



## Post-doctoral position

Applications are welcome for a postdoctoral position on **the mechanics of tumor infiltrating lymphocytes**. The project is mainly **experimental**, will begin **early 2020**, and is funded by a Bettencourt-Schueller Biomedical Engineering Seed Grant for **one year that might be extended another year**. The project will be conducted in a large part in the Hydrodynamics Laboratory, Ecole polytechnique (Palaiseau, France) with tight interactions with Institut Curie (Paris, France).

### Profile of the candidate

The successful candidate will hold a PhD and a strong record in experimental biophysics. She/he will be strongly motivated by experiments at the single-cell level and have a background in image analysis and coding (e.g. Python). The project also requires basic cell culture knowledge as cells from patients in limited amount will be manipulated. Candidates should be skilled to interact with several groups including medical doctors, biologists, and physicists/engineers: a clear taste for interdisciplinary research is needed.

### Partners of the project

Dr. Julien Husson, Hydrodynamics Laboratory (LadHyX), Ecole polytechnique – CNRS, Palaiseau, France.

Dr. Emanuela Romano, MD PhD, Center of Cancer Immunotherapy, Department of Medical Oncology, INSERM U932, Institut Curie, Paris, France.

Dr. Claire Hivroz, Institut Curie – INSERM U932, Institut Curie, Paris, France.

### Contact

A high personal motivation to develop a challenging project is required. To apply please send the following documents as a single PDF file: detailed CV with description of expertise in biophysics, motivation letter, publication list including preprints, and contact details of three referees.

Inquiries can be addressed to Julien Husson, [julien.husson@ladhyx.polytechnique.fr](mailto:julien.husson@ladhyx.polytechnique.fr)

### Aims

Our vision is that quantifying cell mechanical properties can be used as an innovative readout of cell signaling<sup>1</sup>, and our aim is to use it to better characterize the functional state of T cells in cancer. Tumors contain Tumor Infiltrating Lymphocytes (TILs), including cytotoxic T lymphocytes, but instead of killing tumor cells, TILs are inhibited by the tumor microenvironment in particular by immune checkpoints (ligand-receptor interactions that can lead to T cell inhibition). The recent development of immune checkpoint blockers has represented a significant clinical breakthrough. Antibodies are used to lift the inhibition of TILs by blocking immune checkpoints such as PD-1/PD-L1. Although immune checkpoint blockade led to unprecedented durable response rates in some cancers, some patients are resistant to these immunotherapies. Innovative tools are needed to investigate the functional responses of TILs from patients. The specific goal of the present application is to establish that lymphocytes extracted from tumors have a characteristic mechanical signature.

We recently established a detailed sequence of morphological changes and force generation that T lymphocytes undergo during activation<sup>1,2</sup>. We further quantified viscoelastic changes in T cell during



activation, and established that the large viscoelastic changes that we observe correlate with specific morphological changes such as shape change and area expansion<sup>3</sup>. Both **micropipette-based single-cell micromanipulation techniques**<sup>1-5</sup> and **image analysis** will be used to characterize the morpho-mechanical signature of lymphocytes exposed to immune checkpoint inhibitors or purified from tumors (TILs). We hereby expect to reveal new parameters characterizing dysfunctional lymphocytes that might be a useful biomarker for therapeutic intervention.

### References

1. Basu, R. *et al.* Cytotoxic T Cells Use Mechanical Force to Potentiate Target Cell Killing. *Cell* **165**, 100–110 (2016).
2. Sawicka, A. *et al.* Micropipette Force Probe to quantify single-cell force generation: application to T cell activation. *Mol. Biol. Cell* **28**, mbc.E17-06-0385 (2017).
3. Zak, A. *et al.* Single-cell immuno-mechanics : rapid viscoelastic changes are a hall- mark of early leukocyte activation. *bioarxiv* (2019). doi:10.1101/851634
4. Guillou, L. *et al.* T lymphocyte passive deformation is controlled by unfolding of membrane surface reservoirs. *Mol. Biol. Cell* **27**, 3574–3582 (2016).
5. Guillou, L., Babataheri, A., Puech, P.-H., Barakat, A. I. I. & Husson, J. Dynamic monitoring of cell mechanical properties using profile microindentation. *Sci. Rep.* **6**, 21529 (2016).