HumTranscriptom: The anatomy of the human transcriptome in health and disease

Description

Gene expression determines the identity of cells and it thus governs the process by which organs and tissues are formed and organized in an individual. Furthermore, differences in gene expression between individuals are known to play a crucial role in determining disease risk. However, the mechanisms of how such differences in gene expression are associated with disease status and even progression are poorly understood. This is mostly due to the fact that most studies that address how differences in gene expression are associated with disease status focus on specific tissues and/or phenotypes on a limited number of individuals. Thus, for most diseases, how the variation of gene expression across individuals influences disease risk and disease progression remains poorly understood.

This project aims to unravel the drivers of gene expression differences between individuals under different disease conditions to gain insight into disease mechanism and progression. To do this, we will take advantage of 14,891 human transcriptome samples from 838 individuals across 49 tissue types together with available single-cell RNA-sequencing data to address this question. We hypothesize that by studying thousands of transcriptomes from an organismal perspective -across individuals for which we have many tissues- we will be able to not only gain deeper insights into the disease biology but also decisively contribute to our understanding on how general phenotypic differences between individuals arise. To do this, we will apply cutting-edge computational tools and develop novel statistical approaches to systematically characterize the interplay of disease status and three main factors contributing to expression variability: changes in gene expression (objective 1), changes in alternative splicing (objective 2), and changes in cell type composition (objective 3).

We anticipate that the results of the project will have a strong impact in the field of biomedical research by gaining fundamental insights into how some of the most common diseases affect the human transcriptome. Indeed, the diseases studied in this project represent a huge burden in developed and undeveloped countries in terms of health impact and economic cost.

PID2019-107937GA-I00/ AEI/10.13039/501100011033

Barcelona Supercomputing Center - Centro Nacional de Supercomputación