

Marseille, 10 Mai 2022

**PhD student (H/F)**

**Starting 2022/10/01**

**Project title:** Deciphering the tissue imprinting of plasmacytoid dendritic cells in homeostasis and during viral infections

**Working context**

The CIML is a joint research unit of the CNRS, INSERM and Aix-Marseille University. It is composed of about 200 people and 16 research teams and is located in the Luminy Science and Technology Park in Marseille (France). Within the CIML, the student will work in the research team "Dendritic cells and antiviral immunity" led by Marc Dalod, and more precisely in the group led by Elena Tomasello. The recruited student will interact closely with an engineer recruited on the same research project and with the genomic facility of the CIML directed by Pierre Milpied.

**Missions**

The student will study the molecular and cellular mechanisms governing the functional heterogeneity of plasmacytoid dendritic cells (pDC) residing in different organs.

During systemic viral infections, plasmacytoid dendritic cells (pDCs) promote antiviral immunity via the production of type I/III interferons (IFN). This function is mainly exerted by splenic pDCs (Zucchini et al. Int Immunol 2008), whereas liver and intestine pDCs induce tolerance (Reizis, Immunity 2019). The first aim will be to determine whether organ-specific cell niches instruct distinct functions in the pDCs. During in vivo infection with murine cytomegalovirus, IFN-producing pDCs in the spleen sequentially acquire 5 activation states with different functions and microanatomical locations (Abbas et al. Nat Immunol 2020). The second aim will be to determine whether niches specifically induced by MCMV infection regulate the generation of different pDC activation states. These studies will be performed by using a systems biology approach, combining novel mutant mice specifically targeting pDCs with state-of-the-art genomics technologies and bioinformatics analyses (Guilliams et al, Cell 2022).

**Activities**

- 1) Isolation of different mouse organs, preparation of sections of these organs, immunofluorescent labelling to perform "spatial transcriptomics" experiments
- 2) RNA sequencing at the single cell or single nucleus level
- 3) Sample preparation, labelling and acquisition by multiparametric flow cytometry
- 4) Sample preparation, labelling and acquisition by multiparameter confocal spectral microscopy
- 5) Animal experimentation (mouse handling, intravenous injection, intraperitoneal injection)
- 6) Breeding and PCR genotyping of different mouse lines required for the research project experiments

## Skills

- 1) Excellent level of knowledge of Immunology
- 2) Very good knowledge of histology and microscopy techniques, preferably confocal, and/or of flow cytometry (strongly wished)
- 3) Proven experience in molecular biology: DNA and RNA extraction, PCR, qPCR (strongly wished)
- 4) Experience in care and use of mice for experimentation (practitioner/operator level wished)
- 5) Good knowledge of the English language, presentation in English of own results during team meetings
- 6) Management of mouse lines, genotyping

## Degrees

Bac +5/M2

## Contrat duration

3 ans/3 years, ANR contract

## Deadline for application

30/06/2022

## Contact

Send a CV, a motivation letter and contact information (e-mail, telephone) of two referees (e.g. M2 internship supervisor, master teacher) to:

**Elena Tomasello**, [tomasell@ciml.univ-mrs.fr](mailto:tomasell@ciml.univ-mrs.fr)

## Bibliography

- **Individual plasmacytoid dendritic cells are major contributors to the production of multiple innate cytokines in an organ-specific manner during viral infection.** Zucchini N, Bessou G, Robbins SH, Chasson L, Raper A, Crocker PR, Dalod M. *Int Immunol.* 2008 20:45-56.
- **Plasmacytoid Dendritic Cells: Development, Regulation, and Function.** Reizis B. *Immunity.* 2019 50:37-50.
- **The activation trajectory of plasmacytoid dendritic cells in vivo during a viral infection.** Abbas A, Vu Manh TP, Valente M, Collinet N, Attaf N, Dong C, Naciri K, Chelbi R, Brelurut G, Cervera-Marzal I, Rauwel B, Davignon JL, Bessou G, Thomas-Chollier M, Thieffry D, Villani AC, Milpied P, Dalod M, Tomasello E. *Nat Immunol.* 2020 21:983-997.
- **Spatial proteogenomics reveals distinct and evolutionarily conserved hepatic macrophage niches.** Guilliams M, Bonnardel J, Haest B, Vanderborght B, Wagner C, Remmerie A, Bujko A, Martens L, Thoné T, Browaeys R, De Ponti FF, Vanneste B, Zwicker C, Svedberg FR, Vanhalewyn T, Gonçalves A, Lippens S, Devriendt B, Cox E, Ferrero G, Wittamer V, Willaert A, Kaptein SJF, Neyts J, Dallmeier K, Geldhof P, Casaert S, Deplancke B, Ten Dijke P, Hoorens A, Vanlander A, Berrevoet F, Van Nieuwenhove Y, Saeys Y, Saelens W, Van Vlierberghe H, Devisscher L, Scott CL. *Cell.* 2022 185:379-396.