Multiomic profiling of patients with inflammatory bowel disease and other inflammatory diseases

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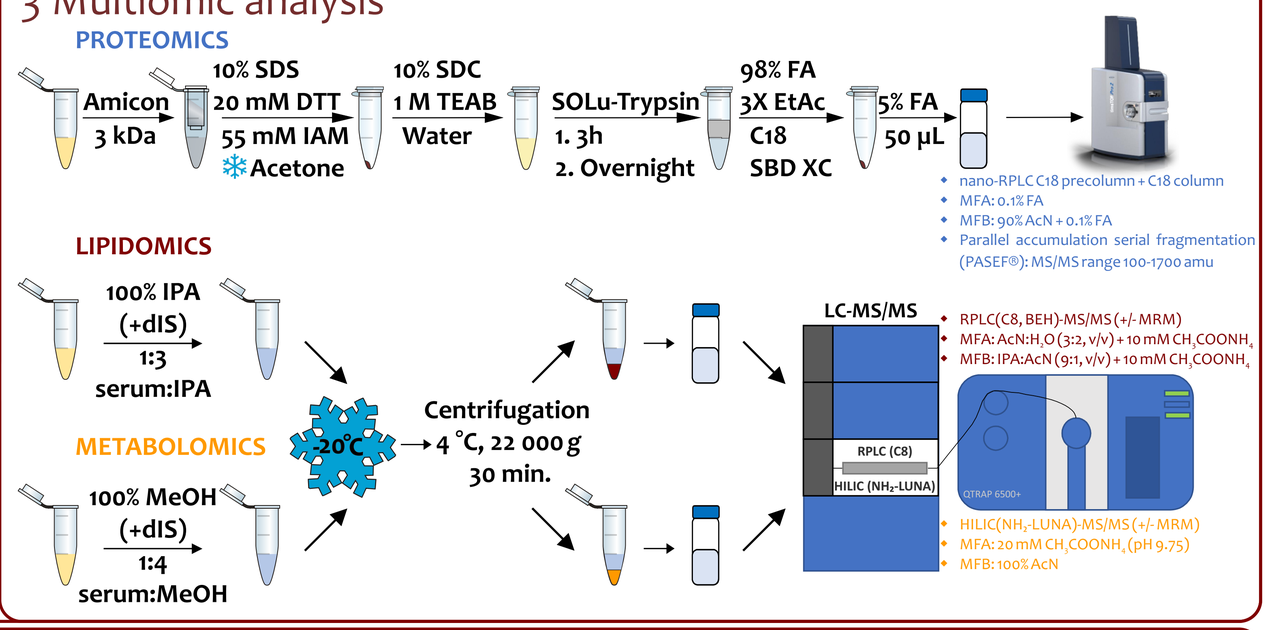
1 Aim

- Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic autoimmune disorders affecting the gastrointestinal tract. Despite their increasing incidence and clinical complexity, diagnostic and prognostic tools remain limited. Systems-level approaches such as lipidomics, metabolomics, and proteomics offer new opportunities to identify molecular signatures associated with disease progression and immune-mediated pathology. This study is focused on characterisation of the molecular landscape of IBD and related autoimmune diseases by integrating lipidomic, metabolomic, and proteomic analyses of pediatric and adolescent patient serum samples.

2 Patient cohort

- Serum samples were obtained from IBD pediatric patients (7-18 years old) suffering from CD (n = 43) and UC (n = 31), alongside with healthy controls (CTRL; n = 38). All samples were collected from Pediatric Clinic at Faculty Hospital Olomouc, Czech Republic.

3 Multiomic analysis



4 Results

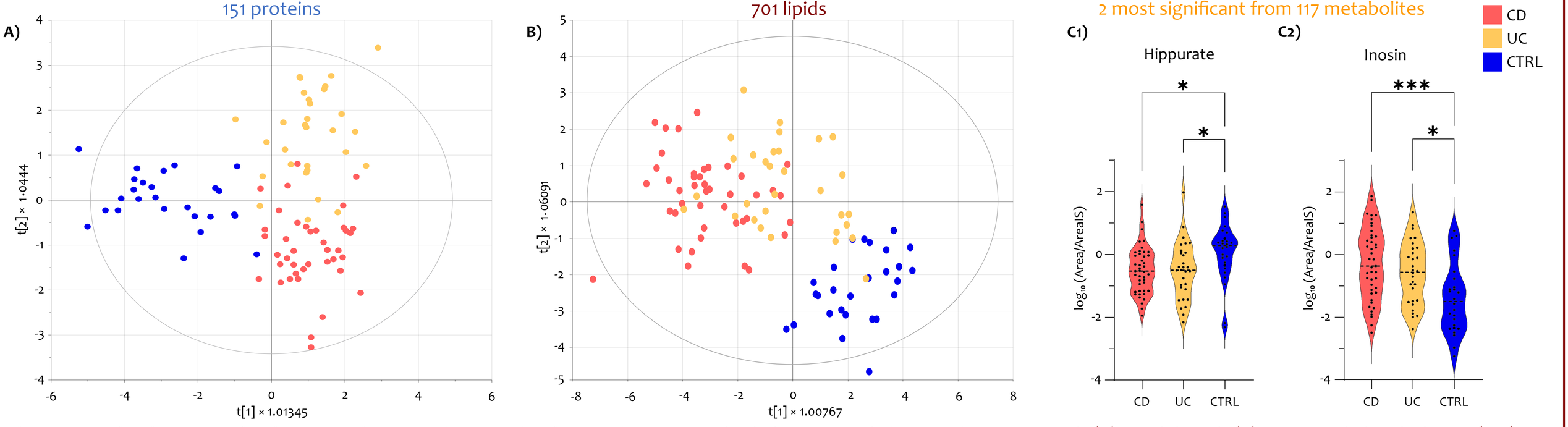
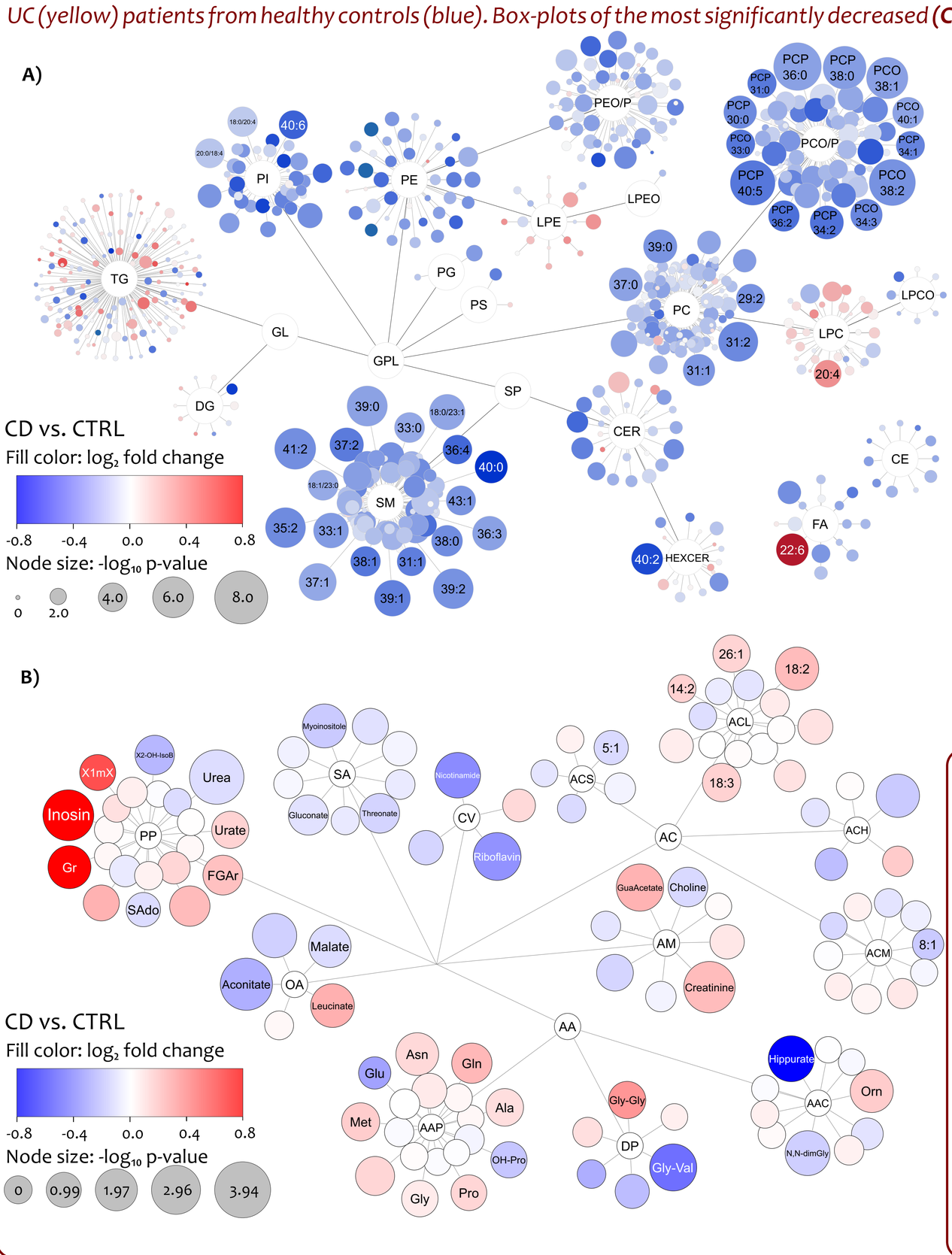


Figure 1: Multivariate and univariate statistical analysis of multiomic data. *Orthogonal discriminant analysis OPLS-DA from proteomic **(A)** and lipidomic **(B)** analyses distinguishing CD (red) and UC (yellow) patients from healthy controls (blue). Box-plots of the most significantly decreased **(C1)** and increased **(C2)** metabolites in both IBD patients compared to healthy controls.*



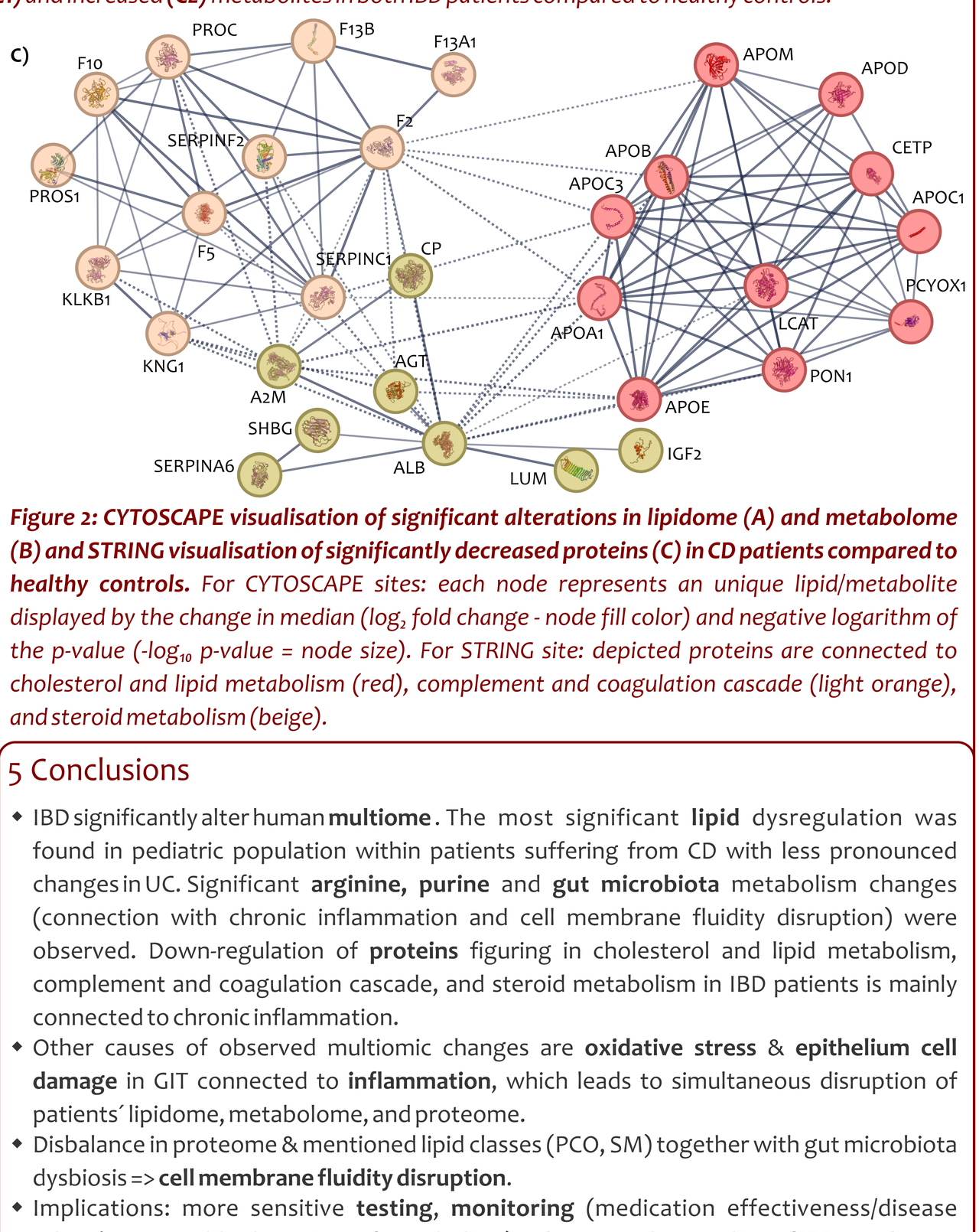


Figure 2: CYTOSCAPE visualisation of significant alterations in lipidome (A) and metabolome (B) and STRING visualisation of significantly decreased proteins (C) in CD patients compared to healthy controls. *For CYTOSCAPE sites: each node represents an unique lipid/metabolite displayed by the change in median (log_2 fold change - node fill color) and negative logarithm of the p-value ($-log_{10}$ p-value = node size). For STRING site: depicted proteins are connected to cholesterol and lipid metabolism (red), complement and coagulation cascade (light orange), and steroid metabolism (beige).*

5 Conclusions

- IBD significantly alter human **multiome**. The most significant **lipid** dysregulation was found in pediatric population within patients suffering from CD with less pronounced changes in UC. Significant **arginine, purine** and **gut microbiota** metabolism changes (connection with chronic inflammation and cell membrane fluidity disruption) were observed. Down-regulation of **proteins** figuring in cholesterol and lipid metabolism, complement and coagulation cascade, and steroid metabolism in IBD patients is mainly connected to chronic inflammation.
- Other causes of observed multiomic changes are **oxidative stress** & **epithelium cell damage** in GIT connected to **inflammation**, which leads to simultaneous disruption of patients´ lipidome, metabolome, and proteome.
- Disbalance in proteome & mentioned lipid classes (PCO, SM) together with gut microbiota dysbiosis => **cell membrane fluidity disruption**.
- Implications: more sensitive **testing**, **monitoring** (medication effectiveness/disease relaps/new possible alterations of metabolism) => **better understanding of IBD patology**.