Bayesian networks and deconvolution methods to study the influence of aging and chronic diseases on the immune system

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Increasing life expectancy is creating new challenges related to age-related diseases. Moreover, chronic diseases like hypertension and diabetes are influenced by lifestyle factors, which increase the risk of these diseases and can accelerate the normal aging process.

The aim is to identify clinical parameters that best correlate with age, body mass index (BMI), and chronic diseases and to determine how these factors relate to gene expression across tissues. It is also known that populations of certain leukocyte cell types decrease with normal aging and we want to analyze how this is influenced by the presence of chronic disease markers such as high BMI. In addition, we will investigate whether sex influences these age-related processes.

By extracting data from GTEx, we constructed a Bayesian network (BN) that models dependencies between clinical variables to identify those that are most correlated with age, BMI, and chronic diseases. We used deconvolution to study the proportion of leukocytes in the different tissues and understand how these change with normal aging, high BMI, and the presence of chronic diseases. We performed lasso-penalized regression to select important genes that can classify the tissue between normal-and disease-related aging in the presence of chronic diseases. The results were compared with those obtained from methylation data.

Conditional probabilities extracted from the BN suggest hypertension as a key mediator, linking age, ischemic heart disease, type II diabetes, and renal failure. Furthermore, deconvolution of the whole blood transcriptome revealed a difference in the proportion of monocytes across age groups between normal-and overweight subjects.

This study will help determine how chronic diseases affect leukocyte subtypes during aging. Genes and methylation marks will provide further insights into the distinct molecular signatures and regulatory mechanisms underlying aging and disease-related changes.

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