

Position Title	Post-doctoral fellow (<u>two years contract</u>)
Supervisor	Charles-Antoine DUTERTRE
Laboratory	Inserm U1015 (Tumour Immunology and anti-cancer immunotherapy unit) Director: Laurence ZITVOGEL Team: Myeloid Cell Development Laboratory Team leader: Florent GINHOUX
Location of Work	Gustave Roussy Institute (IGR) 114 rue Edouard Vaillant, 94800 Villejuif, France

Qualifications

Candidate must:

- Hold a Ph.D. degree in Immunology or Cancer Biology
- Expertise in mononuclear phagocytes and/or T-cell biology
- Training with 2D primary cell culture (3D would be an advantage)
- Training with multi-parametric flow cytometry
- Must be able to communicate in English (official language in the laboratory)

To apply

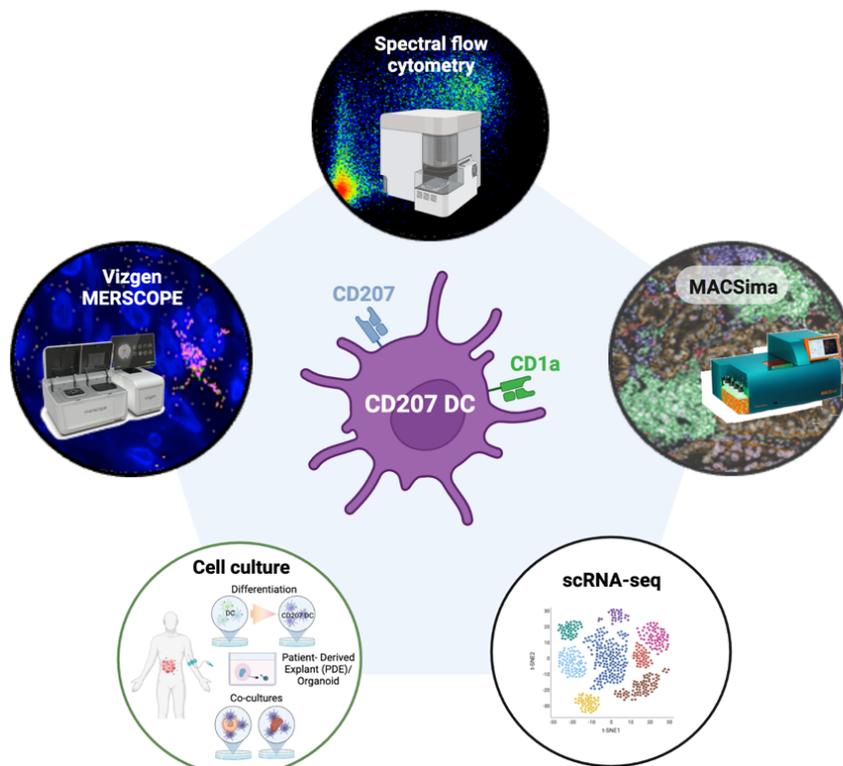
Send a motivation letter, a curriculum vitae and the name and email of two to three reference mentors to Charles-Antoine Dutertre (cadutertre@gmail.com)

Research activity of the team

Our research focuses on human mononuclear phagocytes (MNP), including dendritic cell (DC), monocyte and macrophage (Mac) subsets, in steady state and in pathologic settings. A common aspect of pathologies we study is their association with chronic inflammation, a hallmark of cancer progression. Over the last 4 years, we have been evaluating the heterogeneity and pathophysiological involvement of MNP subsets in several human solid tumours, which led to discoveries that have been published (Sharma *et al.*, Cell 2019; Mulder *et al.*, Immunity 2021) or that are submitted or in revision. Over the last 10 years, we have been pioneering in the development of high dimensional flow cytometry analyses, as well as single-cell RNA sequencing data generation and analysis, which both require robust machine learning-based analytic tools.

Proposed project

Evaluation of the immunosuppressive functions of CD207⁺ dendritic cells in human carcinomas



Proposed project outline

The presence of intra-tumoral cytotoxic CD8⁺ T cells is associated with a good prognosis in most cancers. Dendritic cells (DC) and monocyte/macrophages (MoMac) are key regulators of the anti-tumour T cell response and populate most tumours. Following our multi-omic analysis of tumour MoMac (Mulder *et al.*, Immunity 2021), we integrated 38,293 DC from 13 tissues across 40 datasets to generate a DC single-cell RNA compendium (DC-VERSE) (Mulder*, Kong* *et al.*, in revision). We found that all neoplastic tissues included in the study contained CD207⁺ DCs, and their abundance was inversely correlated with tumour CD8⁺ resident memory T cells (T_{RMS}), T cell clonality, and were associated with lower patient survival.

The proposed project's aim is to unravel the mechanism by which CD207⁺ DCs could lead to the poor anti-tumour T cell response, focusing on human carcinomas (Breast, Lung, colon, Stomach, Liver, Head & Neck, and Pancreas).

This will be addressed using:

- 2D cultures, 3D cultures (tumour spheroids) and fresh tumour explants
- Spectral flow cytometry (Cytek Aurora)
- scRNAseq (10X Genomics, BD Rhapsody)
- LegendScreen and InfinityFlow (Dutertre *et al.*, Immunity 2019)

Relevant publications of the team

1. Guilliams M*, Dutertre CA*, ..., Ginhoux F. Unsupervised High-Dimensional Analysis Aligns Dendritic Cells across Tissues and Species. *Immunity*, 2016, 20, 669-684. *co-1st authors
2. See P*, Dutertre CA*, ..., Ginhoux F. Mapping the human DC lineage through the integration of high dimensional techniques. *Science*, 2017, 356, 6342. *co-1st authors
3. Tan-Garcia A, ..., Dutertre CA. Intrahepatic CD206⁺ macrophages accumulate and drive inflammation in advanced viral-related liver disease, *J Hepatol*, 2017, 67, 490.
4. Becht E, McInnes L, Healy J, Dutertre CA, Kwok I, Ng LG, Ginhoux F, Newell E. Evaluation of UMAP as an alternative to t-SNE for single-cell data, *Nature Biotech*, 2018, 37, 38-44.
5. Dutertre CA, ..., Ginhoux F. Single-Cell Analysis of Human Mononuclear Phagocytes Reveals Subset-Defining Markers and Identifies Circulating Inflammatory Dendritic Cells, *Immunity*, 2019, pii: S1074-7613, 30334-6.
6. Tan-Garcia A, ..., Dutertre CA. GM-CSF neutralisation suppresses pro-inflammatory CD206⁺ macrophage accumulation in viral-related liver disease, *J Hepatol Reports*, 2019, 2, 100062.
7. Mulder K*, Patel AS*, Kong WT*, ..., Dutertre CA** and Ginhoux F**. The MoMac-VERSE: Dissecting the diversity of human monocytes and macrophages in health and disease. *Immunity*. 2021 Aug 10;54(8):1883-1900.e5. *co-1st authors, **co-senior authors.
8. Becht E, Tolstrup D, Dutertre CA, ..., Headley MB. High-throughput single-cell quantification of hundreds of proteins using conventional flow cytometry and machine learning. *Sci Adv*. 2021 Sep 24;7(39):eabg0505. doi: 10.1126/sciadv.abg0505.
9. Anderson DA 3rd, Dutertre CA, Ginhoux F, Murphy KM. Genetic models of human and mouse dendritic cell development and function. *Nat Rev Immunol*, 2020, doi: 10.1038/s41577-020-00413-x.
10. Ginhoux F*, Yalin A*, Dutertre CA*, Amit I*. Single-cell immunology: past, present and future. *Immunity*, 2022 Mar 8;55(3):393-404. doi: 10.1016/j.immuni.2022.02.006. * co-corresponding authors