Universitat Pompeu Fabra Barcelona

Master in Bioinformatics for Health Sciences

Master project 2024-2025

Personal Information

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Project

Computational systems biology

Project Title:

Environmental triggers of immune-mediated diseases: identification through population-scale analyses of polygenic risk scores and human antibody repertoires

Keywords:

IMIDs; Microbiome; Polygenic Risk Score; Phage display; Disease Risk

Summary:

Immune-mediated inflammatory diseases (IMIDs) are a prevalent group of common diseases (>5% of European population) characterized by the chronic activation of the immune system against cells and tissues of the organism. They are the main cause of morbidity in women, they significantly reduce the quality of life of patients and therefore have a very high socioeconomic impact. IMIDs are caused by a complex interplay between a genetic basis of risk and an environmental exposure. Genome-wide association studies have allowed a formidable advance in the characterization of the genetic risk variants associated with IMIDs. The causal environmental factors, however, have been very poorly characterized so far. Antibodies are the primary effector molecules and are highly adaptable and influenced by environmental factors. Exposure to pathogenic microbial antigens leads to the expression of antibodies many years after the original infection, thereby providing a unique record of the environmental history of an individual. In the present study our aim will be to associate the genetic risk for common IMIDs with antibody profiles. Genetic risks will be determined through polygenic risk score (PRS) analysis of GWAS data from a cohort of 1,400 individuals. Antibody repertoire will be determined on those same individuals using Phage-display immunoprecipitation sequencing (PhIP) analysis of reactivities to >340,000 different peptides generated from a library of a wide range of microbial and environmental antigens. The most strongly associated antibodies will be subsequently tested in the plasma samples of patients of the relevant IMIDs, to validate the causal role in the development of the disease. The present study combines large human datasets, advanced computational analyses and cutting-edge technologies. We expect that the results of this study will allow to better understand the environmental factors that contribute to the risk of this group of highly prevalent and debilitating diseases.

References:

Vogl, Thomas, et al. "Population-wide diversity and stability of serum antibody epitope repertoires against human microbiota." Nature medicine 27.8 (2021): 1442-1450.

Expected skills:

Knowledge of multivariate statistical analysis techniques, multi-omic data analyses. Experience in R and Python environments.

Possibility of funding:

No

Possible continuity with PhD:

To be discussed

Comments:

Our laboratories are located both at the Vall d'Hebron Research Institute and the Barcelona Scientific Park. For a recent work related to the project's topic see: Aterido, Adrià, et al. "Seven chain adaptive immune receptor repertoire analysis in rheumatoid arthritis: association to disease and clinically relevant phenotypes." medRxiv (2021): 2021-11.