Deep phenotyping analyses of immune cell populations in the context of autoimmune clinical trials

Description of the project

The i3 laboratory, located at the Hospital of the Pitié-Salpêtrière in Paris, aims to (i) advance the frontiers of knowledge in immunology and (ii) develop novel immunotherapies using systems biology approaches.

Our laboratory launched in 2015 an observational clinical trial (Transimmunom – NCT02466217) which aims at studying 19 autoimmune and autoinflammatory disorders. The final goal is to guide the development of novel therapeutic strategies and to redefine the nosography of autoimmune and autoinflammatory diseases using bioinformatics and systems biology approaches.

We are focusing our investigations on the process and analysis of deep immunophenotyping (flow cytometry), cytokines (Luminex), microbiome (metagenomics), transcriptome (RNA-seq), TCR repertoire (Rep-seq), and clinical data collected from hundreds of patients and healthy volunteers.

The immune cell phenotyping of patients enrolled in this clinical trial is performed by flow cytometry using 13 standardized panels already developed in the laboratory (Pitoiset et al. 2018). Each of the 13 flow cytometry panel allows the quantification of the expression of 10 cellular markers, for a total of approximately 100 cell markers per sample. These panels allow an in-depth study of T lymphocytes (Tregs included), B lymphocytes, NK cells, MAIT, myeloid cells, monocytes, ILC, and also dendritic cells.

The main objective of the proposed project is to deeply characterize the phenotypes and functions of leukocytes using systems immunology approaches

Bioinformatics approaches are needed to analyze, interpret, and integrate these complex data in an unbiased and efficient manner. More specifically, unsupervised approaches based on automatic clustering algorithms are required to characterize the phenotypic complexity of the patient cell populations.

During the last months, we have developed an analytical pipeline, based on the SPADE and UMAP/kmeans algorithms, to characterize and cross-phenotype immune cell populations. These developments were done in the context of different clinical trials (such as the LUPIL2 trial). Thanks to these algorithms, we are now able to explore in an unbiased way the immune populations that have been determined automatically using multiple bioinformatics tools (volcano plots, heatmap, PCA, MDS, and machine learning methods). Thus, we can identify cell populations having differential abundances between groups of patients or correlated with pathophysiological status of patients.

We now aim to use and extend these approaches to interpret the deep phenotyping data collected in Transimmunom project.

The goals of this M2 internship will be to: (i) process the collected Transimmunom cytometry data using our existing bioinformatics pipeline; (ii) identify and characterize cell populations impacted by the different diseases; and (iii) interpret the results obtained in regards to the literature.

Expected profile

The expected MSc candidate must have a strong interest in Systems Immunology and biomedical research and should justify training in Bioinformatics, Immunology, Computer Science or Biology.

Research environment

The candidate will benefit from a highly interdisciplinary environment, including biologists, immunologists, clinicians, computer scientists, and bioinformaticians. The internship should ideally start in January/February/March/April 2021. This project can be extended as part of a PhD thesis.

Contacts

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