

Postdoctoral position available: single-cell multi-omics in oncoimmunology.

Offer: The laboratory of Dr Nathalie Bonnefoy, Immunity and Cancer team, at the research cancer institute of Montpellier (IRCM, INSERM U1194: <https://www.ircm.fr>) is looking for a full-time postdoctoral research fellow to take on an exciting highly translational project to decipher tumor promoting neutrophils biogenesis in non-small cell lung cancer patients and mouse models.

The position is offered for **24 months with a possible reconduction for 1 year**; selected candidate will work under the supervision of Dr Julien Faget.

Keywords: Neutrophil, lung cancer, immunotherapy, single-cell multi-omics, epigenetics, image mass cytometry, genetic engineered mouse models

Scientific summary:

Immune checkpoint inhibitors (ICIs) constitute the latest revolution in the care of patients with cancer, providing long-term survival benefit in only a subset (25 to 40%) of treated patients. Our recent work together with findings from others highlighted the critical involvement of tumor-associated neutrophils (TANs) in resistance to ICIs in lung cancer. Especially, we observed that a massive TAN infiltration occurs in about 20% of patients and is associated with tumor immune exclusion, a key feature of resistance to ICIs[1,2]. We also showed, in a genetic engineered mouse model of lung cancer, that neutrophil depletion remodels the tumor microenvironment (TME) and favors response to anti-PD1 treatment. Furthermore, accumulation of tumor-promoting TANs in mouse lung tumors requires a remote alteration of neutrophil biogenesis in the bone marrow [3,4].

Using state-of-the-art technologies, our research focuses on deciphering TAN related resistance to ICI, with a special interest on the link between neutropoiesis alteration in lung cancer, TAN functional diversity and the architecture of the TME. Through single-cell RNAseq and single-cell ATACseq analyses on lung cancer patients blood samples and tumors, together with image mass cytometry (Hyperion) we expect to identify novel predictive markers based on circulating neutrophil epigenetics, to better understand neutrophil plasticity and finally to propose innovative therapeutic strategies that will be evaluated in mice.

Lab location and description:

The IRCM (INSERM U1194) currently hosts 16 teams dedicated to cancer research and located in ICM Cancer Hospital Campus allowing optimal interaction with clinicians. IRCM hosts several technical facilities (proteomics, cellular screening, cytometry, microscopy, organoids) some being part of the Montpellier Biocampus network. It offers a unique pipeline dedicated to the generation and in vivo use of preclinical models (including syngeneic grafts, cell-line and patient-derived xenografts models), and their most comprehensive analysis by small animal imaging (IPAM), targeted or whole-body irradiation and histology (RHEM). IRCM has developed top notch innovative platforms to generate genetically engineered monoclonal antibodies (GenAc), to exploration of tissue ecosystems by imaging mass cytometry (CIM) and the PLATON platform dedicated to metabolomic analysis. IRCM is also characterized by its efforts to valorize its research activity through the creation/housing of biotech.

Candidate profile:

We are seeking a highly motivated PhD/MD-PhD who wants to develop its own research project in an independent way while having a good team-working spirit. The candidate must be strongly motivated for importing / developing / learning bioinformatics for sing-cell multi-omics.

- Expertise on bioinformatics and single-cell analyses (RNAseq, ATACseq) will be strongly appreciated
- Expertise on human sample handling, flow cytometry and cell purification methods will be a good point however technical support for wet-lab and mouse work will be offered.
- Knowledge on cancer immunology would be welcome but not mandatory

Application: Please send a concise cover letter with a statement of research interests and a summary of previous research activity and achievements. We will also require detailed *curriculum vitae* and two reference letters. Applications should be sent to Julien Faget: Julien.faget@inserm.fr

References:

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2. **Faget J**, Peters S, Quantin X, Meylan E, Bonnefoy N. Neutrophils in the era of immune checkpoint blockade. *J Immunother Cancer*. 2021 Jul 1;9(7):e002242.
3. Engblom C, Pfirschke C, Zilionis R, Da Silva Martins J, Bos SA, Courties G, Rickelt S, Severe N, Baryawno N, **Faget J**, Savova V, Zemmour D, Kline J, Siwicki M, Garriss C, Pucci F, Liao HW, Lin YJ, Newton A, Yaghi OK, Iwamoto Y, Tricot B, Wojtkiewicz GR, Nahrendorf M, Cortez-Retamozo V, Meylan E, Hynes RO, Demay M, Klein A, Bredella MA, Scadden DT, Weissleder R, Pittet MJ. Osteoblasts remotely supply lung tumors with cancer-promoting SiglecFhigh neutrophils. *Science*. 2017 01;358(6367).
4. Zilionis R, Engblom C, Pfirschke C, Savova V, Zemmour D, Saatcioglu HD, Krishnan I, Maroni G, Meyerovitz CV, Kerwin CM, Choi S, Richards WG, Rienzo AD, Tenen DG, Bueno R, Levantini E, Pittet MJ, Klein AM. Single cell transcriptomics of human and mouse lung cancers reveals conserved myeloid populations across individuals and species. *Immunity*. 2019 May 21;50(5):1317-1334.e10.