HOSTING RESEARCH LABS

Centre d'Immunologie de Marseille-Luminy

Home | CIML (univ-mrs.fr)

Founded in 1976, the Centre d'Immunologie de Marseille-Luminy is a research institute internationally renowned in its discipline. From worm to man, from molecules to the whole organism, from nanosciences to system biology, from physiology to pathology, the CIML addresses all areas of contemporary immunology. These include the genesis of numerous cell populations, their modes of differentiation and activation, their implication in cancers, infectious and inflammatory diseases.

The CIML brings together 16 research teams and cutting-edge technological platforms and employs around 180 people, including scientists of many different nationalities.

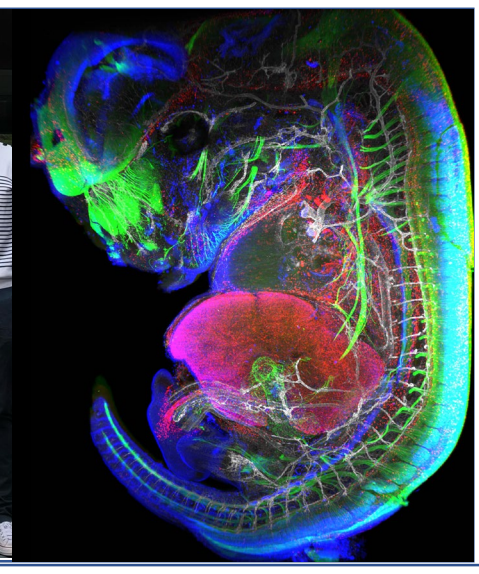
The CIML is located on the Luminy campus of Aix-Marseille University (Amu), in the exceptional environment of the Calanques National Park.

CIML,Parc Scientifique et Technologique de Luminy
Case 906, F 13288 Marseille cedex 09, FRANCE

Applications : Candidates should send a CV + letter of motivation with indications on the lab(s) and projects(s) they are interested in and the dates/duration they would be available for the internship to Dr Béatrice Nal-Rogier (nalrogier@ciml.univ-mrs.fr). *Applications are open until* ***March 31st 2025***.

Funding : up to 3 « *International Immunology at Amu » A*Midex fellowships* will be available for successful international candidates for short (1 to 2 months) and longer stays (up to 6 months). Candidates are encouraged to also apply to local funding in their home university and to ERASMUS fellowships, when possible.

Innate Lymphoid Cells in fetal and neonate immunity



Team Serge van de Pavert

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The Innate lymphoid cell (ILC) family play critical roles in early defense, tissue repair, and maintaining immune balance. They act as the innate counterparts to T cells, responding rapidly to infections and environmental cues without antigen-specific receptors. Of this family, the Lymphoid Tissue inducer (LTi) cell is critically involved in lymph node (LN) formation. LN are crucial for adaptive immunity and develop early in the fetus through interactions between hematopoietic and stromal cells. Our team is offering three exciting research projects focused on understanding Innate Lymphoid Cell (ILC) ontogeny and LN development:

Project 1: Maternal Diet Impact on Fetal ILC differentiation

This project aims to analyze the role of key components of the maternal diet on LN differentiation in the offspring. Our previous work demonstrated that Vitamin A within the maternal diet affects fetal LTi cell differentiation[5]. Besides Vitamin A, other dietary products are thought to affect fetal LTi cell differentiation. You will analyze lymph nodes differentiation in embryos from mouse knockout strains strains for key metabolic enzymes. You will also explore how a high-fat diet affects fetal ILC and lymph node formation in offspring.

Project 2: Neuronal Influence on Lymph Node Formation

This project aims to determine the role of the nervous system in lymph nodes formation. We hypothesize that neurons provide crucial signals controlling LTi localization and differentiation. If neurons are absent or misplaced, lymph nodes may develop in incorrect locations or not at all. In this project, you will investigate the relationships between neurons and LTi cells and concomitant LN formation in embryos using mouse models with specific neuronal deletions.

Project 3: ILC Ontogeny and LTi Cell Differentiation

Lymphoid Tissue Inducer (LTi) cells are the predominant ILC type in the fetus, but the mechanisms behind this preference to differentiate into LTi cells within the embryo remain unclear. This project aims to uncover how precursor cells differentiate into LTi cells and other ILCs. Using various reporter mouse models, you will study the stages of ILC development and analyze their localization within the embryo.

Techniques You Can Learn:

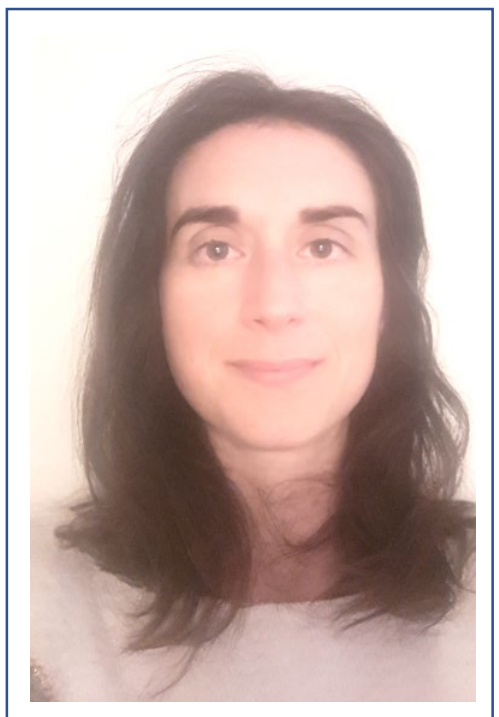
- Whole-mount immunofluorescence, analysis with Imaris
- Section immunofluorescence, processing using ImageJ
- (Spectral) Flow cytometry, analysis by FlowJo

Selected publications

1. Siret C, van de Pavert SA. **Methods Mol Biol.** 2024; 2713:297-306
2. Wang S, *et al.*, **Journal of Neuroinflammation** 2023 20-8
3. Siret C, *et al.*, **Nature Communications** 2022 13:7366
4. Simic M. *et al.*, **Cell Reports** 2020 Aug 11;32(6):108004.
4. Vivier E, van de Pavert SA, *et al.,* **Nature Immunology** 2016 17(7):790-794
5. van de Pavert SA, Ferreira M, *et al.*, **Nature** 508(7494):123-7 (co-first author)

http://www.ciml.univ-mrs.fr/science/lab-serge-van-de-pavert/development-immune-system

INNATE IMMUNITY AT MUCOSAL SITES



Julie TOMAS

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Achille Broggi and his team study the interplay between the immune system, commensal microbes, and the mucosal layer: http://www.ciml.univ-mrs.fr/publications/by-team/33837. Evolving in AB's team, I am particularly exploring how malnutrition affects mucosal homeostasis, microbiota and immune response.
Early emergence of malnutrition has disastrous consequences later in life and must be assessed at very early stages to fully understand the pathogenesis and associated side effects such as recurrent infections and noncommunicable diseases. We developed a Severe Acute Malnutrition (SAM) mouse model in males starting at weaning that reproduces the main physiological, immunological, microbial and metabolic features of SAM in children. In addition, we have identified key markers to monitor under nutritional intervention: the mucosal immune system and the intestinal microbiota, which remain dysbiotic unlike physiological parameters. Today, using this system, we are studying how to compensate for the side effects of SAM with probiotics, bacterial metabolites, combined or not with nutritional intervention, and how malnutrition favors infections and impairs vaccine efficacy.

Fanny Hidalgo-Villeda, Matthieu Million, Catherine Defoort, Thomas Vannier, Flavie Sicard, Margaux Lagier, Camille Wagner, Cynthia Arroyo-Portilla, Lionel Chasson Jean-Pierre Gorvel, Hugues Lelouard*, **Julie Tomas*** (2023). *Prolonged dysbiosis and altered immunity under nutritional intervention in a physiological mouse model of severe acute malnutrition*, iScience. DOI : 10.1016/j.isci.2023.106910

Cynthia Arroyo Portilla, Romain Fenouil, Camille Wagner, Cécilia Luciani, Margaux Lagier, Clément Da Silva, Fanny Hidalgo-Villeda, Lionel Spinelli, Mathieu Fallet, **Julie Tomas**, Jean-Pierre Gorvel, Hugues Lelouard (2023). *Peyer's patch phagocytes acquire specific transcriptional programs that influence their maturation and activation profiles*, Mucosal Immunoglogy. DOI: 10.1016/j.mucimm.2023.05.009

Julie Tomas, Yoon Koo, Dimitri Popoff, Vilma Arce-Gorvel, Sean Hanniffy, Jean-Pierre Gorvel, Cyrille Mionnet (2021). PTX Instructs the Development of Lung-Resident Memory T Cells in Bordetella pertussis Infected Mice, Toxins. DOI: 10.3390/toxins13090632

Camille Wagner, Johnny Bonnardel, Clément Da Silva, Lionel Spinelli, Cynthia Arroyo Portilla, **Julie Tomas**, Margaux Lagier, Lionel Chasson, Marion Masse, Marc Dalod, Alexandre Chollat-Namy, Jean-Pierre Gorvel, Hugues Lelouard (2020). *Differentiation Paths of Peyer's Patch LysoDCs are Linked to Sampling Site Positioning, Migration, and T Cell Priming*, Cell Reports DOI: 10.1016/j.celrep.2020.03.043

Julie Tomas, Céline Mulet, Azadeh Saffarian, Jean-Baptiste Cavin, Robert Ducroc, Béatrice Regnault, Chek Kun Tan, Kalina Duszka, Rémy Burcelin, Walter Wahli, Philippe J Sansonetti, Thierry Pédron, (2016). High Fat diet induces rapid alteration in the spatial distribution and composition of the small-intestinal microbiota through the PPAR-γ-antimicrobial peptides-CFTR axis. Proc Natl Acad Sci U S A. DOI: 10.1073/pnas.1612559113

Innate immunity in *C. elegans*

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Mechanobiology / aECM / epidermis / skin / cytoskeleton / innate immune system

How is the innate immune response of the epidermis controlled by the mechanical properties of the extracellular matrix? ?

The apical extracellular matrix (aECM) of *C. elegans* exhibits remarkable mechanical properties, reflecting its intricate structure and composition. This protective outer layer is comprised of collagenous proteins forming a complex and periodically organized mesh-like network. aECM damage leads to the reorganization of the cytoskeleton and the activation of immune responses in the underlying epidermis. The mechanical connections between the aECM and the plasma membrane/cytoskeleton are currently uncharacterised. We hypothesise that circumferential periodic collagens increase stretching anisotropy and could sense changes in tension, leading to cytoskeleton assembly. Using a combination of genetics, cell biology and biophysics, we are exploring the links between aECM damage, tension changes, and immune signaling in *C. elegans.* Our studies are expected to give fundamental insights into how the aECM affects immunity in other animals, including mammals.

Body stiffness is a mechanical property that facilitates contact-mediated mate recognition in Caenorhabditis **elegans**. Weng JW, Park H, Valotteau C, Chen RT, Essmann CL, Pujol N, Sternberg PW, Chen CH. **Curr Biol. 2023**

Meisosomes, folded membrane microdomains between the apical extracellular matrix and epidermis. Aggad D, Brouilly N, Omi S, Essmann CL, Dehapiot B, Savage-Dunn C, Richard F, Cazevieille C, Politi KA, Hall DH, Pujol R, Pujol N. **Elife. 2023**

Microtubule plus-end dynamics link wound repair to the innate immune response. Taffoni C, Omi S, Huber C, Mailfert S, Fallet M, Rupprecht JF, Ewbank JJ, Pujol N. **Elife. 2020**

Innate Immunity Promotes Sleep through Epidermal Antimicrobial Peptides. Sinner MP, Masurat F, Ewbank JJ, Pujol N, Bringmann H. **Curr Biol. 2021**

A Damage Sensor Associated with the Cuticle Coordinates Three Core Environmental Stress Responses in *Caenorhabditis **elegans***. Dodd W, Tang L, Lone JC, Wimberly K, Wu CW, Consalvo C, Wright JE, Pujol N, Choe KP. **Genetics. 2018**

Neuroimmune regulations of tissue regeneration

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Evolving in Sophie Ugolini's Team "Neural regulation of Immunity" in CIML, my research focuses on how immune cells respond to sensory neuron cues in periphery and more generally how the central nervous system orchestrates immune defense. Discovering that macrophages emerged very early during embryonic development changed ours views about how macrophages sense and interact with their surroundings, throughout the lifespan. Tissue-resident macrophages are now considered key players in tissue development, repair and regeneration and we are using spectral/light sheet imaging, high dimensional cytometry, and single-cell transcriptomics, to decipher the non-canonical functions allowing macrophages to regulate tissue homeostasis (e.g. in type 2 diabetes and in cancer). We also observed that the central nervous system can integrate peripheral information upon tissue injuries, and orchestrate the myeloid cell healing responses, suggesting an integral brain-to-periphery axis constantly tuning tissue integrity. Deciphering the nature of peripheral and central neuronal circuits promoting tissue integrity and repair will provide new leads for regenerative medicine strategies.
Neuroimmunologie is an emerging field of research at the crossroad between developmental immunologie and neurosciences, providing exciting opportunities for young and creative minds. The campus is also located in the unique and vibrant environment of Luminy, South of France city of Marseille, allowing adventurous fellows to discover the national park of Calanques.

- **Hoeffel G*#,** Debroas G*, Roger A, Rossignol R, Gouilly J, Laprie C, Chasson L, Barbon PV, Balsamo A, Reynder A, Moqrich A and Ugolini S#. Sensory neurons derived TAFA4 promotes dermal macrophage tissue repair functions. Nature 2021. Jun; 594(7861):94-99. (#co-corresponding author; *co-first author).
- **Hoeffel G*** & Ginoux F*. Fetal Monocytes and the Origins of Tissue-resident Macrophages. Cell. Immunol. 2018 (*co-corresponding author).
- **Hoeffel G,** Chen J, Lavin Y, Low D, Almeida FF, See P, Beaudin AE, Lum J, Low I, Forsberg C, Podinger M, Zolezzi F, Larib A, Ng LG, Chan JKY, Greter M, Becher B, Samokhvalov IM, Merad M, and Ginhoux F. C-Myb+ erythromyeloid progenitors-derived fetal monocytes give rise to tissue-resident macrophages. Immunity. 2015 Apr 21;42(4):665-78.
- Thion MS, Low D, Silvin A, Chen J, Grisel P, Schulte-Schrepping J, Blecher R, Ulas T, Squarzoni P, **Hoeffel G**, Coulpier F, Siopi E, David FS, Scholz C, Shihui F, Lum J, Amoyo AA, Larbi A, Poidinger M, Buttgereit A, Lledo PM, Greter M, Chan JKY, Amit I, Beyer M, Schultze JL, Schlitzer A, Pettersson S, Ginhoux F and Garel S. Microbiome influences prenatal and adult microglia in a sex-specific manner. Cell. 2018 Jan 18 172 (3):500-516. 330:5-15.
- Reynders A*,Anissa Z Jhumka A, Gaillard S, Mantilleri A, Malapert P, Magalon K, Salio C, Ugolini S, Castets F, Saurin AJ, Serino M, **Hoeffel G** and Aziz Moqrich A* Gut microbiota promotes pain chronicity in Myosin1A deficient male mice BioxRiv 2023.