Graduation proposal Student: Project: Contact: Address: Starting: Matthijs Knigge Interplay between gut microbiome and immune system Asst. Prof. Dr. S. Sanna, s.sanna@umcg.nl, 050 361 7100 UMCG department of Genetics, Antonius Deusinglaan 1, 9713 AV Groningen February 5, 2018

The body of a human is a complex interconnected ecosystem, and the gut is where the body acts as a first line of defence. Where it interacts with the "outside world", functioning as a frontline of the immune system, which is constantly exposed to new microbes and molecules. [1] The whole assortment of microbes that are present in and on the human body is known as the microbiota. [2] The microbiome refers to the whole set of genes within these microbes. The role of the microbiome composition/function is considered as an acting organ in the body's operation. It has an impact on aging, digestion, the immune system, mood, and cognitive function. [3]

The immune system a defensive system from the host entailing many biological structures and processes within an organism to protects against diseases. The function of the immune system relies on the ability to detect and distinguish a wide arrange of agents known as pathogens, viruses, and parasites from self and non-self.^[4]

The aim of this research is to find causality links between the microbiome composition/function and immune system, does the microbiome influence the immune system (cell counts, cytokines, globulin levels), or/and does the immune system influence the microbiome.

By using gene expression data, transcriptomic data from the 500 Functional Genomic cohort^[5] a model is constructed that explains immune traits/functions between gene expression data and 500FG with elastic net regularization^[6], and cross-validation. The constructed model will be used to predict immune function/traits in BIOS data which contains genetic data from a large number of individuals which lacks immunogenic information. After the immune phenotypes are predicted, a causal link between microbial composition/function and immune phenotypes can be predicted with one-sample Mendelian Randomization, here microbial metagenomic data will be used and the predicted immune phenotypes, see figure 1.

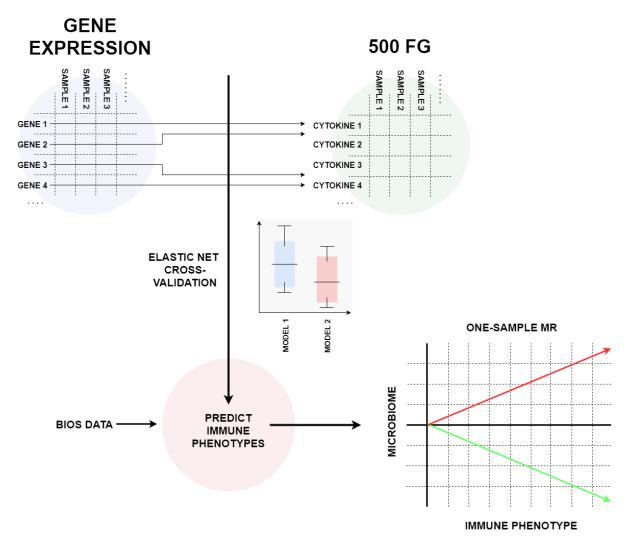


Figure 1: overview of the research workflow. A model will be constructed that explains the relation between gene expression and immune phenotypes in 500FG. This constructed model will be used to predict immune phenotypes in BIOS data, which will be used to predict causal links with the microbiome.

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