Proteomics deconvolution of pediatric IBD

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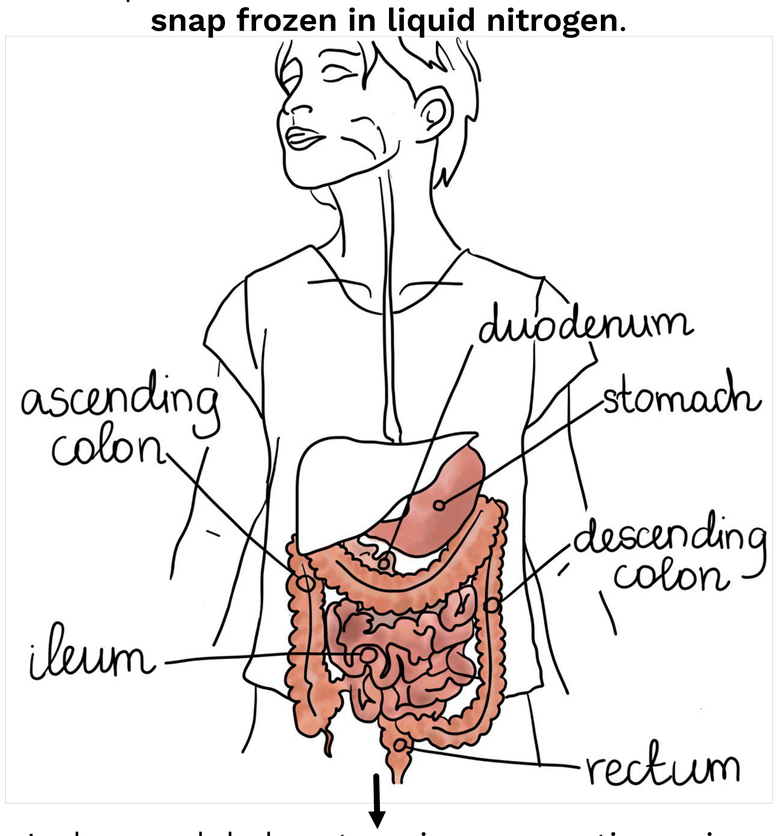
Background and objectives

There has been a significant increase in the incidence of **pediatric inflammatory bowel disease (IBD)** over the last 25 years. However, etiology and mechanistic understanding of the changes occurring in pediatric IBD are yet to be revealed. In this study we perform **in-depth global proteomics profiling** of a unique biobank of pediatric biopsies collected in collaboration with Uppsala University hospital from children **naïve to IBD treatment**, to provide insights into pathophysiology of pediatric IBD and aid in development of novel diagnostic and therapeutic modalities.

Workflow and methods

Biopsies collection at the Uppsala University hospital - **mucosal at 6 anatomical sites snap frozen in liquid nitrogen**.



In-house global proteomics preparation using HT96 Preomics iST kit.

Analysed in-house using high resolution mass-spectrometry based global proteomics in bespoke **data-independent acquisition mode** using Orbitrap Q Exactive HF.

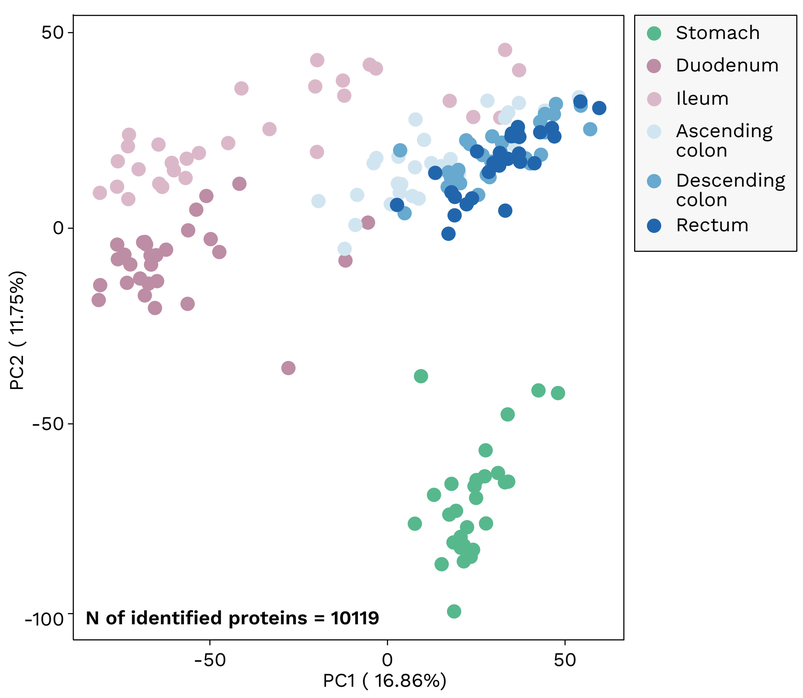
Protein identification was performed using **DIANN software**, whilst subsequent data analysis was executed in R and Amica.

Conclusions and perspective

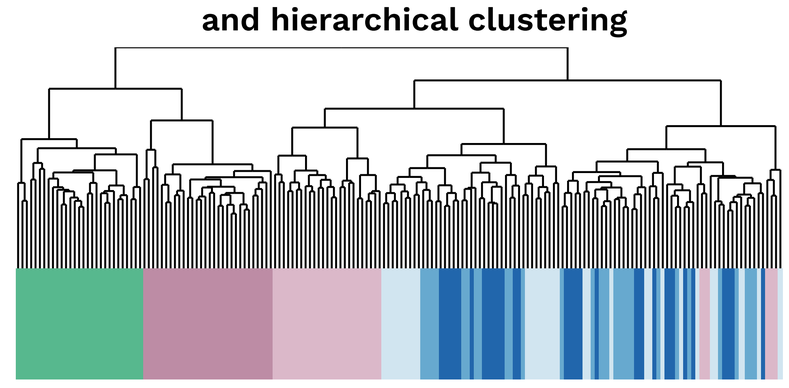
To our knowledge, no studies have performed **comprehensive global proteomics profiling** of newly diagnosed paediatric patients along gastro-intestinal tract. Here we aim to provide an extensive resource of knowledge that has the **potential of improving the mechanistic understanding of paediatric IBD**, as well as to aid in the development of novel IBD diagnostics. In addition, we create a unique atlas of paediatric GIT proteomes, that could be further applied in physiologically based pharmacokinetic (PBPK) modelling of paediatric population.

Preliminary results of global proteomics analysis

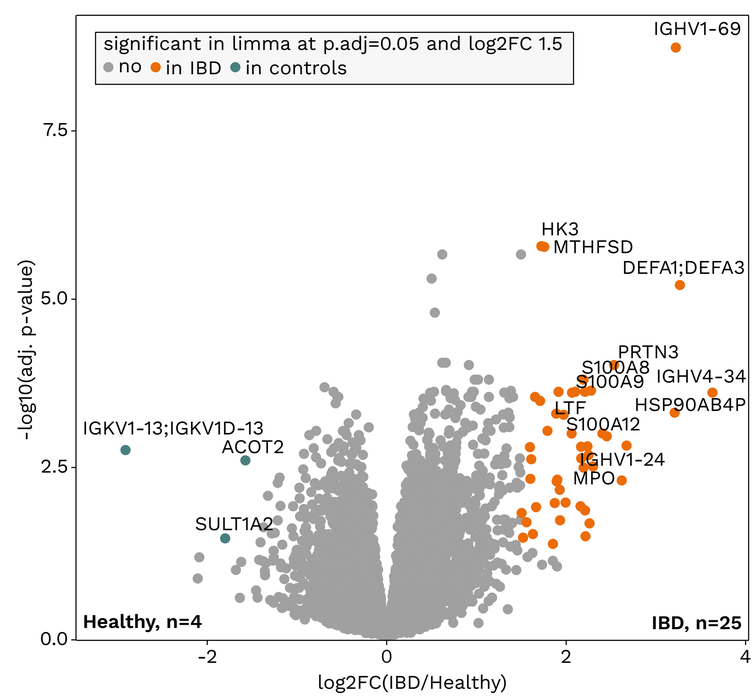
Overview of the samples: Principal component analysis



and hierarchical clustering



What proteins are differentially expressed in children diagnosed with IBD vs controls?



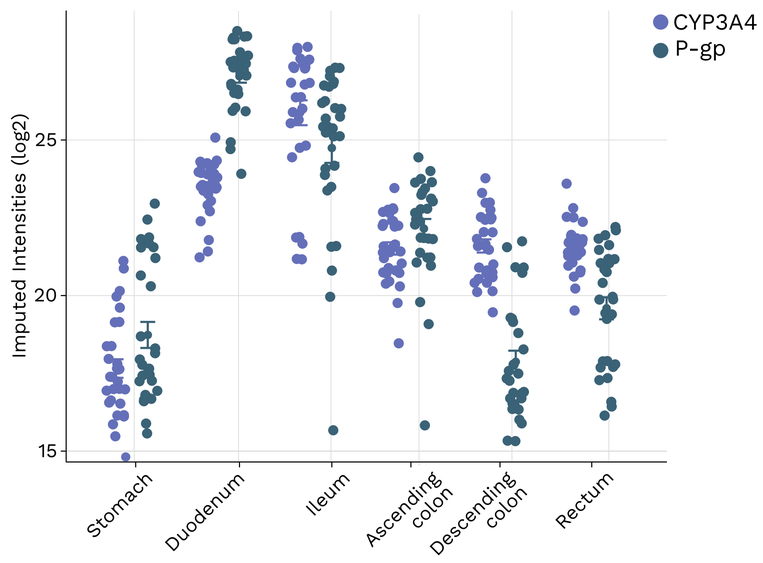
What is known about these proteins?

Potential therapeutic targets
Arginase 1: *doi.org/g9xwhr*
CEACAM8: *doi.org/grkb9d*
Dual oxidase 2: *doi.org/qd56*
Neutrophil elastase: *doi.org/gnscnj*
Nitric oxide synthase: *doi.org/qd57*

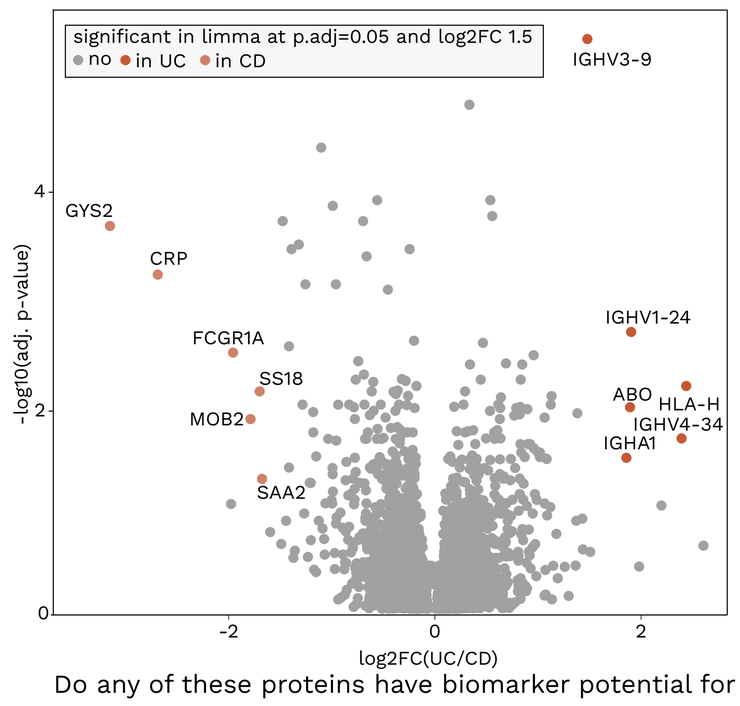
Potential and known biomarkers
Lactotransferrin: *doi.org/dkqwvx*
Myeloperoxidase: *doi.org/gf434v*
Chitinase-3 like protein: *doi.org/qd58*
Myeloblastin (pediatric biomarker!): *doi.org/g6v59w*
Resistin: *doi.org/qd6b*
Calprotectin and S100A12: *doi.org/b42ppz*

As well as **immunoglobulins, inflammation** and **innate immune system response**

ADME protein expression profile along GIT

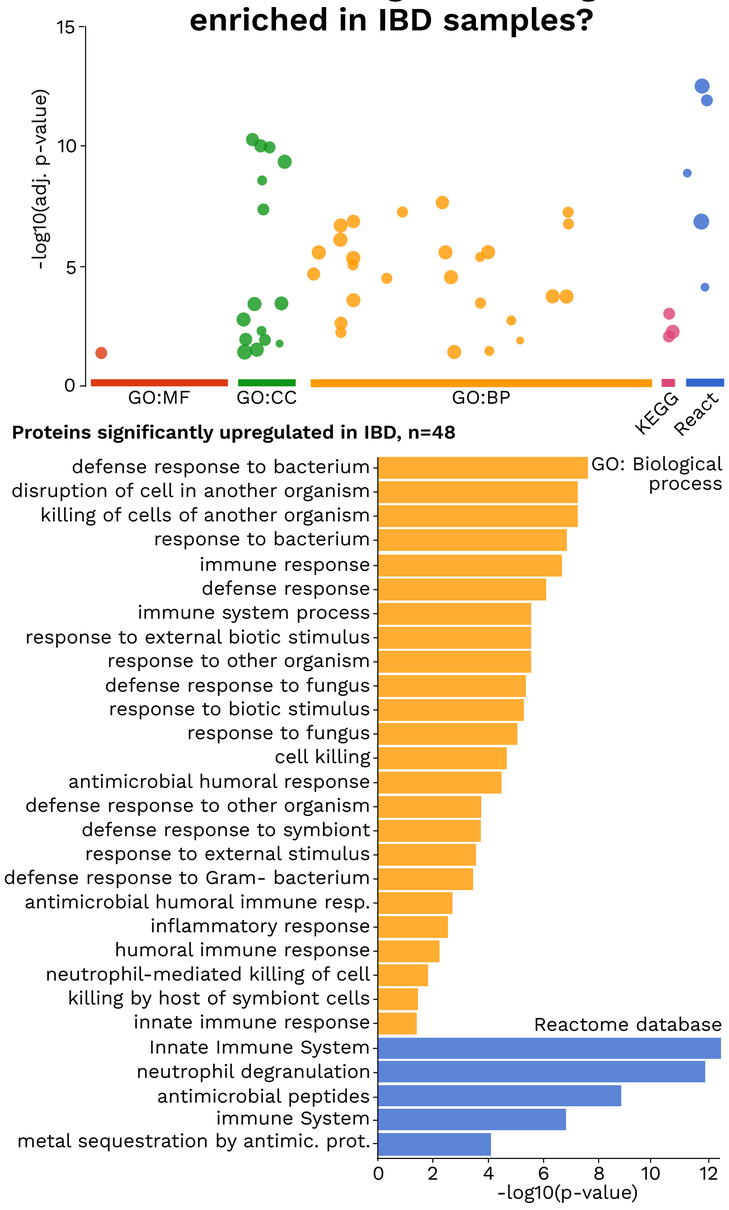


Exploring metadata parameters



Do any of these proteins have biomarker potential for differentiating UC and CD?

Which functional categories are significantly enriched in IBD samples?



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