Title: Master 2 Internship - Systems biology and gene network analysis of autoimmune and inflammatory disorders

Keywords: Immunology, Bioinformatics, transcriptome analysis, RNAseq, network analysis

Project Summary:
The i3 laboratory launched in 2015 an observational clinical trial, Transimmunom (NCT02466217), which aims at studying nineteen autoimmune and inflammatory disorders. The final goal is to guide the development of novel treatments and redefine the nosography of autoimmune and autoinflammatory diseases. Our strategy is to integrate clinical and "omics" data to identify and understand the complexity of the immune responses underlying these immunopathologies by applying a systems biology approach. In particular, we focused our investigations on processing, analysing and creating solutions to integrate transcriptome (RNA-seq), TCR repertoire (Rep-seq), deep immunophenotyping (ten flow cytometry panels), microbiome (metagenomics), cytokines (Luminex) and clinical data. Currently, we processed samples from 200 patients (affected by one of the nineteen pathologies) and 50 healthy donors. Data have been generated and stored in dedicated servers and Laboratory Information Management Systems (LIMS).

The project proposal for a Master 2 internship aims at developing, under the supervision of a bioinformatician and an immunologist, analysis and modelling methods for transcriptomic data obtained as part of the Transimmunom research program. We already implemented an automated pipeline that addresses all the conventional steps of RNA-seq data processing and first-level analysis (quality control of sequences until quantification of gene expression, as well as differential gene expression analysis). Additionally, we previously developed an algorithm for gene signature detection (Pham et al. 2014) based on Independent Component Analysis and Gene Set Enrichment Analysis (ICA-GSEA) for microarray data currently adapted for RNA-Seq data.

The Master 2 candidate will design and apply systems immunology approaches to identify relevant gene signatures able at stratifying patients in subgroups. The developed methods must also be able to extract relevant immunological information out of these complex data. Especially, the proposed strategies should perform cell type deconvolution analysis, generate gene co-expression networks, and predict patient's responses to treatments. A specific focus should be placed on gene networks analysis and gene community identification based on hypothesis free approaches. These network analyses will be refined and completed by resources from the literature. Predictions can be validated by bootstrapping techniques and by integrating transcriptomic data with other –omics data. The Transimmunom dataset is extremely valuable in the context of biomedical research and consists of multiple existing challenges in both computational biology and systems immunology.
The expected MSc candidate will justify training in Computer Science / Bioinformatics / Biostatistics and/or Immunology, with interest for Systems Biology. Experience with R or other programming languages (Python, C++…) are expected. The candidate will benefit from an interdisciplinary environment, including biologists, immunologists, clinicians, computer scientists, and bioinformaticians. This project is part of the laboratory funded projects (LabEx Transimmunom - www.i3-immuno.fr, www.transimmunom.fr. This research work can possibly be extended in the context of a PhD project. The internship should ideally start in January/February/March/April 2020.

References:
- Philippe Mauffrey, Nicolas Tchitchek, Vilma Barroca, Alexis Bemelmans, Virginie Firlej, Yves Allory, Paul-Henri Roméo and Claire Magnon (2019) Progenitors from the central nervous system drive neurogenesis in cancer. Nature. 569, 672-678 (doi:10.1038/s41586-019-1219-y).
- Pierre Rosenbaum, Nicolas Tchitchek, Candie Joly, Lev Stimmer, Hakim Hocini, Nathalie Dereuddre-Bosquet, Anne-Sophie Beignon, Catherine Chapon, Yves Levy, Roger Le Grand, and Frédéric Martinon (2018). Molecular and Cellular Dynamics in the Skin, the Lymph Nodes, and the Blood of the Immune Response to Intradermal Injection of Modified Vaccinia Ankara Vaccine. Front in Immunology 9: 870 (doi: 10.3389/fimmu.2018.00870).
- Nicolas Dérian, Bertrand Bellier, Hang-Phuong Pham, Eliza Tsitoura, Dorothea Kazazi, Christophe Huret, Penelope Mavromara, David Klatzmann and Adrien Six (2016) Early transcriptome signatures from immunized mouse dendritic cells predict late vaccine-induced T-cell responses. PLoS Computational Biology, 12, e1004801 (doi:10.1371/journal.pcbi.1004801).
- Yamina Hamel, François-Xavier Mauvais, Hang-Phuong Pham, Roland Kratzer, Christophe Marchi, Emilie Barilleau, Emmanuelle Waeckel-Enée, Jean-Baptiste Arnoux, Agnès Hartemann, Corinne Cordier, Jérome Mégret, Benedita Rocha, Pascale de Lonlay, Jacques Beltrand, Adrien Six, Jean-Jacques Robert and Peter van Endert (2016) A unique CD8+ T lymphocyte signature in pediatric type 1 diabetes. Journal of Autoimmunity, 73, 54–63 (doi: 10.1016/j.jaut.2016.06.003).
- Hang-Phuong Pham, Nicolas Dérian, Wahiba Chaara, David Klatzmann and Adrien Six (2014) A novel strategy for molecular signature discovery based on independent component analysis. International Journal of Data Mining and Bioinformatics 9, 277-304 (doi: 10.1504/IJDMB.2014.060052).

Dates

Durée du poste:6 mois
Localisation:Inserm UMRS959 & Sorbonne Université
Adresse: Hôpital Pitié-Salpêtrière, Bâtiment Cervi - 83 boulevard de l'Hôpital,75013 Paris

Contacts

Nicolas Tchitchek (nicolas.tchitchek@sorbonne-universite.fr)
Adrien Six (adrien.six@sorbonne-universite.fr)