Dalod Marc, PhD
Team leader at CIML
Tel : +33 (0)4.91.26.94.51
dalod@ciml.univ-mrs.fr

Marseille, February 28th 2022,

Post-doctoral position in Immuno-oncology,
in the team of Marc Dalod (CIML, Marseille, France),

Provisional start date: 01/06/2022
Contract duration: 2,5 years (30 months)

The CIML (Centre d'Immunologie de Marseille-Luminy, AMU UM2, CNRS UMR7280; Inserm U1104), is a dynamic research center located in Marseille that comprises internationally recognized groups focusing on Immunology.
The team of Marc Dalod has made major contributions in the identification and functional study of mouse and human dendritic cell types (http://www.ciml.univ-mrs.fr/science/lab-marc-dalod/experts), including participating to the discovery of mouse plasmacytoid dendritic cells (pDC) (1,2), to the alignment of mouse and human DC types, including the type 1 conventional DC (cDC1) that excel in cross-presentation of cell-associated antigens to cytotoxic CD8 T lymphocytes (3, 4), and their functional study in infection (5-8) or cancer (9-12) settings.

We seek to hire a highly motivated postdoctoral fellow to investigate the role of pDC, cDC1 and interferons, in mouse models of breast cancer, in tight **collaboration with the groups of Nathalie Bendriss-Vermare and Jenny Valladeau-Guillemond in the laboratory of Christophe Caux** at the Cancer Research Center of Lyon.

The applicant will work under the supervision of Drs. Marc Dalod and Elena Tomasello, in collaboration with a PhD student in the team, Ramazan Akyol. The aim will be **to decipher the early cellular and molecular mechanisms of immune surveillance against triple-negative breast cancer** (TNBC). We use transplantable models of preneoplastic organoids, and regressive or progressor cell lines, derived from spontaneous mouse mammary adenocarcinoma. We will study them by combining i) deep characterization of the tumor-associated DC types, including by single cell RNA sequencing, and ii) proprietary mutant mice as graft recipients to specifically manipulate DC types. We will pursue 3 objectives. (1) To identify common candidate immune surveillance pathways and targets in human and mouse tumor-associated DC. (2) To analyze the role of cDC1 and pDC in early immune surveillance against TNBC. (3) To decipher the importance during breast cancer immune surveillance of cell-intrinsic signaling in DC types by type I or III interferons, interferon-γ, and other newly identified pathways/targets. This project should lead to the identification of immunotherapy targets able to promote the anti-tumor functions of cDC1, pDC and IFNs, complementary to the targets currently evaluated in clinical trials that have shown limited efficacy so far in TNBC.

Benefits
The applicant will benefit from a strong collaborative environment. The CIML (http://www.ciml.univ-mrs.fr) is composed of 18 research teams, 6 core facilities, administration and technical services. It is located on the Luminy campus regrouping fundamental research laboratories in life sciences, informatics, physics, chemistry and mathematics, and biotech start-up companies, including several that emerged from CIML work: Immunotech, Innate Pharma, Oz Bioscience and HalioDX/Veracyte. The Dalod team also belongs to the CenTuri Institute (http://centuri-livingsystems.org/) that fosters tight collaborations between biologists, mathematicians, physicists and bio-informaticians to understand how biological function emerges from the organization and dynamics of living systems.

Eligibility criteria
The candidate must have a PhD in Immunology or Cancerology, with **advanced experience in high content flow cytometry**, and **expert proficiency in experimentation *in vivo* in mice**, including treatment of mice through intraperitoneal or intravenous injections, harvest of various organs, and preparation of cell suspensions from these organs for flow cytometry. The project will require flexibility in working hours. **Documented expertise in the generation of bulk and single cell RNA sequencing data will also be valuable.** The candidate will have to

contribute to the management of the mouse lines required for the project, including their genotyping. The candidate must have demonstrated an ability to work well both independently and as a member of a team.

Publications related to the project:

1. Asselin-Paturel et al. Mouse type I IFN-producing cells are immature APCs with plasmacytoid morphology. Nat Immunol. 2001. doi: 10.1038/ni736.
2. Dalod et al. Interferon alpha/beta and interleukin 12 responses to viral infections: pathways regulating dendritic cell cytokine expression in vivo. J Exp Med. 2002. doi: 10.1084/jem.20011672.
3) Robbins et al. Novel insights into the relationships between dendritic cell subsets in human and mouse revealed by genome-wide expression profiling. Genome Biol. 2008. doi: 10.1186/gb-2008-9-1-r17.
4) Crozat et al. The XC chemokine receptor 1 is a conserved selective marker of mammalian cells homologous to mouse CD8alpha+ dendritic cells. J Exp Med. 2010. doi: 10.1084/jem.20100223.
5) Abbas et al. The activation trajectory of plasmacytoid dendritic cells in vivo during a viral infection. Nat Immunol. 2020. doi: 10.1038/s41590-020-0731-4. *Co-first authors. **Co-senior authors.
6) Valente et al. A novel mouse model based on intersectional genetics enables unambiguous in vivo discrimination between plasmacytoid and other dendritic cells and their comparative characterization. bioRxiv 2022.01.07.475382; doi: https://doi.org/10.1101/2022.01.07.475382. **Co-senior authors.
7) Alexandre et al. XCR1+ dendritic cells promote memory CD8+ T cell recall upon secondary infections with Listeria monocytogenes or certain viruses. J Exp Med. 2016. doi: 10.1084/jem.20142350.
8) Ghilas et al. Natural killer cells and dendritic epidermal γδ T cells orchestrate type 1 conventional DC spatiotemporal repositioning toward CD8+ T cells. iScience. 2021. doi: 10.1016/j.isci.2021.103059.
9) Cancel et al. Are Conventional Type 1 Dendritic Cells Critical for Protective Antitumor Immunity and How? Front Immunol. 2019. doi: 10.3389/fimmu.2019.00009.
10) Ghislat et al. NF-κB-dependent IRF1 activation programs cDC1 dendritic cells to drive antitumor immunity. Sci Immunol. 2021. doi: 10.1126/sciimmunol.abg3570.
11) Hubert et al. IFN-III is selectively produced by cDC1 and predicts good clinical outcome in breast cancer. Sci Immunol. 2020. doi: 10.1126/sciimmunol.aav3942.
12) Mattiuz et al. Type 1 conventional dendritic cells and interferons are required for spontaneous CD4+ and CD8+ T-cell protective responses to breast cancer. Clin Transl Immunology. 2021. doi: 10.1002/cti2.1305.

REQUIRED EDUCATION LEVEL

Biological sciences: PhD in Immunology or Cancerology

REQUIRED LANGUAGES

FRENCH: Good
ENGLISH: Excellent (strong writing and oral communication skills in English will be needed).

Skills/Qualifications

The applicant must have:
*a PhD in Immunology or Cancerology,
*Proficiency in animal experimentation (intraperitoneal or intravenous injections on vigil animals; euthanasia of animals; harvesting of organs ...),
*Expert skills in high content flow cytometry,
*Ability to manage mouse colonies, including their genotyping,
*A minima, experience in RNA extraction from tissues and gene expression profiling by qRT-PCR; ideally documented expertise in the generation of bulk and single cell RNA sequencing data.

Application process:

Please send by email to dalod@ciml.univ-mrs.fr:
1) a CV,
2) a list of publications,
3) a short description of previous research projects and experience,
4) the contact information for at least two referees, including the PhD mentor,
5) a motivation letter.

Deadline for application

31/03/2022