

Post-doctoral position at the Cancer Research Center of Lyon FRANCE.

Team : Inflammasome and Cancer

Application Deadline October the 15th 2020.

A **postdoctoral position** is available at the **CRCL - INSERM U1052 CNRS UMR5286** in the research team of **Dr Virginie Petrilli** to work on the **characterization of the regulation of the ATM pathway by the Pattern Recognition Receptor NLRP3**. The team interest focuses on the biology of the NLRP3 receptor and the inflammasome (Guey, *in press*; Guey et al., 2014; Muruve et al., 2008; Pétrilli et al., 2007...), a major complex of the innate immunity. The NLRP3 protein is well-known for its role in the formation of the inflammasome complex which controls caspase-1 activation, proinflammatory cytokine production and pyroptosis in myeloid cells. Recently, the team also discovered a novel non immune function for NLRP3 in the DNA Damage Response pathway.

ATM is the central kinase orchestrating the DDR. The molecular mechanism leading to ATM activation upon formation of double strand breaks remains poorly understood. Dr Petrilli's team has recently demonstrated that NLRP3 is crucial to reach optimal ATM activation, and its knock-down renders the cells more resistant to chemotherapy-induced apoptosis (Bodnar-Wachtel et al., 2020). Furthermore, the team showed that its expression is strongly impaired in Non-Small Cell Lung Cancers suggesting oncosuppressive properties. The proposed project aims at deciphering more precisely the molecular mechanisms by which NLRP3 controls ATM activation, and at further characterizing the functional consequences of NLRP3 loss on the DDR pathway. For instance, the candidate will address whether this interaction is regulated by post-translational modifications, determine the specific functions of NLRP3 associated with its different subcellular localizations, and phenotype the NLRP3 knock-out cells.

The candidate profile :

- PhD in Biochemistry or Cell biology
- Strong expertise in working with proteins (co-immunoprecipitation, proteomic, analysis of post-translational modifications)
- Expertise in cell biology (tissue culture of immortalized cells, lentivirus production and transduction)
- knowledge on the DNA damage response or DNA repair field.

- good communication skills
- rigor
- autonomy

We are looking for a **highly motivated** candidate. The initial funding is for 18 months but the laboratory will support the candidate to apply for postdoctoral funding in order to extend the contract.

Please send your CV to virgine.petrilli@inserm.fr including at least 2 referees to be contacted for recommendation, a list of publications and an cover letter describing the work you have performed so far and your career objectives.

Bodnar-Wachtel, M., Huber, A.-L., Gorry, J., Hacot, S., Gerossier, L., Guey, B., Goutagny, N., Bartosch, B., Ballot, E., Ghiringhelli, F., Py, B., Couté, Y., Ballesta, A., Lantuejoul, S., Hall, J., & PETRILLI, V. (2020). NLRP3 controls ATM activation in response to DNA damage. *BioRxiv*, 2020.05.12.087015. <https://doi.org/10.1101/2020.05.12.087015>

Guey B., Bodnar-Wachtel M., Drouillard A., Eberhardt A., Pratviel M., Goutagny N., Bendriss-Vermare N., Puisieux I., Caux C., Walzer T., and Petrilli V. Inflammasome deletion promotes anti-tumor NK cell function in an IL-1/IL-18 independent way in murine invasive breast cancer. *Frontiers in Oncology*. In press

Guey, B., Bodnar, M., Manié, S. N. S. N., Tardivel, A., & Petrilli, V. (2014). Caspase-1 autoproteolysis is differentially required for NLRP1b and NLRP3 inflammasome function. *Proceedings of the National Academy of Sciences of the United States of America*, 111(48), 17254–17259. <https://doi.org/10.1073/pnas.1415756111>

Muruve, D. a D. A., Petrilli, V., Zaiss, A. K. A. K., White, L. R. L. R., Clark, S. a, Ross, P. J. J., Parks, R. J. R. J., Tschopp, J., Pétrilli, V., Zaiss, A. K. A. K., White, L. R. L. R., Clark, S. a, Ross, P. J. J., Parks, R. J. R. J., & Tschopp, J. (2008). The inflammasome recognizes cytosolic microbial and host DNA and triggers an innate immune response. *Nature*, 452(7183), 103–107. <https://doi.org/10.1038/nature06664>

Pétrilli, V., Dostert, C., Muruve, D. a D. A., Tschopp, J., Petrilli, V., Dostert, C., Muruve, D. a D. A., & Tschopp, J. (2007). The inflammasome: a danger sensing

complex triggering innate immunity. *Current Opinion in Immunology*, 19(6), 615–622. <https://doi.org/10.1016/j.coi.2007.09.002>