenia Gravis
6	Petitpre Charles	Compartmentalized cytotoxic CD4 T cell responses in anti-Yo paraneoplastic cerebellar degeneration
7 Flash	Cazaubieilh Mathilde	Constitutive expression of ISGs shapes the intrinsic antiviral immunity of brain endothelial cells
8	Babise Manon	Decoding the local short-term immune response induced by the yellow fever vaccine at the injection site.
9	Sabino Albaniza	Evaluation of the potential of Saccharomyces cerevisiae extracellular vesicles for antifungal vaccine development
10	Marion Huré	Fighting Inflammatory Bowel Diseases with mutualistic bacteria isolated from the gut microbiota
11	Pothlichet Julien	Human Papillomavirus 18 replication reshapes innate immune receptors expression in 3D epithelial cultures
12	Dos Santos-Toinet Camille	Identification and characterization of a novel Chlamydia trachomatis growth inhibitor
13	Dauvilliers Annouk	IgA-mediated phagocytosis of mucosally acquired viruses stimulates innate memory in effector phagocytes, providing protection against subsequent, unrelated viral infections
14 Flash	De Laval Bérengère	Immunobiography of hematopoietic stem cells
15	Richier Quentin	Impaired type I interferon response early after SARS-CoV-2 infection is associated with the occurrence of persistent COVID-19 in solid organ transplanted recipients.
16	Camard Marion	Major depressive episodes and psychiatric symptoms among HIV controllers compared with antiretroviral-treated people living with HIV
17	Cormontagne Delphine	Mfd, a multifunctional protein as a new target for the development of innovative antimicrobials
18	Pukar KC	Microbiome-Mediated Regulation of Monocyte Differentiation by Dietary Cholesterol Restrains Enteropathogen Dissemination.
19	Lecouffe Aurane	Nasal nanoparticle vaccine induces a cross-strain immune response against Toxoplasma gondii
20	Haigh Oscar	NK-cell-dependent immune conditioning during HSV-1 latency establishment irreversibly biases trigeminal ganglion reservoirs toward non-reactivation

21 Flash	Motet Christian	*P. aeruginosa* complex infections treated with bacteriophage therapy in France: Experience from the "PHAGEinLYON Clinic" program
22	Hosmalin Anne	Plasmacytoid dendritic cell discrete subpopulations with contrasting functions are elicited by CD4+ T cells infected or not by HIV-1 or HIV-2
23	Jacoutot Manon	Proinflammatory strains of Mediterraneibacter gnavus are enriched during spondyloarthritis (SpA) and modulate disease during experimental SpA
24	Dégardin Maurane	Role of the SucBA metabolic complex in biofilm formation and flea-borne transmission of Yersinia pestis
25	Schimmich Cécile	Set-up of non-human primate precision cut lung slices: an ex vivo model to study infectious respiratory diseases
26	Da Silva Teixeira Igor	Superinfection Interference of Insect-Specific Virus GUAPV in Chikungunya Virus Replication in Mosquito Cell Lines
27	Bordas Clément	The gut microbiota as a determinant of host susceptibility to respiratory infection in old individuals
28 Flash	Sakanwi Joy	The impact of prenatal maternal stress on antitumoral immune responses in offspring: toward an exposome-driven understanding of immune programming
29	Provôt Quentin	The lysosomal glutamine transporter SLC38A7/SNAT7 modulates SAMHD1 antiviral activity and promotes HIV-1 production in human macrophages.
30	Coux Rémi-Xavier	Tlr7-biallelism defines a hyperfunctional state of female B lymphocytes
31	Fremont-Debaene Zoé	One virus, multiple strategies: how the common cold virus inhibits macrophage secretion

A Neisseria-specific surface lipoprotein contributes to endothelial dysfunction and lethality in invasive meningococcal disease

Maeva Gauduin *[1], Isabel Dos Santos Souza [1], Youssouf Diallo [1], Jason Ziveri [1], Samuel Walter [2], Elodie Le Seac'h [1], Haniaa Bouzinba-Segard [1], Camille Faure [1], Taliah Schmitt [3], Brigitte Izac [1], Franck Letourneur [1], Thomas Rattei [2], Xavier Nassif [4], Mathieu Coureuil [4], Philippe Morand [1], Sandrine Bourdoulous [1]

[1] Institut Cochin – Inserm U1016-CNRS UMR8104-Université Paris Cité – France
[2] University of Vienna, Centre for Microbiology and Environmental Systems Science – Autriche
[3] Clinique Sainte Geneviève – - – France
[4] Institut-Necker-Enfants-Malades – Inserm, CNRS, Université Paris Cité – France

Neisseria meningitidis is a human nasopharyngeal commensal that can cause invasive diseases such as meningitis and fatal sepsis upon bloodstream invasion. A critical step in meningococcal pathogenesis is the adhesion to human endothelium via Type IV pili (T4P), which triggers endothelial dysfunction and can lead to fatal outcomes. T4P are dynamic filamentous structures that rapidly elongate and retract, enabling bacterial motility, competence and host cell interactions. Emerging evidence indicate that T4P retraction acts as a mechanical signal in both bacteria and host cells. However, the consequences of this process in disease progression remain poorly understood.
Using a humanized mouse model of invasive meningococcal disease, consisting in SCID mice grafted with human skin, we recently demonstrated that a retraction-defective meningococcal strain (*pilT)* failed to induce lethality, despite achieving vascular colonization and systemic inflammation comparable to the wild-type strain (WT). This strongly suggested that T4P retraction potentiates bacterial virulence. Transcriptomic analysis of the WT and *pilT* strains during *in* vivo infection revealed 20 transcripts significantly more abundant in the WT strain, including a putative surface-exposed lipoprotein (Lp). Given the established role of surface-exposed lipoproteins (SLPs) in meningococcal virulence, we investigated the function of Lp during infection.

Structural analysis revealed that Lp is unique to the *Neisseria* genus, with no homology to known protein structures and exhibits typical SLP features. Unlike other characterized SLPs that contribute to bacterial survival, host colonization or evasion, Lp expression was not required for bacterial growth or colonization of host microvascular endothelial cells. However, Lp deletion significantly reduced endothelial cell alterations and death *in vitro*. *In vivo*, Lp deletion attenuated vascular alterations, thrombosis, signs of acute organ injury and lethality, without affecting bacteremia, systemic inflammation or vascular colonization. Conversely, Lp overexpression exacerbated vascular damage, organ injury and lethality. Current work aims at characterizing candidate endothelial receptors for this novel SLP.
These findings identify Lp as a novel virulence factor that uniquely drives vascular dysfunction and progression to lethal sepsis.

Mots-Clés: Neisseria meningitidis, surface lipoprotein, endothelial dysfunction, sepsis, virulence factor

*Intervenant

A novel cystic fibrosis-mimetic Pseudomonas auxotrophic vaccine is protective in vivo and is associated with Th17 and IgA mucosal immunity

Youssouf Sereme1,2,¶,*,Bérengère Villeret1,2,¶, Ségolène Caboche3,Samuel Ikeh1,2, Delphyne Beury3, Florence Maurier3, Christophe Desterke4, Maëlys Born-Bony 1,2, Zhou Xing5,6, Romé Voulhoux7, Jean-Michel Sallenave1,2,*.

1) Institut National de la Santé et de la Recherche Médicale,
2) U1149 (Centre de Recherche sur l'Inflammation), Université Paris-Cité, Paris, France
3) Université de Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, US41-UAR 2014, F-59000, Lille, France
4) University Paris Saclay, Faculty of Medicine, INSERM UMRS-1310, Villejuif, France.
5) McMaster Immunology Research Centre, McMaster University, Hamilton, ON, Canada;
6) Department of Medicine, McMaster University, Hamilton, ON, Canada.
7) Laboratoire de Chimie Bactérienne LCB-UMR7283, CNRS, Aix Marseille Université, IMM, Marseille, France.

Pseudomonas aeruginosa (P.a) is a Gram-negative opportunistic pathogen that poses a major global health threat, particularly in immunocompromised individuals, patients with cystic fibrosis, and those with burn injuries or ventilator-associated pneumonia. Despite intense efforts, no vaccine is available for human use. In this context, live attenuated vaccines represent a promising but underexplored approach, offering the potential to elicit robust, long-lasting, and multifaceted immune responses including inducing trained immunity. Here, our rationale was to develop, for the first time to our knowledge, an auxotrophic P.a strain phenotypically as close as possible to clinical strains present in sputa secretions from patients with CF (pwCF), with reduced virulence while being robustly immunogenic. To that aim, we developed a live auxotrophic P.a vaccine ('V') by sub-culturing a genetically-modified P.a (ΔLasB-PAO1, (a P.a strain we have previously shown to have reduced virulence) in artificial sputum medium (ASM), a culture medium mimicking CF sputum. We show by RNA seq and whole genome sequencing that 'V' up-regulated pathways involved in energy metabolism, redox reaction, cofactor biosynthesis, biosynthetic precursors, stress response and virulence regulation in bacteria, closely mirroring the nutrient-restricted and redox-challenged environment of cystic fibrosis, by shifting metabolic resources from virulence toward a persistence mode of community behavior and survival. Furthermore, we showed that this vaccine was indeed auxotrophic, less virulent, had characteristics of 'small colony' CF-like strain, and had the ability to secrete high amounts of filamentous phages (mainly Pf4). Crucially, 'V' induced in vivo in mice both local (IgA) and systemic humoral responses as well as memory Th17 immune responses, and could, when administered in the lung, but not intra-muscularly, fully protect mice against a lethal PAO1-WT infection. Overall, the present study demonstrates that our vaccine formulation, in addition to providing an advantageous auxotrophic phenotype adapted to the CF setting, was efficient, when given mucosally, in preferentially inducing secretory IgA and Th17 pathway at mucosal surfaces, a critical barrier that neutralizes pathogens before tissue invasion.

Mots-Clés: Vaccine, P. aeruginosa, cystic fibrosis

*Intervenant

3

Characterisation of the inflammatory response and its impact on brain damage during Streptococcus agalactiae meningitis

Madalina Stretcu * [1], Julie Guignot [1]

[1] Institut Cochin – 1Institut Cochin, INSERM U1016, UMR 8104 CNRS, Université de Paris – France

Streptococcus agalactiae or Group B streptococcus (GBS) is the leading cause of neonatal meningitis, often resulting in neurological sequelae. We hypothesised that cerebral inflammation plays a significant role in the brain damage that causes sequelae. My project, based on a mouse model of GBS meningitis, aims to characterise the cerebral immune response, identify neuronal lesions and establish a causal link between inflammation and neuronal damage during GBS meningitis. While there is weak and delayed reactivity of brain immune cells (microglia), transcriptomic analyses (bulk RNA-seq and spatial transcriptomics) have revealed strong and early induction of the type I interferon (IFN-I) pathway throughout the brain. Cerebral vessels were identified as the main source of IFN-I, suggesting a pivotal role for cerebral endothelial cells. In addition, alterations in glutamatergic synapses were observed in several brain areas (cortex, thalamus, striatum). We have shown that these alterations do not result from a direct effect of bacteria on neurons, supporting an inflammatory origin. These alterations are no longer detected in mice lacking the IFN-I receptor, confirming the involvement of this pathway. Taken together, our findings provide new insights into the interaction between GBS and the central nervous system and may contribute to the development of new neuroprotective strategies in the long term.

Mots-Clés: Group B Streptococcus, Meningitis, Type I interferon

*Intervenant

Characterization of AI-designed peptides targeting the FtsQBL complex of the cell division machinery of Escherichia coli

Pauline Rémont *[1], Xiaosong Liu [1], Federico Croci [1], Ariel Mechaly [2], Minh Ha Nguyen [3], Iñaki Guijarro [3], Ahmed Haouz [2], Jeanne Chiaravalli [4], Daniel Ladant [5], Olivier Sperandio [1]

[1] Structural Bioinformatics Unit, Institut Pasteur, – Université de Paris Cité, CNRS UMR3528 – France

[2] Cristallographie (Plateforme) - Crystallography (Platform) – Institut Pasteur [Paris], Centre National de la Recherche Scientifique, Université Paris Cité – France

[3] Plateforme Technologique de RMN Biologique et HDX-MS - Biological NMR and HDX-MS Technological Platform – Institut Pasteur [Paris], Centre National de la Recherche Scientifique, Université Paris Cité – France

[4] Criblage chémogénomique et biologique (Plateforme) - Chemogenomic and Biological Screening Platform – Institut Pasteur [Paris], Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique, Université Paris Cité – France

[5] Biochimie des Interactions Macromoléculaires / Biochemistry of Macromolecular Interactions – Institut Pasteur [Paris], Centre National de la Recherche Scientifique, Université Paris Cité – France

The discovery of antibiotics has significantly improved public health. However, due to antibi-otic misuse and limited drug diversity, antimicrobial resistance has significantly risen. Despite the urgent need for new antibiotics, fewer are approved each year, and innovative approaches are required for combating Gram-negative bacteria (1). The bacterial divisome is an essential machinery for cell division and it is composed of more than 12 essential proteins. Among them, the core ternary complex FtsQ/FtsB/FtsL, represents a promising target for novel classes of an-tibiotics (2) . To inhibit the assembly of this core complex, we used RF diffusion (3), an artificial intelligence (AI)-based method, to design peptides targeting the FtsB binding site on the FtsQ protein from *Escherichia coli (4).*

The interactions between the designed peptides and FtsQ were characterized both in bacteria using a Bacterial Two-Hybrid (BACTH) genetic assay and *in vitro* using a Fluorescence Polarization assay (FP). Further optimizations were performed *in silico* to increase peptides affinity for FtsQ and positively charged amino acid were introduced to facilitate their penetration through bacteria cell wall. In parallel, peptides' binding site on FtsQ has been confirmed by X-ray crystallography. The impact of peptides on *E. coli*lptD4213 (imp) strain growth and cell morphology was assessed using phase contrast microscopy and OD-based culture monitoring. . The potential cytotoxicity of the peptides was measured using Luminescent Cell viability assay on MRC5 human cells.

We demonstrated that the designed peptides are specifically t argeting t he F tsB b inding s ite of FtsQ. In addition, the optimized peptides induce a cell elongation phenotype and growth inhibition of the lptD4213 (imp) *E. coli* strain. The best candidate targets FtsQ with an affinity of 0.1μM and has a Minimal Inhibitory Concentration of 6.25μM. In conclusion, our results show that the RF diffusion-designed p eptides c an i nteract s pecifically wi th th e Ft sB bi nding si te on FtsQ and interfere with the proper assembly of the divisiome leading to bacteria growth inhibition. These peptides are non-toxic for human cells. They thus represent good leads for the further development of potential cell division inhibitors.

Mots-Clés: Antimicrobial Resistance, Cell division, Artificial Intelligence, Peptides, Gram Negative

*Intervenant

5

Characterization of gamma delta T cells in Autoimmune Myasthenia Gravis

Léa Lippens * [1], Edouard Hemery [1], Frédérique Truffault [1], Anthony Behin [2], Antoine Gueguen [3], Elie Fadel [4], Dominique Gossot [5], Sophie Demeret [6], Rozen Le Panse [1]

[1] Association Institute of Myology, Center of Research in Myology, UMRS 974 – Sorbonne University, INSERM – France
[2] Referral center for neuromuscular disorders, Institute of Myology – AP-HP [Groupe hospitalier Pitié - Salpêtrière] – France
[3] Hospital Foundation Adolphe de Rothschild – Hospital Foundation Adolphe de Rothschild – France
[4] Marie Lannelongue Hospital – paris saclay university – France
[5] Montsouris Mutualist Institute – Montsouris Mutualist Institute – France
[6] Neuro-intensive care Unit, Sorbonne University – AP-HP [Groupe hospitalier Pitié - Salpêtrière] – France

Gamma delta ($\gamma\delta$) T cells have attracted considerable interest in cancer research, and an increasing number of studies start to report their involvement in autoimmune diseases. Myasthenia Gravis (MG), is characterized by muscle weakness caused by autoantibodies targeting the acetylcholine receptors at the neuromuscular junction. Previous work from our group revealed altered $\gamma\delta$ T-cell subpopulations in MG patients. Our aim is therefore to perform an in-depth study of $\gamma\delta$ T cells in MG, a disease associated with thymic abnormalities: lymphofollicular hyperplasia or thymoma.
$\gamma\delta$ T cells were analyzed by CyTOF in fresh whole blood from healthy controls (HC, n=8), MG (n=8) and corticosteroid-treated MG (n=7) patients. To increase cohort size and include thymoma patients, an optimized flow cytometry panel was applied on PBMC from HC (n=24), MG subgroups (n=43), and thymoma patients without MG (n=15). The same panel was used on thymocytes from HC (n=7) and patients with MG, MG with thymoma, or thymoma alone (n=17).

Our analyses revealed a decreased frequency of $\gamma\delta$ T cells in the thymus and the blood of MG patients, persiste after thymectomy. While thymoma did not affect overall $\gamma\delta$ T-cell abundance, it promoted an expansion of thymic Vδ1 cells and an inversion of the peripheral Vδ1/Vδ2 ratio.
Our analyses revealed a decreased frequency of $\gamma\delta$ T cells in the thymus and blood of patients with myasthenia gravis (MG), which persists after thymectomy. Although the thymoma did not affect the overall abundance of $\gamma\delta$ T cells, it promoted an expansion of thymic Vδ1 cells and an inversion of the peripheral Vδ1/Vδ2 ratio. The Vδ1 cells differentiated into TEMRA cells, which were identified as potentially cytotoxic via the presence of the CD57 marker based on WBC results.
These findings suggest that inflammatory and tumorous thymic environments remodel $\gamma\delta$ T cell differentiation.

Mots-Clés: Myasthenia Gravis, Thymoma, $\gamma\delta$ T cells, cytometry

*Intervenant

6

Compartmentalized cytotoxic CD4 T cell responses in anti-Yo paraneoplastic cerebellar degeneration

Charles Petitpre * [1]

[1] CIC CHU Lyon (inserm) – Université Claude Bernard Lyon 1, Institut National de la Santé et de la Recherche Médicale – France

Paraneoplastic cerebellar degeneration with anti-Yo antibodies (Yo-PCD) is a rare neurological disorder associated with breast and gynecological cancers. Although T cell–mediated immunity against Purkinje cell antigens CDR2/CDR2L has been implicated, the precise mechanisms remain undefined. Here, we applied single-cell RNA sequencing and paired T cell receptor profiling to cerebrospinal fluid (CSF) and peripheral blood mononuclear cells (PBMCs) from six Yo-PCD patients and five ovarian cancer patients without paraneoplastic disease, with additional controls from individuals with multiple sclerosis or idiopathic intracranial hypertension. PBMCs from both cancer cohorts exhibited pro-inflammatory signatures. However, uniquely in Yo-PCD, antigen-presenting cells (APCs) and regulatory T cells showed reduced expression of tolerance-associated genes, including key components of the TGF-β pathway. Moreover, Yo-PCD APCs showed compartment-specific programs, with peripheral APCs enriched for MHC-I and inflammatory mediators, whereas CSF APCs upregulated MHC-II and interferon-stimulated genes. Yo-PCD CSF subclustering revealed no disease-specific expansion of CD8 T cells. In contrast, CD4 cytotoxic T cells were clonally expanded, spanned graded cytotoxic states, expressed central nervous system homing signatures, and overlapped with helper T cell clones, consistent with local reprogramming. Supporting their pathological relevance, CD4 granzyme B T cells were identified in patient cerebellar tissue. Together, these findings define a dual-compartment immunopathology in Yo-PCD, highlighting CD4 cytotoxic T cells as biomarkers and therapeutic targets.

Mots-Clés: single cell RNA sequencing, Yo, PCD

*Intervenant

Constitutive expression of ISGs shapes the intrinsic antiviral immunity of brain endothelial cells

Mathilde Cazaubieilh * [1], Julian Buchrieser [2], Haniaa Bouzinba-Segard [3], Nicolas Perrière [4], Nicolas Vabret [5], Olivier Schwartz [6], Sandrine Bourdoulous [7]

[1] Vascular Cell Biology in Infection Inflammation and Cancer - Cochin Institute - INSERM U1016, Paris, France – Inserm U1016 – France
[2] Virus et immunité - Virus and immunity – Institut Pasteur [Paris], Université Paris Cité – Département Virologie, 25-28 rue du Docteur Roux - 75724 Paris CEDEX15, France
[3] Institut Cochin – Inserm U1016-CNRS UMR8104-Université Paris Cité – France
[4] BrainPlotting – - – France
[5] Icahn School of Medicine at Mount Sinai [New York] – États-Unis
[6] Institut Pasteur, Université Paris Cité, Virus and Immunity Unit – Institut Pasteur de Paris – France
[7] Institut Cochin (IC UM3 (UMR 8104 / U1016)) – Institut National de la Santé et de la Recherche Médicale, Université Paris Cité – 22 rue Méchain, 75014 Paris, France

The blood–brain barrier (BBB) is a highly specialized vascular interface that protects the central nervous system by tightly regulating exchanges between the blood and the brain parenchyma. Brain endothelial cells (BECs), which form the core of the BBB, constitute the first line of defense against blood-borne pathogens, including neurotropic viruses. However, the intrinsic molecular mechanisms by which BECs resist viral invasion remain poorly understood.
Here, we identified a constitutive antiviral program in BECs characterized by constitutive expression of interferon-stimulated genes (ISGs) in the absence of any exogenous stimulation. Comparative transcriptomic analyses of endothelial cells isolated from brain and skin microvasculature revealed a strong enrichment of ISGs in BECs

Cross-species single-cell transcriptomic analyses from six vertebrate species showed that this endothelial antiviral signature seems conserved across mammals but absent in non-mammalian species, suggesting an evolutionary link with BBB specialization. Developmental analyses of human fetal brains showed that ISG expression in BECs emerges early during embryogenesis and increases with postnatal maturation, paralleling BBB development. Consistently, in vitro exposure of human brain endothelial cells to shear stress, a key driver of endothelial differentiation and barrier formation, led to enhanced ISG expression.

Mechanistically, we show that tonic ISG expression in BECs partially depends on JAK1/2 signaling and IFNAR1 expression. Importantly, we identified endogenous transposable elements as potential intrinsic triggers of this antiviral state. Transposable element–derived transcripts are enriched in BECs, and pharmacological inhibition of endogenous reverse transcriptase activity reduced ISG expression, increased susceptibility to viral infection (Zika virus and Modified Vaccinia Ankara virus), and altered endothelial junctional organization.
Together, our findings reveal a previously unrecognized, intrinsic antiviral state of brain endothelial cells that contributes to BBB protection and may also participate in barrier maturation. This

*Intervenant

work highlights a novel link between endothelial innate immunity, genome-derived elements, and BBB integrity, with implications for neuroinvasion and neuroinflammatory diseases.

Mots-Clés: brain blood barrier, endothelial cells : transposable elements, anti, viral immunity, Interferon Stimulated Genes

8

Decoding the local short-term immune response induced by the yellow fever vaccine at the injection site.

Manon Babise * [1], Matthieu Maisch [1], Suzanne Figueiredo [1], Bénédicte Charmeteau-De Muylder [1], Yoann Martin [2,3], Benjamin Saint Pierre [4], Stevenn Volant [5], Anne Couëdel-Courteille [4], Rémi Cheynier [4], Giovanna Barba-Spaeth [6], Jacques Dutrieux [4]

[1] Université Paris Cité, Institut Cochin, INSERM U1016, CNRS, UMR8104 – Université Paris Cité, CNRS : UMR8104, Institut National de la Santé et de la Recherche Médicale - INSERM, Institut National de la Santé et de la Recherche Médicale - INSERM : U1016 – France
[2] plateforme GENOM'IC – INSERM U1016, Institut Cochin, CNRS UMR 8104, Université de Paris Cité – France
[3] Cancer Research and Personalized Medicine - CARPEM [Paris] – Hôpital Européen Georges Pompidou [APHP], Hôpital Cochin [AP-HP], Université Paris Descartes - Paris 5, Institut National de la Santé et de la Recherche Médicale, CHU Necker - Enfants Malades [AP-HP] – France
[4] Université Paris Cité, Institut Cochin, INSERM U1016, CNRS, UMR8104 – 1Institut Cochin, INSERM U1016, UMR 8104 CNRS, Université de Paris – France
[5] Institut Pasteur, Université Paris Cité, Bioinformatics and Biostatistics Hub, F-75015 Paris, France – Institut Pasteur de Paris – France
[6] Institut Pasteur, Unité de Virologie Structurale [Paris] (IP) – Université Paris Cité, CNRS UMR3569 – 25-28, rue du docteur Roux, 75724 Paris cedex 15, France

INTRODUCTION AND OBJECTIVES:
Yellow fever is a serious arbovirus disease endemic in Africa and South America. Due to urbanization and global warming, mosquito vectors are now colonizing new regions such as Europe. Although an effective vaccine (strain YF17D) provides lifelong protection with a single dose, global stocks remain limited. Our study aims to describe the early immune response induced in situ by this vaccination in order to better understand the mechanisms of protection initiation, which are still poorly understood.

MATERIALS AND METHODS:

A cohort of 29 healthy volunteers was recruited and vaccinated with the YF17D strain. Skin biopsies were taken 48 hours post-vaccination at the injection site and on the contralateral arm (viremia, RNAseq, HES, spatial transcriptomics). Longitudinal follow-up was performed by blood sampling up to 28 days post-vaccination (seroneutralization, cytokine assay, cytometry).

RESULTS AND CONCLUSION:

All vaccinated volunteers developed seroneutralizing antibodies within 14 days post-vaccination. Cutaneous RT-qPCR revealed viral genome in 7 vaccinees 48 hours after injection. No significant difference in vaccine efficacy was observed between these individuals and those in whom the virus was not detectable. In addition, a strong cellular infiltrate was observed at the injection site. The Bulk RNAseq profile shows massive induction of the immune response: IFN-stimulated genes,

*Intervenant

pro-inflammatory cytokines, antigen presentation, and JAK/STAT signaling pathways. These results were refined by spatial transcriptomics, allowing us to precisely map the expression of these markers at the histological level and characterize the immune infiltrate, thus confirming their specific expression within infected areas. We highlight the importance of the skin as the founding and initiating center of the protective and lasting immune response induced following infection by the YF17D vaccine strain.

Mots-Clés: Vaccine, Yellow Fever, Orthoflavivirus, Immune Response

9

Evaluation of the potential of Saccharomyces cerevisiae extracellular vesicles for antifungal vaccine development

Leandro Honorato [1], Albaniza Sabino * [1], Natalia Silva [1], Allan J. Guimarães [2], Leonardo Nimrichter [1]

[1] Universidade Federal do Rio de Janeiro [Brasil] = Federal University of Rio de Janeiro [Brazil] = Université fédérale de Rio de Janeiro [Brésil] – Brésil
[2] Universidade Federal Fluminense [Rio de Janeiro] – Brésil

Fungal infections represent an increasing global health concern, particularly among immunocompromised or seriously ill individuals. Despite advances in antifungal therapies, treatment options remain limited, highlighting the need for effective preventive strategies such as vaccines. Previous studies from our research group have demonstrated that fungal pathogens release extracellular vesicles (EVs) containing immunogenic molecules capable of inducing protective immune responses and that *Candida albicans* EVs activate phagocytes and can induce a protective response, promoting full protection against systemic candidiasis in immunosuppressed mice. However, the presence of virulence factors in EVs derived from pathogenic fungi may limit their applicability as vaccine candidates, especially considering that this fungus is part of the human microbiota. Therefore, this study aimed to evaluate the potential of EVs produced by *Saccharomyces cerevisiae*, a non-pathogenic yeast, as a vaccine platform against systemic fungal infections. Initially, the protective capacity of *S. cerevisiae* EVs was assessed using the *Galleria mellonella* model. Larvae were immunized with optimized concentrations of EVs and subsequently challenged with clinically relevant fungal pathogens, including *C. albicans*, *Candida auris*, *Cryptococcus neoformans*, *Candida parapsilosis*, *Histoplasma capsulatum*, and *Sporothrix brasiliensis*. Survival was monitored daily to evaluate protection. Following the observation of protective effects in the insect model, the immunoprotective potential of *S. cerevisiae* EVs was further evaluated in a murine model. Eight-week-old BALB/c mice were immunized intraperitoneally with EVs four times at one-week intervals. One week after the final immunization, mice were challenged intraperitoneally with lethal doses of *C. albicans* or *C. auris*, and survival was monitored. In the *G. mellonella* model, immunization with *S. cerevisiae* EVs resulted in 100% survival following challenge with C. albicans, 60% survival with *C. neoformans* and *C. parapsilosis*, 40% survival with *C. auris* and *H. capsulatum*, and 30% survival with *S. brasiliensis*. In the murine model, EV-immunized mice exhibited 80% survival following *C. albicans* infection, whereas no significant protection was observed against *C. auris*. Overall, these findings demonstrate that *S. cerevisiae* EVs confer cross-protective effects against multiple fungal species and support their potential application as a safe and promising platform for antifungal vaccine development.

Mots-Clés: Extracellular vesicles, antifungal vaccines, Saccharomyces cerevisiae

*Intervenant

10

Fighting Inflammatory Bowel Diseases with mutualistic bacteria isolated from the gut microbiota

Noémie Gloanec [1,2], Marion Huré [2,3], Moïse Coëffier [2,4,5], David Ribet * [2,4]

[1] U1073-Nutrition, Inflammation et axe Microbiote-Intestin-Cerveau – Université de Rouen Normandie, Institute for Research and Innovation in Biomedicine, Institut National de la Santé et de la Recherche Médicale – France
[2] Université de Rouen Normandie – Normandie Université – France
[3] U1073-Nutrition, Inflammation et axe Microbiote-Intestin-Cerveau – Université de Rouen Normandie, Institute for Research and Innovation in Biomedicine, Institut National de la Santé et de la Recherche Médicale – France
[4] U1073-Nutrition, Inflammation et axe Microbiote-Intestin-Cerveau – Université de Rouen Normandie, Institute for Research and Innovation in Biomedicine, Institut National de la Santé et de la Recherche Médicale – France
[5] Service de Nutrition [CHU Rouen] – CHU Rouen, Université de Rouen Normandie – France

Inflammatory Bowel Diseases (IBD), including Crohn's disease and ulcerative colitis, are chronic diseases marked by recurrent inflammation of the gastrointestinal tract. Targeting the gut microbiota has recently emerged as a promising therapeutic approach for treating IBD, given that patients often exhibit gut dysbiosis. We have recently created a biobank containing gut bacteria isolated from healthy volunteers, whi[Flash acc]reened in order to identify bacterial strains with anti-inflammatory properties. These bacteria were screened in addition for their ability to produce short- or branched-chain fatty acids, which are bacterial metabolites playing key roles in intestinal physiology. Using various in vitro intestinal cell lines, we have identified several bacterial strains with strong anti-inflammatory properties. This screen led more particularly to the identification of a strain, named PR1121, belonging to a yet unknown bacterial species. PR1121 is a potent producer of butyrate, a short-chain fatty acid known for its anti-inflammatory properties, but also exhibits butyrate-independent anti-inflammatory effects. We are currently using murine models of colitis to evaluate the anti-inflammatory potential of these different bacterial strains in vivo, both individually and as a consortium, and obtained promising preliminary data. In conclusion, our work has led to the identification of several mutualistic bacteria from the gut microbiota that play essential roles in intestinal homeostasis. These bacteria constitute potential candidates for developing Live Biotherapeutic Products for IBD treatment.

Mots-Clés: Inflammatory Bowel Disease, Gut microbiota, host, bacteria interactions, inflammation

*Intervenant

11

Human Papillomavirus 18 replication reshapes innate immune receptors expression in 3D epithelial cultures

Celia Kemmat [1], Ocimek Morgan [1], Marta Lagana [1], Alexie Ouchakoff [1], Françoise Mercier-Nomé [1,2], Géraldine Schlecht-Louf [1], Claire Deback [1], Mïchael Herfs [3], Françoise Bachelerie [1], Julien Pothlichet * [1]

[1] Inflammation, Microbiome and Immunosurveillance Unit, MI2, UMR-S 996 INSERM, Team CreatIVe, Chemokines, Immunoregulation and Virome, Paris-Saclay University, Orsay, France – Institut National de la Santé et de la Recherche Médicale - INSERM, Université Paris Sud, Université Paris Saclay – France

[2] Ingénierie et Plateformes au Service de l'Innovation Thérapeutique, Inserm, Paris-Saclay University, Orsay, France – Institut National de la Santé et de la Recherche Médicale - INSERM, Université Paris Sud, Université Paris Saclay – France

[3] Experimental Pathology - GIGA Cancer - Université de Liège – Belgique

Human papillomaviruses (HPVs) are commensal viruses of stratified epithelia that replicate in human keratinocytes, most often asymptomatically. However, nearly 5% of cancers are associated with HPV. Host, viral, and environmental factors can promote the transition of the virus from a commensal to a pathogenic state. We hypothesize that dysfunctions of the innate immune response, involving in particular a dysregulation of the protein expression profile of innate immune receptors (PRRs), may participate in the transition of HPVs replication towards pathogenesis. Thus, we characterized the protein expression of the 5 main epithelial PRRs that could sense HPV-DNA using Western-blot and Immunohistofluorescence (IHF): (i) within three-dimensional epithelial cultures (3D-EpC)1, the only model to study the replicative cycle of HPV18; and (ii) in healthy human skin and a tumor associated with HPV52. Our results suggest that HPV18 replication is associated with modifications of the expression levels and tissue distribution of certain PRRs, as revealed by our newly developed IHF layer analysis technique. In addition, the PRR expression profiles observed in 3D-EpC in the absence or presence of HPV18 correspond, respectively, to those detected in healthy skin and in tissues adjacent to the HPV5-associated tumor. These results support the hypothesis of a contribution of some PRRs in the control of HPV infections and pave the way for more in-depth studies that would lead to the identification of new biomarkers or treatments for HPV-associated cancers.

Mots-Clés: Human papillomavirus (HPV) replication and cancer, Keratinocytes, Innate immunity, Pattern recognition receptors (PRRs) tissue distribution and regulation, Skin, 3D epithelial cultures (3D EpC)

*Intervenant

12

Identification and characterization of a novel Chlamydia trachomatis growth inhibitor

Camille Dos Santos-Toinet * [1,2,3], Ludovic Halby [4], Valérie Huteau [4], Karen Druart [5], Yongzheng Wu [1], Mariette Matondo [5], Paola Arimondo [4], Agathe Subtil [1]

[1] Biologie cellulaire de l'Infection microbienne - Cellular Biology of Microbial Infection – Institut Pasteur [Paris], Centre National de la Recherche Scientifique, Université Paris Cité – France
[2] ANRS - Maladies infectieuses émergentes – Institut National de la Santé et de la Recherche Médicale – France
[3] ED 515 - Complexité du vivant – Sorbonne Universite – France
[4] Chimie biologique épigénétique - Epigenetic Chemical Biology – Institut Pasteur [Paris], Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique, Université Paris Cité – France
[5] Spectrométrie de Masse pour la Biologie – Mass Spectrometry for Biology – Institut Pasteur [Paris], Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique, Université Paris Cité – France

In the current context of a global antimicrobial resistance threat, new narrow-spectrum antibiotics are needed. A microscopy-based screen of small molecules identified A79 as a potent narrow-spectrum drug preventing *Chlamydia trachomatis* (*Ct*) growth in culture cells. We confirmed A79 potency to inhibit *Ct* replication at micromolar concentration, while being well tolerated by human cells. This molecule does not affect the growth of four other bacterial species tested, including *Lactobacillus crispatus* and *Gardnerella vaginalis*, commonly found in the vaginal microbiota. A79's derivatives were synthesized and tested, leading to the identification of derivatives working at nanomolar concentrations and presenting a good metabolic stability. Thermal proteome profiling (TPP) of infected cells in the presence and absence of A79 suggested that inhibition of a specific metabolic synthesis pathways might account for A79's activity on *Ct* development. To confirm this hypothesis by an orthogonal approach, we grew Ct over several generations in increasing concentrations of A79. Cross-examination of the genome of the A79-resistant clones which emerged from these cultures with the TPP data should identify the biological activity inhibited by A79. In summary, we have identified a chemical scaffold that constitutes a promising lead for the development of a narrow-spectrum anti-*Ct* antibiotic.

Mots-Clés: Chlamydia trachomatis, Sexually Transmitted Infection (STI), Drug discovery

*Intervenant

13

IgA-mediated phagocytosis of mucosally acquired viruses stimulates innate memory in effector phagocytes, providing protection against subsequent, unrelated viral infections

Annouk Dauvilliers * [1], Morgan Noiret [1], Daniela Tudor [1], Morgane Bomsel [2]

[1] [Institut Cochin] Departement Infection, immunité, inflammation – Institut cochin – France
[2] [Institut Cochin] Departement Infection, immunité, inflammation – CNRS, Institut National de la Santé et de la Recherche Médicale - INSERM, Université de Paris Cité (UPC) – France

Trained immunity describes the capacity of innate immune cells, including phagocytes, to undergo long-term functional reprogramming after an initial encounter with a pathogen, resulting in enhanced non-specific responses to subsequent, unrelated challenges. This process is classically driven by the engagement of pattern-recognition receptors (PRRs) and is mediated by coordinated metabolic and epigenetic remodelling. Beyond direct microbial sensing, pathogen-specific antibodies may also contribute to the induction of trained immunity by modulating innate cell activation through Fc receptor engagement, although this possibility remains poorly explored. In the context of viral infections, antibodies typically confer protection through neutralization but also, as we have shown earlier, by recruiting innate phagocytes via antibody-dependent cellular phagocytosis (ADCP) or antibody-dependent viral phagocytosis (ADVP). These mechanisms may additionally shape long-term innate immune programming.
We recently found that HIV-1 envelope-specific neutralizing IgA efficiently triggered elimination of HIV-1-infected cells by ADCP unlike its IgG counterpart. IgA-mediated HIV-1 ADCP reprograms monocytes into macrophages with a mixed inflammatory phenotype that enhances HIV-1 antigen cross-presentation, leading to virus-specific CD8 T-cell responses (Cottignies-Calamarte et al, Mucosal Immunol 2025, doi:10.1016/j.mucimm.2025.09.004).

We now show in a study addressing both HIV-1 and COVID that ADCP of HIV-1 infected cell but also ADVP of HIV-1 and SARS-CoV-2 mediated by IgA specific for corresponding viral envelope (referred to HIV-1 ADCP, HIV-1 ADVP and SARS-CoV-2 ADVP, respectively) induce trained immunity in effector monocytes compared to untrained cells. Indeed, trained monocytes produce high level of lactate and respond to a new bacterial LPS or priming-unrelated virus challenge by secreting TNF-α/IL-6. As functional consequences of training, monocytes trained by SARS-CoV-2 ADVP resisted to new HIV-1 infection. Furthermore, the conditioned media from these SARS-CoV-2 ADVP-trained monocytes but also that of HIV-ADVP-trained monocytes specifically reduced HIV-1 infection of CD4+ T cells, indicating that trained phagocytes secret factors which confer a protective antiviral effect to other immune cells.
Together, effector phagocytes acquire an innate memory following specific IgA-mediated phagocytosis of HIV-1, but also SARS-CoV-2, resulting in protection against distinct viral infections. Thus, a first viral infection could appear protective from new unrelated infections, which might have beneficial consequence after the COVID pandemic.

Mots-Clés: Trained immunity, ADCP, ADVP, IgA, HIV, 1, SARS, CoV, 2, mucosa

*Intervenant

Immunobiography of hematopoietic stem cells

Lucas Ruffinatto [1], Yann Groult [1], Johanna Iacono [1], Marie-Lou Leqdes [1], Mathilde Leriguier [1], Michael H Sieweke [2], Sandrine Sarrazin [1], Bérengère De Laval * [1]

[1] Centre d'Immunologie de Marseille - Luminy – Aix Marseille Université, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique – France
[2] Center for Regenerative Therapies TU Dresden (CRTD) – Allemagne

Innate immune memory, or trained immunity, is referred to as the capacity of innate cells to respond better to a subsequent challenge (Ruffinatto et al., 2024). This memory involves long-term epigenetic reprogramming and has been discovered in monocytes and macrophages, where primary stimulation increases their phagocytic capacities. The long-term effect observed in epidemiological analyses has led to focusing on long-lived immune progenitors such as hematopoietic stem cells (HSCs). Discoveries made during the last decades have highlighted the importance of HSCs in pathogen, PAMP, and cytokine recognition, resulting in emergency myelopoiesis. We have previously found that, in addition to their immediate response to LPS, mimicking bacterial infection, HSCs also exhibited hallmarks of trained immunity, allowing the long-term maintenance of epigenetic memory and functional improvement in response to a second challenge, such as increased myeloid differentiation (de Laval et al., 2020).
Given the central role of HSCs and their ability to respond to multiple inflammatory stimuli, it is essential to better characterize external stimuli capable of reprogramming them and potentially modifying hematopoiesis. This raises the question of whether this memory reflects a universal trained state or is stimulus-specific. To address this, we mimicked different infections using PAMPs such as LPS, zymosan, and Lyovec poly(I:C). We observed that all the stimuli triggered transient HSC activation, immune response programs, and proliferation, albeit with varying magnitudes, both in vivo and ex vivo. Importantly, each stimulus led to chromatin remodeling in HSCs, suggesting that diverse signals can induce innate immune memory. This leads to modified HSC activation, immune programs, and emergency hematopoiesis in response to different types of secondary stimulation. In parallel, macrophages derived from HSCs of primarily exposed mice also exhibited modulated phagocytic responses, indicating that this memory is transmitted during differentiation.
These data suggest that different types of stimulation can reprogram HSCs, modulate emergency hematopoiesis in cases of re-exposure, and lead to the long-term production of macrophages with distinct functions.

Mots-Clés: epigenetic memory, hematopoietic stem cell, inflammation, emergency myeloipoisis

*Intervenant

15

Impaired type I interferon response early after SARS-CoV-2 infection is associated with the occurrence of persistent COVID-19 in solid organ transplanted recipients.

Quentin Richier * [1], Fabrice Carrat , Guillaume Martin-Blondel , Anne-Geneviève Marcelin , Karine Lacombe [2], Darragh Duffy

[1] Translational Immunology Unit – Darragh Duffy – France
[2] Institut Pierre Louis d'Epidémiologie et de Santé Publique (iPLESP) – Institut National de la Santé et de la Recherche Médicale, Sorbonne Universite, Institut National de la Santé et de la Recherche Médicale : U1136 – 56, boulevard Vincent Auriol - CS 81393 - 75646 Paris Cedex 13, France

Background:
Immunocompromised patients may experience persistent symptoms of COVID-19 because of impaired viral clearance and sustained viral replication. This clinical scenario is a possible source for evolution of new viral variants of concern, or the emergence of antiviral resistance. An improved understanding of persistent COVID-19 (pCOVID-19) is required to better define, predict and treat it.

Methods:

From the multi-centric and prospective ANRS 0003S CoCoPrev cohort study, we selected a homogeneous group of patients with solid organ transplantation (SOT) treated by sotrovimab. We defined pCOVID as a positive SARS-CoV-2 RT-PCR with ct $<$ 30 at day 21 after sotrovimab initiation. We used digital ELISA to measure serum interferon responses and Luminex for inflammatory cytokines and soluble markers of lymphocytes anergy or activation.

Results:

We enrolled 81 patients with SOT and treated by sotrovimab. Among them 67 presented as aCOVID-19 and 14 as pCOVID-19. The mean duration of symptoms between the COVID-19 onset and the sotrovimab administration was 3.22 and 2.57 days in the two groups, respectively (p= 0.23). At day 0 (before the sotrovimab initiation) nasopharyngeal viral load was significantly higher in the pCOVID-19 group (ct = 18 *vs* ct = 21.9, p = 0.02), and the type 1 interferon response was significantly lower in the blood of pCOVID-19 (p = 0.014). The type 2 interferon response, PD-1, TIM-3, CD27, CXCL13, CXCL10, CCL2, and CCL3 were not significantly different between the two groups.

Conclusion:
In immunocompromised patients, high viral load and impaired type 1 interferon response after a SARS-CoV-2 infection are significantly associated with the occurrence of pCOVID-19. This finding could allow us to early identify the patients most at risk of viral persistence and adapt

*Intervenant

the treatment by combining antivirals or extending the duration of treatment. Finally, these results highlight the potential role of interferon-based therapy specifically in immunocompromised patients.

Mots-Clés: Interferon, COVID, 19, Immunocompromised

16

Major depressive episodes and psychiatric symptoms among HIV controllers compared with antiretroviral-treated people living with HIV

Marion Camard * [1,2], Samia Hendou [3], Marie Bitu [1], Christelliah Mouanga [1], Faroudy Boufassa [3], Salomé Laurens [1], Jérôme Le Chenadec [3], Léo Plaçais [1,4], Véronique Avettand-Fenoël [5,6], Laurence Meyer [3,7], Christine Bourgeois [1], Emmanuelle Corruble [8,9], Olivier Lambotte [1,4], Romain Colle [8,9], Nicolas Noel [1,4]

[1] Université Paris-Saclay, Inserm, CEA, Center for Immunology of Viral, Auto-immune, Hematological, Bacterial Diseases (IMVA-HB/IDMIT/UMR1184), Le Kremlin-Bicêtre, France – CEA, Universit Paris-Sud, INSERM, U1184 – France
[2] AP-HP, Hôpital Bicêtre, Service de Médecine Interne et Immunologie Clinique, Le Kremlin-Bicêtre, France – AP-HP, Service de Medecine Interne-Immunologie Clinique, Hôpitaux Universitaires Paris Sud, Le Kremlin Bicêtre, France – France
[3] Université Paris-Saclay, Inserm, Centre for Research in Epidemiology and Population Health (CESP), INSERM U1018, Le Kremlin-Bicêtre, France – INSERM U1018, Université Paris-Sud – France
[4] AP-HP, Hôpital Bicêtre, Service de Médecine Interne et Immunologie Clinique, Le Kremlin-Bicêtre, France – AP-HP, Service de Medecine Interne-Immunologie Clinique, Hôpitaux Universitaires Paris Sud, Le Kremlin Bicêtre, France – France
[5] CHU d'Orléans, Virologie, Orléans, France – CHU Orléans – France
[6] Université d'Orléans, LI2RSO, Orléans, France – Université d'Orléans – France
[7] AP-HP, Hôpital Bicêtre, Service de Santé Publique, Le Kremlin-Bicêtre, France – Hôpital Bicêtre [AP-HP, Le Kremlin-Bicêtre], Hôpital Bicêtre [AP-HP, Le Kremlin-Bicêtre] – France
[8] AP-HP, Hôpital Bicêtre, Service Hospitalo-Universitaire de Psychiatrie de Bicêtre, Mood Center Paris Saclay, Le Kremlin-Bicêtre, France – Hôpital Bicêtre [AP-HP, Le Kremlin-Bicêtre] – France
[9] MOODS Team, Université Paris-Saclay, Inserm, Centre for Research in Epidemiology and Population Health (CESP), INSERM U1018, Le Kremlin-Bicêtre, France – INSERM U1018, Université Paris-Sud – France

Background. Major depressive episodes are highly prevalent among people living with HIV (PWH), including those with sustained virological suppression under antiretroviral therapy (ART). However, psychiatric outcomes among HIV controllers (HIC), who maintain long-term spontaneous control of viral replication without ART, remain poorly characterised. As HIC represent a distinct immunovirological phenotype, understanding their psychiatric profile may help clarify the contribution of viral and immunological factors to mental health outcomes in HIV. We aimed to assess the frequency of major depressive episodes and psychiatric symptom profiles in HIC compared with ART-treated PWH and to identify associated factors.
Methods. We conducted a prospective observational study recruiting HIC from the French multicentre ANRS CO21 CODEX cohort and comparing them with PWH receiving suppressive ART. Major depressive episodes were assessed using the Mini-International Neuropsychiatric Interview (M.I.N.I.), and psychiatric symptoms were evaluated using the Symptom Checklist-90–Revised. Between-group comparisons and univariable analyses were performed to identify factors associated with psychiatric outcomes.

*Intervenant

Findings. Ninety-eight participants were included, comprising 57 HIC and 41 ART-treated PWH. The prevalence of lifetime major depressive episodes was high in both groups and did not differ significantly between HIC and ART-treated participants (35% vs 41%). Overall, SCL-90-R symptom dimension scores were generally low in both groups (Figure 1). HIC had higher scores for interpersonal sensitivity and for a composite psychopathology dimension mainly reflecting appetite and sleep symptoms, whereas immunovirological parameters showed no significant associations. In both groups, reported pre-existing psychiatric history, alcohol use, and sociocultural factors were associated with adverse psychiatric outcomes, whereas immunovirological parameters showed no significant associations.

Interpretation. Despite spontaneous control of HIV replication, HIC do not exhibit more favourable psychiatric outcomes than PWH receiving suppressive ART. The prevalence of depressive disorders observed across groups, which remains higher than that reported in the general population, appears primarily driven by behavioural factors, pre-existing psychiatric conditions, and contextual factors related to geographic origin rather than by immunovirological parameters. These findings support the need for routine identification and comprehensive management of psychiatric disorders for all PWH, including HIC.

Mots-Clés: HIV controllers, Depression, Psychiatric disorders, Psychological symptoms, Antiretroviral therapy

17

Mfd, a multifunctional protein as a new target for the development of innovative antimicrobials

Delphine Cormontagne * [1], Lucie Lebreuilly , Seav-Ly Tran , Samantha Samson , Thu Ba To [2], Marie Stosskopf , Rozenn Dervyn , Anne Grießhammer , Jacobo De La Cuesta-Zuluaga , Lisa Maier , Thierry Naas [3], Simona Mura , Didier Rognan [4], Julien Nicolas , Gwenaëlle Andre-Leroux , Nalini Ramarao

[1] Département Microbiologie et Chaîne Alimentaire - INRAE – Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement – France
[2] Institute Galien Paris-Saclay – Institut Galien Paris-Saclay, UMR CNRS 8612, Orsay, France – France
[3] Service de Bactériologie, AP-HP, CHU de Bicêtre, EA7361, Labex LERMIT, Université Paris Sud, CNR résistance aux antibiotiques – Thierry Naas – France
[4] Laboratoire d'Innovation Thérapeutique (LIT) – université de Strasbourg, Centre National de la Recherche Scientifique : UMR7200 – Université de Strasbourg Faculté de Pharmacie 74 route du Rhin BP 60024 67401 Illkirch Cedex, France

Mfd is a conserved bacterial protein implicated in various processes such as DNA repair, mutagenesis and virulence. Due to its role in virulence and mutagenesis, Mfd is a promising target for the development of new antimicrobial drugs. We identified an inhibitor of Mfd called NM102 showing an antimicrobial activity against *K. pneumonia* and *P. aeruginosa* exclusively in a context of infection, without inducing toxicity to the host. Furthermore, NM102 also inhibits Mfd's function in mutagenesis leading to a decrease of antimicrobial resistance. This represents a promising alternative therapeutic strategy to fight against antimicrobial resistance which constitutes an urgent and alarming health issue.

Mots-Clés: Antivirulence, Drug Discovery, ESKAPEE pathogens, Host–pathogen interaction

*Intervenant

18

Microbiome-Mediated Regulation of Monocyte Differentiation by Dietary Cholesterol Restrains Enteropathogen Dissemination.

Mathias Chamaillard * [1], Pukar Kc *

, Wenhui Zhang , Lucy Biber , Juan-José Martinez-Garcia , Pablo Pelegrin , Thomas Kufer , Philippe Lesnik , Maryse Guerin

[1] Inserm U1366 - CRCLille – Univ. Lille, Inserm, CHU Lille, CNRS, U1366-UMR9020 – CRCLille – Cancer Research Center of Lille, F-59000 Lille, France – France

The intestine integrates nutritional and microbial cues for coordinating host metabolism although little is known how it may in turn prevent an innapropriate response leading to a heightened postprandial risk to enteric infection. Here, we demonstrate that the protection to the intestinal pathogen Salmonella enterica serovar Typhimurium is tightly regulated by a microbiome-mediated response to dietary cholesterol in mice. This relies on a heightened generation of microbiota-generated metabolites that restrains the molecular control of monocyte fate decision. As a consequence, monocyte-dependent replenishment of migratory phagocytes is heightened in mice supplemented by cholesterol. By contrast, high-fat diet outperforms this microbiome-dependent transition of monocytes into non-migratory phagocytes that are endowed with the ability to capture bacteria in mice. Accordingly, circulating monocytes showed a lowered transcriptional regulation of monocyte differentiation in response to a high-calorie diet in humans. Altogether, these findings highlight how dietary cholesterol shape host-microbiome dynamics influencing susceptibility to Salmonella infection.

Mots-Clés: Cholesterol, Enteric infection, Microbiote, Mocyte fate.

*Intervenant

19

Nasal nanoparticle vaccine induces a cross-strain immune response against Toxoplasma gondii

Aurane Lecouffe * [1], Angelo Scuotto [1], Christophe Barnier-Quer [1], Didier Betbeder [1]

[1] Vaxinano – 84 rue du Docteur Yersin, 59120, Loos, France – France

T. gondii infection can lead to severe clinical outcomes in humans, including congenital and ocular toxoplasmosis, and causes significant mortality in highly susceptible species such as New World primates (1).
Vaxinano has developed a vaccine candidate (VXN-Toxo) composed of maltodextrin nanoparticles formulated with an inactivated *T. gondii* parasite (2). In an initial field study, squirrel monkeys housed in zoos were vaccinated with VXN-Toxo, resulting in a reduction in toxoplasmosis-associated mortality, together with the induction of a strong and durable systemic cellular immune response, characterized by IFN-γ secretion from peripheral blood mononuclear cells (3). These findings were subsequently confirmed through large-scale vaccination of wildlife animals across 32 zoological parks in Europe and the Americas, leading to the near-complete elimination of toxoplasmosis-related deaths following vaccination (4).

These findings suggest that VXN-Toxo induces broad protective immunity against *T. gondii* strains circulating in diverse geographical regions (5). Therefore, in this study, we further investigate this hypothesis by vaccinating C57BL/6 mice and analysing the cellular immune responses following restimulation with antigens derived from multiple *T. gondii* strains representing the major haplogroups (Type I, Type II, Type III, and atypical strains). ELISPOT analysis demonstrated robust antigen-specific IFN-γ and IL-17 responses not only against the vaccine strain, but also against all heterologous strains tested.

Together, these results support the capacity of VXN-Toxo to induce a cross-reactive cellular immune response and highlight its potential as a promising vaccine candidate for both human and veterinary applications.

(1). Denk, D. et al. Toxoplasmosis in Zoo Animals: A Retrospective Pathology Review of 126 Cases. *Animals* (2022).
(2). Ducournau, C. *et al.* Synthetic Parasites: A Successful Mucosal Nanoparticle Vaccine Against Toxoplasma Congenital Infection in Mice. *Future Microbiol.* (2017).
(3). Ducournau, C. *et al.* Vaccination of squirrel monkeys (Saimiri spp.) with nanoparticle-based Toxoplasma gondii antigens: new hope for captive susceptible species. *Int. J. Parasitol.*(2023).
(4). Scuotto, A. *et al.* Retrospective Analysis of the Impact of Vaccination with an Inacti-vated Vaccine on Toxoplasmosis-Associated Mortality in Captive Wildlife. *Vaccines* (2025).
(5). Barbosa, I. M. F. N. et al. Toxoplasma gondii Genotypes Isolated from Humans: A Sys-tematic Review. Contrib. LAS Cienc. Soc., (2023).

Mots-Clés: Toxoplasma gondii, Nanoparticle Vaccine, Nasal, Cellular Immunity, Cross, reactive immunity

*Intervenant

20

NK-cell–dependent immune conditioning during HSV-1 latency establishment irreversibly biases trigeminal ganglion reservoirs toward non-reactivation

Oscar Haigh *[1], Kenza Breton [1], Paul Mazet [1], Alba Gonzalez Sanchez [1], Rafael Boucher [1], Nolwenn Poccardi [1], Seonhee Kim [1], Noemie Oziol [1], Franceline Julliard [2], Patrick Lomonte [2], Jean Armengaud [3], Antoine Rousseau [1], Marc Labetoulle [1]

[1] Université Paris-Saclay, Inserm, CEA ; Immune Diseases, Microbiology and Innovative Therapies (IDMIT/UMRS1184) ; Fontenay-aux-Roses & Le Kremlin-Bicêtre, France

[2] Université Claude Bernard Lyon 1, CNRS UMR 5310, Lyon, France – Université Claude Bernard - Lyon I (UCBL) – France

[3] Laboratory Innovative technologies for Detection and Diagnostics (LI2D) – French Alternative Energies and Atomic Energy Commission (CEA), DFR, Joliot Institute, DMTS, SPI – France

Herpes simplex virus type 1 (HSV-1) establishes lifelong neuronal DNA reservoirs in the trigeminal ganglia (TG) that periodically reactivate to drive recurrent mucocutaneous and oc-ular disease. While T cell surveillance constrains latency exit, determinants acting during the latency-establishment window to influence reactivation potential remain poorly understood. Using our clinically relevant lip infection model, we previously showed that contralateral prim-ing with a replication-defective thymidine kinase deletion mutant (TKdel) prevented subsequent wild-type (WT) HSV-1 reactivation. Protection was not reproduced by priming with an alter-native attenuated reporter mutant, indicating that immune conditioning quality, rather than priming per se, is critical. Protection correlated with enhanced NK-cell infiltration into the chal-lenged lip and TG during early infection, implicating NK cells as candidate effectors.

Here, we tested whether NK cells act during WT challenge to enforce a non-reactivating la-tent state and examined their role in tissue programming during latency establishment. TKdel priming did not prevent WT latent genome establishment in TG, yet it abolished explant-induced reactivation, confirming selective enforcement of reactivation incompetence. Depletion of asialo-GM1–expressing NK cells at WT challenge abrogated TKdel-mediated protection, to restore reactivation-prone latency, whereas CD8 depletion did not. Thus, a critical NK cell–dependent decision point was established. Phenotypic profiling revealed that TKdel priming calibrated early NK responses at the lip challenge site, enriching mature CD11bCD27 NK cells, while alternative priming skewed toward terminally differentiated TIGIT phenotypes. Under protected conditions, NK effector activity was largely confined to the lip, whereas during naïve WT challenge it oc-curred prominently in the TG, consistent with early containment of lytic permissiveness within TG.

*Intervenant

Whole-TG proteomics with causal network inference demonstrated that reactivation-prone naïve WT challenge was associated with IFN/NF-B–permissive inflammatory and chromatin-accessibility programs. In contrast, TKdel priming installed an NK-dependent restrictive architecture char-acterised by integrated stress response activation, metabolic checkpoint control, chromatin re-pression and post-transcriptional restraint. NK depletion dismantled this state, reverting toward a permissive profile resembling naïve challenge.
Together, these data position licensed NK cells as upstream determinants of latent HSV-1 reac-tivation fate, acting during establishment to durably bias viral episomes toward deep repression and non-reactivation.

Mots-Clés: herpes, NK cells, latency, reactivation, proteomics

P. aeruginosa complex infections treated with bacteriophage therapy in France: Experience from the "PHAGEinLYON Clinic" program

Christian Motet * [1], Thomas Briot [2], Tiphaine Roussel-Gaillard [3], Cécile Batailler , Myrtille Le-Bouar [1], Florent Valour [1], Rafael Gomes , Maya Merabishvili [4], Florence Ader , Mathilde Lherm [5], Fabien Craighero [6], Ani Horikian [3], Guillaume Henry [5], Claire Merveilleux [7], Philippe Reix [8], Olivier Martin [9], Sandrine Roux [1], Sébastien Lustig [10], Tristan Ferry [1]

[1] Service de Maladies Infectieuses et Tropicales [Hôpital de la Croix-Rousse - HCL] – Hôpital de la Croix-Rousse [CHU - HCL] – France
[2] Pharmacie à usage intérieur, Groupement Hospitalier Nord, Hospices Civils de Lyon (HCL) – HCL – France
[3] Institut des Agents Infectieux, Laboratoire de Bactériologie – Hospices Civils de Lyon – France
[4] Queen Astrid Military Hospital [Brussels] – Belgique
[5] Service de chirurgie des brûlés, plastique, reconstructrice et esthétique – Hospices Civils de Lyon – France
[6] Service de Radiologie [Hôpital de la Croix-Rousse - HCL] – Hôpital de la Croix-Rousse [CHU - HCL] – France
[7] Services de Pneumologie, Exploration Fonctionnelle Respiratoire et Cardiologie – Hospices Civils de Lyon – France
[8] Service de pneumologie, allergologie, mucoviscidose – Hôpital Femme Mère Enfant, HCL, Bron, France, mère enfant – France
[9] Service d'anesthésie-réanimation – Hôpital Edouard Herriot - HCL - France – France
[10] Service de chirurgie orthopédique et médecine du sport – Hôpital de la Croix-Rousse [CHU - HCL] – France

Background

Bacteriophages are natural viruses that target specific bacteria and their biofilm. *P. aeruginosa* is: (i) a pathogen frequently involved in severe bacterial infections; (ii) a strong biofilm producer; (iii) associated with increasing antimicrobial resistance; and (iv) responsible for high morbidity and mortality. Few data about the potential added value of phage therapy in complex *P. aeruginosa* infections are available.

Methods

"PHAGE*in*LYON *Clinic*" is a dedicated program to develop clinical phage therapy at Hospices Civils de Lyon (HCL) that includes a multidisciplinary team that is able to (i) answer to phage requests; (ii) validate the indication of phage therapy as compassionate use within the framework of early access authorization in France; (iii) propose specific therapeutic scheme; (iv) order and prepare bacteriophages locally; with the aim of treating and monitoring each patient who needs it. Phage susceptibility testing was performed by each phage producer. We analyzed data from "PHAGE*in*LYON *Clinic*" cohort study (NCT06185920) to describe patients with *P. aeruginosa* infections who received this treatment.

Results

Between 2017 and August 2025, 148 requests were received for phage therapy in patients with *P.*

*Intervenant

aeruginosa infections. Afte assessment, phage therapy was performed finally in 42 of them; 33 were treated at HCL and 9 were treated externally under HCL supervision, mainly with phages PP1450 and PP1777 (Figure 1). Indications for phage therapy were mainly biofilm-associated infections (Figure 2). Over half of *P. aeruginosa* isolates were at least multidrug resistant strains. No serious adverse event attributed to phage therapy was detected. The majority of patients who have undergone phage therapy had a favorable outcome (clinically and/or microbiologically) (Table 1). Five patients needed at least a second line of phage therapy of which two of them had a favorable outcome.

Conclusions

There is a significant development of phage therapy in France thanks to the set-up of the "PHAGE*in*LYON *Clinic*" program. Complex *P. aeruginosa* infections were successfully treated with adjunctive phage therapy. In the context of growing antimicrobial resistance, phage therapy could be a crucial adjuvant in selected patients with difficult-to-treat infections.

Mots-Clés: Phage therapy, biofilm related infections, antibiotic resistance

Plasmacytoid dendritic cell discrete subpopulations with contrasting functions are elicited by CD4+ T cells infected or not by HIV-1 or HIV-2

Khelfa, M., Xing , E., Apostol, D. and Hosmalin, A.* [1]

[1] Institut Cochin, CNRS UMR8104, Inserm U1016, Université Paris-Cité – Inserm U1016 – France

Introduction

Plasmacytoid dendritic cells (pDC) are major interferon (IFN)-α _producing-cells in response to viruses. After maturation, they stimulate T cells. We found that they cross-present antigens from HIV-1-infected CD4+ T cells to specific cytotoxic T cells. During primary HIV infection, IFNs are essential to decrease viral loads, but during chronic infection, they induce immune suppression and metabolic syndrome. Free influenza or Sars-Cov2 viruses were shown by cytometry to induce pDC diversification. Because HIV is rarely free, we stimulated pDC by HIV-1 or 2-infected H9 CD4+ T cells to assess diversification.

Methods

Human pDC were purified from buffy coats by immunomagnetic depletion and CD304+ BD Aria III sorting, stimulated for 16h by H9 cells, tested by flow cytometry (BD LSR2), multiparametric spectral cytometry (Cytek Aurora, Omics) and single-cell RNA sequencing (scRNAseq, Chromium Next Gem-X Flex 10xGenomics, Illumina NextSeq2000, Human genome GRCh38-2024-1, R v4.05, Seurat, DGE, UMAP, GOE, pseudo-trajectory).

Results

HIV-infected CD4+ T cells induced diversification of pDC into IFN-α and IFN-λ-producing, or mature pDC with T-cell stimulatory potential (CD83), or cytotoxic cells (CD107a, target H9HIV cell apoptosis). Spectral cytometry showed diversification into 10 subpopulations with different functions. scRNAseq showed that H9 cells induced pDC with TLR7/9 signaling pathway, HIV-1 or-2-infected H9 cells induced additional subpopulations with IFN-α and -λ _(more with HIV-2), IFN-Stimulated Genes (more with HIV-1), cytotoxicity, T cell activation and regulation genes.

Conclusion

H9 cells induced pDC primed for viral activation, HIV-infected H9 cells induced more populations with surprisingly contrasted functions and differences between HIV-1 and 2 infections which may explain HIV-2 lower pathogenicity. Understanding pDC diversification will enable development of targeted immunotherapeutic strategies to control HIV through adequate modulation of IFN production and cytotoxic T cell responses.

Mots-Clés: HIV, 1, HIV, 2, Interferon, alpha, Interferon, lambda, plasmacytoid dendritic cells

*Intervenant

23

Proinflammatory strains of Mediterraneibacter gnavus are enriched during spondyloarthritis (SpA) and modulate disease during experimental SpA

Manon Jacoutot * [1,2,3], Danielle Dias Munhoz [1,2], Marie Beaufrère [1,2,4], Guillaume Gautreau [5], Anne-Sophie Bergot [6], Roula Said-Nahal [1,2,4], Véronique Robert [7], Aïda Boukamel [1,2], Paul Karpman [1,2], Eva Frison [1,2], Dominique Lamarque [1,2,8], Thomas Bazin [1,2,9], Teddy Manuello [3,10], Emilie Dumas [3,10], Pierre Maraquin [1,2], Jena-Marc Chatel [7], Philippe Langella [7], Dirk Elewaut [3,10], Ranjeny Thomas [6], Maxime Breban [1,2,4], Simon Glatigny [1,2]

[1] Infection et inflammation – Université de Versailles Saint-Quentin-en-Yvelines, Institut National de la Santé et de la Recherche Médicale – France
[2] INFIBREX – Université Paris Cité – France
[3] VIB-UGent Center for Inflammation Research – Belgique
[4] Service de rhumatologie – Assistance publique - Hôpitaux de Paris (AP-HP), Hospital Ambroise Paré, Boulogne-Billancourt – France
[5] Mathématiques et Informatique Appliquées du Génome à l'Environnement [Jouy-En-Josas] – Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement, Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement : UPR1404 – France
[6] Frazer Insitute, University of Queensland – Australie
[7] U1319, MICrobiologie de l'ALImentation au Service de la Santé – AgroParisTech, Université Paris-Saclay, Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement – France
[8] Service de Gastro-entérologie – Assistance publique - Hôpitaux de Paris (AP-HP), Hospital Ambroise Paré, Boulogne-Billancourt – France
[9] Service de Gastro-entérologie – Assistance publique - Hôpitaux de Paris (AP-HP), Hôpital Beaujon, Clichy – France
[10] Department of Rheumatology, Ghent University Hospital – Belgique

Introduction. Spondylarthritis (SpA) is a chronic inflammatory disorder characterized by osteoarticular and extra-articular manifestations, including inflammatory bowel disease (IBD). It is well-established that intestinal microbiota dysbiosis plays an important role in IBD pathophysiology. We recently evidenced an intestinal dysbiosis during SpA characterized by a decreased bacterial diversity associated to an increased relative abundance of the bacterium *Mediterraneibacter gnavus* (*MG*). In this study, our goal was first to determine if specific *MG* strains are present during SpA. Second, we tested if *MG* strains isolated from SpA patients were more toxic and proinflammatory than those from healthy controls (HC). Finally, we assessed *in vivo* pathogenicity of those *MG* strains.

Methods. *MG* colonies were isolated from colonic biopsies and/or stools from SpA patients and HCs. Isolated *MG* strains were sequenced by next generation sequencing-. Functional assays were conducted by stimulating peripheral blood monocytes from SpA patients with the isolated strains to assess *MG* toxicity and pro-inflammatory function through tumor necrosis

*Intervenant

factor (TNF) induction. Germ-free SKG mice were monocolonized with *MG* strains isolated either from SpA patients or HC, challenged with curdlan and the development of arthritis and colitis were evaluated.

Results. A total of 44 *MG* strains were isolated and sequenced (37 from SpA patients and 7 from HC), with no shared strains between groups. Phylogenetic analysis revealed 2 clades with one containing exclusively strains from SpA patients. Functional studies showed that SpA patients were enriched in *MG* strains displaying toxic and proinflammatory functions on monocytes. *MG* monocolonization restored SpA susceptibility in GF SKG mice. *MG* strains from SpA patients were associated with higher arthritis severity and bone remodeling than *MG* strains from HCs.

Conclusions. Our work demonstrates a broad *MG* diversity in stools and biopsies from SpA patients and HCs. Enhanced toxic and proinflammatory potential of *MG* strains isolated from SpA patients was associated with higher pathogenicity in SKG mice *in vivo* supporting a possible pathogenic role of *MG* during SpA. Further research will investigate the underlying pathogenic mechanism to clarify the contribution of *MG* strains to SpA.

Mots-Clés: Spondyloarthritis, Mediterraneibacter gnavus, Microbiota

24

Role of the SucBA metabolic complex in biofilm formation and flea-borne transmission of Yersinia pestis

Maurane Dégardin * [1], Amélie Dewitte [1], Catherine Robbe-Masselot [2], Florent Sebbane [1], Sébastien Bontemps-Gallo [1]

[1] Centre d'Infection et d'Immunité de Lille - INSERM U 1019 - UMR 9017 - UMR 8204 – Institut Pasteur de Lille, Institut National de la Santé et de la Recherche Médicale, Université de Lille, Centre Hospitalier Régional Universitaire [CHU Lille], Centre National de la Recherche Scientifique – France
[2] Unité de Glycobiologie Structurale et Fonctionnelle - UMR 8576 – Université de Lille, Centre National de la Recherche Scientifique – France

Plague, caused by *Yersinia pestis*, is a vector-borne disease transmitted through the bites of infected fleas. Successful colonization of the flea requires the plague bacillus to adapt to the challenging environment of the insect digestive tract and to overcome host defenses, including survival within a bactericidal soft mass produced by the flea at the level of the proventriculus. *Y. pestis* consolidates this mass through the production of a poly-N-acetylglucosamine polymer that obstructs blood flow to the flea midgut. This obstruction process increases the likelihood of bacterial transmission during blood feeding. Production of this extracellular polysaccharide requires metabolic adjustments that sustain both polymer synthesis and bacterial growth. Here, we investigated the contribution of central metabolism, and in particular the tricarboxylic acid cycle, to this process. We identified the α-ketoglutarate dehydrogenase complex (SucBA) as a major metabolic hub. Loss of *sucBA* resulted in a near-complete loss of the ability of *Y. pestis* to obstruct the flea proventriculus. Integrative transcriptomic and metabolomic analyses revealed that *sucBA* deletion indirectly impairs production of the extracellular polysaccharide *in vitro* through overexpression of the sole c-di-GMP phosphodiesterase, leading to reduced intracellular c-di-GMP levels. This secondary messenger is a key regulator of polysaccharide production and proventricular obstruction. Altogether, our results identify SucBA as a central metabolic node required for establishment of a transmissible flea infection and highlight the importance of metabolic regulation in flea-borne transmission of plague.

Mots-Clés: Plague, Yersinia pestis, Vector borne disease, Metabolism

*Intervenant

25

Set-up of non-human primate precision cut lung slices: an ex vivo model to study infectious respiratory diseases

Cécile Schimmich * [1], Cindy Adapen [2], Camille Pimienta , Sophie Luccantoni , Camille Ludot [3], Quentin Pascal [3], Céline Mayet [4], Thibaut Naninck [4], Nathalie Bosquet [5], Francis Relouzat [3], Roger Le Grand [1], Elisabeth Menu [6]

[1] CEA-Université Paris Sud, INSERM U1184, Immunology of Viral Infections and Autoimmune Diseases, IDMIT departement, IBFJ, Fontenay-aux-Roses, France – CEA-Université Paris Sud-Inserm U1184, IMVA/IDMIT Department/DRF/IBFJ – France
[2] Commissariat à l'énergie atomique et aux énergies alternatives - Fontenay-aux-Roses – CEA-Université Paris Sud-Inserm U1184, IMVA/IDMIT Department/DRF/IBFJ – France
[3] Center for Immunology of Viral, Auto-immune, Hematological and Bacterial Diseases (IMVA-HB/IDMIT), Université Paris-Saclay, Inserm, CEA, Fontenay-aux-Roses, France – CEA IDMIT – France
[4] CEA -IDMIT Laboratoire d'Imagerie de l'Infection et de l'Immunité (CEA-IDMIT-L3I) – CEA – France
[5] Infrastructure IDMIT (CEA/DRF/IBFJ/IDMIT) – CEA, Université Paris Sud - Paris XI, Institut National de la Santé et de la Recherche Médicale - INSERM – France
[6] Immunologie des Maladies Virales et Autoimmunes (IMVA - U1184) – Institut National de la Santé et de la Recherche Médicale : U1184, Université Paris-Sud - Paris 11, Commissariat à l'énergie atomique et aux énergies alternatives : DRF/IMETI – France

Background: Respiratory infections pose a major global burden. Because traditional cell cultures cannot fully replicate complex *in vivo* environments, there is a growing push to find complex alternatives that also reduce animal testing. Precision-cut lung slices (PCLS) are thin live slices of lung tissue that address this need, providing a scalable *ex vivo* model that maintains organotypic structure for several days in *in vitro* culture. By maintaining a multicellular micro-environment, this model allows for the detailed study of various infections, time-course dynamics, and host immune responses.
Methods: Using the Alabama R&D tissue slicer, 600μm thick PCLS were generated from cynomolgus macaques, non-human primates (NHP) lungs after agarose inflating. After an overnight resting period post-slicing, PCLS viability was assessed via LDH release assay and Live/Dead staining imaged by confocal microscopy. PCLS were infected with viruses (respiratory syncytial virus (RSV) and influenza A virus (IAV)) or bacteria (*Streptococcus pneumoniae*) at different timepoints. The pathogen replication was monitored via RTqPCR, qPCR or CFU and the host response was monitored via cytokine release using Luminex technology. Histology staining (H&E) and immunolabelling using antibodies were performed on formalin-fixed paraffin-embedded (FFPE) PCLS sections at different timepoints and conditions. The cryopreservation of PCLS is possible, with a preserved viability post-thawing.

Results: The PCLS remained viable and responsive up to a week after the slicing process, as assessed by LDH assay and live/dead staining observed by confocal microscope imaging. The PCLS support replication of all tested pathogens, after infection and are able to produce cy-

*Intervenant

tokines in response to infection. From FFPE sections, histology analysis allowed to determine cellular organization as well as highlighting senescence over time. No significant structural difference could be observed from infected to non-infected PCLS.
Conclusion: NHP PCLS bridge a gap between preclinical *in vivo* and *in vitro* studies, by displaying a preserved lung micro-environment and allowing the complex cross-talk between multiple local cells in response to a pathogen. This sophisticated *ex vivo* model is highly relevant for studying respiratory diseases and contribute to the 3Rs principles by reducing the need for animal use in *in vivo* experiments.

Mots-Clés: PCLS, respiratory diseases, in vitro model, influenza virus, RSV, pneumonia

26

Superinfection Interference of Insect-Specific Virus GUAPV in Chikungunya Virus Replication in Mosquito Cell Lines

Igor Da Silva Teixeira * [1], Lívia Sacchetto [2], Cecília Banho [1], Cássia Estofolete [1], Nikos Vasilakis [3], Roenick Olmo [4], Maurício Nogueira [1]

[1] Faculdade de Medicina de São José do Rio Preto – Brésil
[2] Universidade Estadual de Campinas – Brésil
[3] The University of Texas Medical Branch – États-Unis
[4] Institut de Biologie Moléculaire et Cellulaire – CNRS UPR9022, Inserm U1257 – France

Vector hosts are frequently infected by viruses sequentially, creating superinfection scenarios that can enhance or decrease viral fitness and replication. Insect-specific viruses (ISVs) show variable prevalence in mosquito populations and are often detected during arbovirus surveillance; recent studies suggest that ISVs are unable to infect vertebrates and can interfere with arbovirus transmission by mosquitoes. Yet most studies target homologous superinfection, whereas heterologous superinfection – in which viruses genetically distinct infect the same host species – remains poorly studied, despite shared vectors among different virus families. Here, we characterized the Guapiaçu virus (GUAPV), an ISV detected in Aedes species from a dengue- and chikungunya-endemic region in Brazil. Phylogenetic analysis of the viral polyprotein placed GUAPV closer to mosquito-borne Orthoflaviviruses such as Yellow fever virus, than to classical ISVs such as CFAV and AeFV. GUAPV replication in Vero cells appeared defective without evidence of replication, but transmission electron microscopy revealed the virus within endocytic vesicles. Importantly, visualization of GUAPV entry into vertebrate cells despite its inability to replicate suggests a feature that highlights its potential as a replication-restricted viral scaffold for vaccine platform development. GUAPV replicated more efficiently in C6/36 than Aag2 cells, showing viral loads tenfold higher in C6/36 cells. Superinfection assays in C6/36 cells showed that GUAPV infection prior to 48 and 96 hours of CHIKV exposure lowered CHIKV titers by 1 log and 2 log at 72 hours, respectively, compared to cells infected only with CHIKV. Interestingly, CHIKV RNA levels dropped 1.5 log at 72 and 96 hours. These results suggest that GUAPV interferes with replication and post-replicative stages of CHIKV, such as assembly or release. The RNA-to-PFU ratio of CHIKV was about 1 log higher in control samples at all time points, indicating fewer infectious particles during superinfection with GUAPV. Our study suggests that the recently discovered GUAPV interferes with CHIKV replication in cells and paves the way to understanding how ISVs may interfere with arbovirus replication in mosquito cells.

Mots-Clés: Insect, specific virus, Superinfection exclusion, Heterologous infection, Chikungunya virus, Guapiaçu virus

*Intervenant

27

The gut microbiota as a determinant of host susceptibility to respiratory infection

Clément Bordas * [1], Clara Valentin [1], Léonard Dubois [2], Lucie Deruyter [1], Séverine Heumel [1], Harry Sokol [2], François Trottein [1]

[1] Université de Lille, CNRS, INSERM, CHU Lille, Institut Pasteur de Lille, U1019-UMR 9017 – Université de Lille, CNRS, INSERM, CHU Lille, Institut Pasteur de Lille, U1019-UMR 9017 – France
[2] Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, AP-HP, Saint Antoine Hospital, Gastroenterology department – Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, AP-HP, Saint Antoine Hospital, Gastroenterology department – France

Aging is associated with increased susceptibility to respiratory infections, but the parameters that determine individual vulnerability remain unclear. Here, we show that age-related changes in the gut microbiota are sufficient to modulate host resistance to *Streptococcus pneumoniae,* the primary causal pathogen of community-acquired pneumonia. Fecal transfer experiments demonstrated that an aged microbiota in young mice increases pulmonary bacterial burden, whereas a young microbiota restores resistance in aged mice. This susceptibility is associated with alterations in the functions of alveolar macrophages, the gatekeepers of pulmonary defense. Microbiota profiling revealed distinct age-associated configurations that robustly predict infection outcomes. Unbiased metabolic analyses and functional studies demonstrated that a microbiota-dependent metabolite, the concentration of which is low in aged individuals, compromises alveolar macrophage phagocytosis and bactericidal activity. Together, these findings establish an age-dependent gut microbiota-lung axis that contributes to age-related vulnerability to bacterial pneumonia.

Mots-Clés: Gut microbiota, aging, gut lung axis, respiratory infection, Streptococcus pneumoniae, alveolar macrophages, microbiota derived metabolites, phagocytosis, bactericidal activity, metabolomics, host–microbe interactions, microbiota targeted interventions

*Intervenant

28 - Flash Talk

The impact of prenatal maternal stress on antitumoral immune responses in offspring: toward an exposome-driven understanding of immune programming

Joy Sakanwi * [1], Rébecca Barascud , Kawthar Mahraoui [1], Matteo Serino , Nicolas Cénac , Abdelhadi Saoudi

[1] Institut Toulousain des Maladies Infectieuses et Inflammatoires – Université Toulouse III - Paul Sabatier, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique – France

Prenatal life represents a critical window during which environmental exposures shape long-term health trajectories. Among these exposures, prenatal maternal stress (PS) is increasingly recognized as a major component of the early-life exposome, with profound consequences on immune development. Epidemiological and experimental studies have linked maternal stress during pregnancy to increased susceptibility to infectious diseases in offspring. However, its impact on antitumoral immunity and the underlying mechanisms remain insufficiently understood.
In this project, we investigate how prenatal stress alters antitumoral immune responses in offspring and aims to identify the cellular and molecular mechanisms involved. Using a validated murine model of prenatal stress, based on repeated restraint and light exposure during mid-gestation, we demonstrate that adult offspring from stressed mothers exhibit increased tumor growth following intradermal injection of B16F10-OVA melanoma cells, and MC38 colorectal carcinoma cells, indicating impaired antitumor immunity. Adoptive transfer experiments into RAG-deficient mice reveal that T lymphocytes from prenatally stressed offspring are sufficient to reproduce the impaired antitumoral phenotype, highlighting a T cell–intrinsic defect. Preliminary data suggest a dysfunction within the CD8 T cell compartment, associated with reduced tumor control and survival.

Given the central role of the microbiota in immune education, we further investigated whether prenatal stress–induced alterations of the gut microbiome contribute to this phenotype. Fecal microbiota transfer experiments demonstrate that microbiota from prenatally stressed offspring is sufficient to increase tumor growth in recipient mice, supporting a microbiota-mediated component of immune reprogramming.
Together, these findings position prenatal maternal stress as a critical exposome factor capable of durably reprogramming antitumoral immunity. Understanding how early-life environmental stressors shape immune competence is essential for developing preventive and therapeutic strategies targeting immune-related diseases, including cancer.

Mots-Clés: Prenatal maternal stress, Antitumoral immunity, B16F10, OVA, CD8 T cell defect, Gut Microbiome, Fecal microbiota transfer

*Intervenant

The lysosomal glutamine transporter SLC38A7/SNAT7 modulates SAMHD1 antiviral activity and promotes HIV-1 production in human macrophages.

Floriane Herit [1], Gabrielle Lê-Bury [2,3], Quentin Provôt * [2], Déborah To-Puzena [2], Julie Haagen [2], T. Matozo De Souza [2], Audrey Dumas [1], Marina Morel [4], Florence Margottin-Goguet [4], Corinne Sagne [5], Asier Saez-Cirion [6,7], Florence Niedergang [8]

[1] Institut Cochin, INSERMU106 - CNRS UMR8104 - Univercité Paris Cité – Institut Cochin, INSERM U1016, UMR 8104 CNRS, Université de Paris – France
[2] Institut Cochin, INSERMU106 - CNRS UMR8104 - Univercité Paris Cité – Institut Cochin, INSERM U1016, UMR 8104 CNRS, Université de Paris – 22 rue Méchain 75014 Paris, France
[3] Cornell University College of Veterinary Medicine, C5-109 Veterinary Medical Center, Ithaca, NY 14853. – États-Unis
[4] Institut Cochin – INSERM U1016. CNRS, UMR8104. Université Paris Descartes, Sorbonne Paris Cité, Inserm, U1016, Cnrs, UMR8104, Université Paris Descartes, Sorbonne Paris Cité – 22, rue Méchain, 75014 Paris, France
[5] Saints-Pères Paris Institute for Neurosciences – Centre National de la Recherche Scientifique, Université Paris Cité – France
[6] Viral Reservoirs and Immune Control Unit – Institut Pasteur – France
[7] HIV Inflammation and Persistence Unit – Institut Pasteur – France
[8] Institut Cochin, INSERMU106 - CNRS UMR8104 - Univercité Paris Cité – Institut Cochin, INSERM U1016, UMR 8104 CNRS, Université de Paris – 22 rue Méchain 75014 Paris, France

HIV-1 is able to infect macrophages which are resistant to the virus's cytopathic effects and exhibit long lifespans making them potent HIV-1 reservoirs. However, the
cellular factors involved in viral production by human macrophages have not been fully identified. In this study, we focused on an amino acid transporter from the solute carrier family called SLC38A7/SNAT7 (small neutral amino-acid transporter 7). It is the main transporter of glutamine, moving it from the lysosome to the cytoplasm. While expression of the SNAT7 protein was increased by HIV-1 infection, we revealed that depletion of SNAT7 using siRNA inhibited viral production, not only at the level of protein synthesis, but also early at the level of retro-transcription. Interestingly, SNAT7 depletion did not affect global RNA or protein synthesis in the cells. We further showed that the restriction factor SAMHD1 (SAM domain- and HD domain-containing protein 1) was activated in SNAT7-depleted cells and was responsible for viral restriction. Finally, supplementation of the extracellular medium with glutamine in the absence of SNAT7 partially restored viral production. Together, our data reveal that glutamine extracted from lysosomes is involved in the early stages of the HIV-1 cycle and that the SNAT7 glutamine transporter acts as a dependency factor for HIV-1 in human macrophages.

Mots-Clés: HIV, 1, Macrophages, SNAT7, Lysosomes, Glutamine

*Intervenant

30

Tlr7-biallelism defines a hyperfunctional state of female B lymphocytes

Rémi-Xavier Coux * [1], Charles-Henry Miquel [2], Mélissa Nieucel [2], Léa Ferrayé [2], Anne Laure Iscache [2], Claire Cenac [2], Bérénice Faz-Lopez [2], Yann Aubert [2], Hugo Garnier [2], Marie-Christine Birling [3], Maxime Dubois [4], Vanja Sisirak [4], Magali Savignac [2], Julie Chaumeil [1], Jean-Charles Guery [2]

[1] [Institut Cochin] Département Développement, Reproduction et Cancer – Institut cochin – France
[2] Institut Toulousain des Maladies Infectieuses et Inflammatoires – Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, Université de Toulouse – France
[3] Institut Clinique de la Souris (ICS) – CERBM-GIE – 1 rue Laurent Fries, 67404 Illkirch, France
[4] Immunology from Concept and Experiments to Translation = Immunologie Conceptuelle, Expérimentale et Translationnelle – Université de Bordeaux, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique – France

Sex disparities in systemic autoimmunity have been associated with enhanced dosage of the X-linked Toll-like receptor *TLR7*. While *TLR7* can escape X chromosome inactivation in female immune cells, its functional contributions to systemic autoimmunity remain unclear. Uusing unique *Tlr7* reporter mouse models, we identified and characterized a novel female-specific subset of mature naive B cells defined by bi-allelic *Tlr7* expression (BiA7). We show that BiA7 B cells express elevated TLR7 protein levels and are intrinsically poised for rapid differentiation into antibody-secreting cells. BiA7 cell development is promoted by type I interferon signaling and occurs independently of B cell receptor self-reactivity. While myeloid differentiation factor 88 (MyD88)-signaling is dispensable for the emergence of BiA7 cells within the follicular B cell compartment, it is critical for their accumulation within atypical memory age-associated B cells that drive lupus pathogenesis. Critically, enforced monoallelic *Tlr7* expression eliminates the BiA7 population and confers protection from *Tlr7*-driven lupus-like disease. Last, despite their naive phenotype, BiA7 B cells display an epigenomic landscape, resembling that of activated and antigen-experienced memory B cells, providing a mechanistic basis for their hyper-responsiveness. Together, our findings establish a direct causal link between X-linked *Tlr7* dosage, epigenetically primed B cell states, and female-biased systemic autoimmunity.

Mots-Clés: systemic autoimmunity, naive B cells, TLR7, epigenetics

*Intervenant

One virus, multiple strategies: how the common cold virus inhibits macrophage secretion

Zoé Fremont-Debaene *[1], Zeyni Mansuroglu [1], Leane Puchot [1], Frédéric Bonhomme [2], Paola B Arimondo [2], Florence Niedergang [1], Suzanne Faure-Dupuy [1]

[1] Institut Cochin – Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, Université Paris Cité – France

[2] Chimie Biologique pour le Vivant / Chemistry for Life Sciences – Institut Pasteur [Paris], Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique, Université Paris Cité – France

LHuman rhinoviruses (HRV), responsible for the common cold, are the main cause of bacterial superinfections in patients with chronic lung diseases, due to impaired macrophage function. We previously showed that macrophages exposure to HRV16 inhibits the secretion of several cytokines (i.e., IL-1β, IL-10, IL-6) following a stimulation mimicking a bacterial superinfection (Jubrail et al., 2018).

To identify the molecular mechanisms responsible for this inhibition, we used a model of human monocyte-derived macrophages exposed to HRV and subsequently stimulated TLR4 with a bacterial ligand, LPS.

Analyses revealed two distinct regulatory profiles. IL-1β and IL-10 showed decreased mRNA expression, indicating inhibition at the transcriptional level or upstream. Using mass spectrometry, we identified eleven epigenetic marks modulated in macrophages exposed to HRV. Among these, the decrease in the activating mark H2AZK4Ac was investigated at the promoters of IL-1β and IL-10 , but no significant variation was observed, suggesting the involvement of alternative regulatory mechanism. We therefore explored disruption of the TLR4 signaling pathway by analyzing the expression of its components and the nuclear translocation of the transcription factors p65 and IRF3. We demonstrated a pre-transcriptional inhibition of these cytokines by HRV.

In contrast, upon HRV exposure, IL-6 exhibited increased mRNA expression (associated with increased H2AZK4Ac at its promoter) without any change in its secretion, suggesting post-transcriptional regulation. We demonstrated cytoplasmic retention of IL-6 after HRV exposure, associated with Golgi apparatus impairment.

Overall, we showed that HRV inhibits cytokine production and secretion by macrophages both at the pre- and post-transcriptional level.

Mots-Clés: Macrophages, Virus, HRV16, cytokines

*Intervenant