

Post-doctoral position at Sorbonne Université
ICM and LIP6
Spatial analysis of gliomas from multiplexed imaging data

Despite advances in cancer immunotherapy, high-grade gliomas (HGGs) remain largely unresponsive to immune checkpoint blockade (ICB) partly because of their immune tumor microenvironment (iTME) with strong immunosuppressive features. Our preliminary data suggest that differences in tumor cell states and iTME spatial organization correlate to HGGs patients' outcomes and mechanisms by which tumors resist to immunotherapy, with differences across glioma types and within tumors from the same subtype.

In order to test the hypothesis that the iTME spatial organization influences immunotherapy response, spatial analysis of tumor-iTME relationships has to be performed. This will be addressed with multiplexed imaging and machine learning in cohorts of interest of tumor samples obtained during the treatment of patients. Correlations will be studied between tumor-iTME interactions, iTME spatial patterns (eg rare lymphocytic infiltrates, perivascular vs parenchymal/perivascular) and survival and response to ICBs.

Data will be acquired by the newly developed imaging mass spectrometry system Hyperion to obtain spatial distribution of 35 molecular markers at a cellular resolution.

The main work during the post-doctoral research will be to develop image analysis method to (1) segment and classify individual cells, (2) analyze their neighborhood and define frequent patterns, (3) establish associations between spatial patterns and tumor type or other information (e.g. age, molecular type, outcome), (4) explore evolution of the tumor from static images. Methods based on morphological analysis, machine learning (including convolutional neural networks and generative models), or combination of those, can be investigated.

Practical information:

Within this interdisciplinary project, the post-doctoral researcher will have to work in close collaboration with ICM at Pitié-Salpêtrière hospital (Mehdi Touat, Franck Bielle, Julie Lerond) and LIP6 (Isabelle Bloch). The two labs are located in Paris, at walking distance from each other.

The post-doc is for one year, and may be renewed for a second year. It could start between December 2022 and January 2023.

Applications:

Applications should include:

- a detailed CV, with a list of publications and a summary of previous achievements,
- a motivation letter,
- a research statement related to the project objectives,

and should be sent before November 30, 2022, in pdf format, to isabelle.bloch@sorbonne-universite.fr, mehdi.touat@aphp.fr, franck.bielle@aphp.fr

A few references:

- Bae et al. Discovery of molecular features underlying the morphological landscape by integrating spatial transcriptomic data with deep features of tissue images. *Nucleic*

Acids Research, 2021, Vol. 49, No. 10 e55

- Chen et al. Classification and mutation prediction based on histopathology H&E images in liver cancer using deep learning. *Precision Oncology* 2020;4:14.
- Efremova et al. CellPhoneDB: inferring cell-cell communication from combined expression of multi-subunit ligand-receptor complexes. *Nat Protoc* 2020;15:1484-1506.
- Hamidinekoo et al. Automated Quantification Of Blood Microvessels In Hematoxylin And Eosin Whole Slide Images. *Proceedings of Machine Learning Research* 156 (2021)
- Kather et al. Continuous representation of tumor microvessel density and detection of angiogenic hotspots in histological whole-slide images. *Oncotarget* 2015;22:19163
- Lin et al. Multiplexed 3D atlas of state transitions and immune interactions in colorectal cancer. *BioRxiv* <https://www.biorxiv.org/content/10.1101/2021.03.31.437984v1>
- Schapiro et al. MCMICRO: A scalable, modular image-processing pipeline for multiplexed tissue imaging. *Nature Methods*, volume 19, pages 311–315 (2022)
- Schürch et al. Coordinated Cellular Neighborhoods Orchestrate Antitumoral Immunity at the Colorectal Cancer Invasive Front. *Cell* 2020;182:1341-1359.e19.
- Schmauch et al. A deep learning model to predict RNA-Seq expression of tumours from whole slide images. *Nature Communications* 2020;11: 3877.
- Touat et al. Mechanisms and therapeutic implications of hypermutation in gliomas. *Nature* 2020;580:517-523
- Väyrynen et al. Composition, Spatial Characteristics, and Prognostic Significance of Myeloid Cell Infiltration in Pancreatic Cancer. *Clin Cancer Res* 2021;27:1069-1081.