Strongest models were faecal HILIC (R2X = 0.129, R2Y = 0.8, Q2Y = 0.596, $p = 6.47 \times 10^{-5}$) and urine HILIC (R2X = 0.164, R2Y = 0.783, Q2Y = 0.526, $p = 7.11 \times 10^{-12}$). Urinary NMRS showed higher isobutyrate, lactate and alanine in the SA group whilst hippurate, 4-cresol sulphate, lysine and citrate were reduced. Secondary bile acids (5B-cholanic acid-3a, 6a-diol-7-one) were higher in the SA group and four secondary bile acids (3-Ketocholanic acid, Lithocholic acid, Isolithocholic acid, 3a-hydroxy-12-ketolithocholic acid) were lower. There were no discriminatory features identified during time point and treatment subgroup analysis.

Conclusions: This prospective, longitudinal inception cohort study demonstrates significant differences driven by ethnicity despite similar diet. SA had more severe disease which maybe a confounding factor. Analysis of paired samples pre- and post-remission are required. Further studies employing metagenomics techniques may define pro-inflammatory pathways specific to SA and justify different treatment approaches.

P057

Proteomic analysis highlights divergences and convergences between ileal and colonic pathological processes involved in Crohn's ulcers

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Background: Crohn disease (CD) affects predominantly the ileum and/or the colon. Previous genome wide association studies have revealed that patients with ileal or colonic disease present partly distinct risk loci. This finding opens new perspectives for the development of personalised treatments and biomarkers based on disease location. To this end, protein-based approaches are needed to discover new tissue-specific proteins associated with CD. The goal of our study was to decipher the relation linking disease location and physiopathological processes by comparing the proteomic picture of ileal/colonic CD ulcers with normal tissues.

Methods: CD patients (n = 16) with ileum (n = 8) or colon (n = 8) ulcers were included. Paired biopsies were taken at the edges of the ulcer (U) and in the nearby endoscopically normal mucosa (N). Label free proteomic differential analysis was run using protein digests obtained with the 16 paired biopsies. Identifications and quantification of proteins were performed using MaxQuant. Paired t-test with Benjamini–Hochberg correction was applied for selection of proteins differentially abundant between N and U tissues. Pathway enrichment analysis was performed with the Database for Annotation, Visualization and Integrated Discovery (DAVID) bioinformatics tool.

Results: We identified and quantified 4652 and 5422 proteins in ileum and colon samples, respectively. Among these proteins, 440 (ileum) and 409 (colon) were differentially distributed between N and U tissues. The well-recognised fecal marker of CD activity, calprotectin, was increased in U, showing consistency of our results with clinical observations. When proteins where ranked by increasing p-value, the calprotectin subunits S100-A9 and S100-A8 appeared respectively at the 266–300th (ileum) and the 142–165th (colon) positions, suggesting that our dataset could reveal new relevant proteins in CD. In both ileum and colon ulcers, pathway enrichment analysis showed that the proteins decreased in lesions, were related to energetic metabolism, whereas the increased ones were mainly involved in the endoplasmic reticulum-Golgi protein processing and the immune response. In the ileum, the over-abundant proteins found in U were also involved in mRNA maturation and protein translation, this was not observed in the colon.

Conclusions: Our proteomic experiment highlights common and distinct physiopathological processes between ileal and colonic CD ulcers, thus indicating a partial segment specificity of the disease. Further investigations are required to confirm these results. Among the 849 proteins differentially abundant between N and U mucosa, new therapeutic targets and new biomarkers could emerge for CD patient management.

P058

Phosphodiesterase 8A domains at the site of leucocyte–endothelial cell adhesion in ulcerative colitis submucosa

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Background: Development of anti-adhesion therapies like Etrolizumab and Alicaforsen highlights the potential for inhibiting recruitment pathways in ulcerative colitis (UC). Recent in vitro mouse work from our group shows that disruption of Phosphodiesterase (PDE) 8A domains inhibits T cell adhesion to ICAM-1 and endothelial cells.[1] PDE inhibitors are known immunosuppressive agents, yet no PDE inhibitors are approved in UC due to dose-limiting side effects. As PDE8A is the most efficient in vivo hydrolyser of cAMP, PDE8A inhibitors are good candidates for overcoming the challenges presented mainly by PDE4 inhibitors. PDE8A expression in colorectal cancer (CRC) is well documented and PDE8A is reported in UC intestinal crypts by gene and protein array. However, the in situ localisation of PDE8A in UC submucosa during recruitment of leukocytes is unknown. Therefore, we developed an image analysis method to highlight PDE8A domains and investigated whether PDE8A domains were present at the site of leucocyte-endothelial cell adhesion in the submucosa of inflamed UC resections.

Methods: PDE8A protein expression in five involved and two uninvolved UC colon resections was determined by immunohistochemistry using anti-PDE8A (ab61815) or IgG isotype (ab125938). Six paired biopsies from CRC (involved and uninvolved) were used as controls. Antibodies were titrated to 1:250 to reveal subcellular domains masked by diffuse staining at 1:100. Images were analysed using the saturation feature (0-255) in Image J software to assign PDE8A staining intensity as a representation of subcellular domains (Figure A).