Gut – IDDF Young Investigator Award

Basic Gastroenterology

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MUCOSAL TISSUE SHORT CHAIN FATTY ACIDS CONTRIBUTE TO PREDICTION OF POUCHITIS IN RESTORATIVE PROCTOCOLECTOMY

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Background Restorative proctocolectomy is a surgical option in patients with ulcerative colitis who become refractory to medical therapy. Various studies have implicated SCFA in both the development of IBD and flares of IBD. Furthermore, it has been shown that SCFA concentrations are significantly lower in faecal samples from patients with pouchitis when compared with healthy controls.

Our study aimed to assess longitudinal changes in SCFA that occur in a pouch to determine if they can predict or are associated with the development of pouchitis. To date no study has analysed short chain fatty acids in mucosal biopsy tissue from these patients.

Methods Patients who underwent restorative proctocolectomy at a single centre underwent pouchoscopy at the time of restoration of continuity and then every 6 months for a year. Biopsies were retrieved from the pouch body. Pouchitis was defined using the pouch disease activity index. The development of pouchitis was assessed at 6 and 12 months. SCFA were measured using an Agilent 7000C Triple Quadrupole GC/MS-MS System. Simca was used for multivariate analysis and T-tests were used for univariate analysis.

Results There were 56 biopsy samples. There were 22 patients (17 males); 16 UC and 6 FAP patients. Median age of the cohort was 40 years (range 20–60 years). Of the UC patients four developed pouchitis within one year.

Comparing UC patients at the time of closure of ileostomy, there were significant decreases in caproic acid (4674uM vs 12217uM $p < 0.01$), valeric acid (1580uM vs 3695uM $p = 0.01$), isovaleric acid (721uM vs 2940uM $p = 0.05$), isobutyric acid 35072uM vs 76074uM $p = 0.03$ and lactic acid (1580uM vs 3732uM $p = 0.02$) between those who developed pouchitis within a year and those who did not develop pouchitis at 1 year.

Conclusions A decrease in SCFA found in the mucosal tissue at time of closure of ileostomy may predict onset of pouchitis within a year. This study is the first to demonstrate that SCFA can be analysed from biopsies. Future studies need to determine factors that may contribute to tissue SCFA levels which may help reduce the incidence of pouchitis.

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ANALYSIS AND PATHOGENIC MECHANISM OF GUT MICROBIOME IN PATIENTS WITH ULCERATIVE COLITIS AND THEIR HEALTHY SPOUSES

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Background In our study, the influence of gender, diet, race, living habits, areas, sample types, sequencing methods and other factors on gut microbiome were included in the criteria of sample collection as far as possible, to fill in the deficiencies of the current research in which many factors are mixed to bias the results, and analyze the structure and function of gut microbiome of UC patients and their healthy spouses, speculating the possible pathogenic mechanism during the development of UC.

Methods The feces and intestinal mucosa of 112 patients with first attack untreated UC and mild-moderate UC and their healthy spouses were collected, including 112 males and 112 females. 112 in urban and 112 in rural areas. The race, dietary structure, living environment and lifestyle of UC patients and their healthy spouses were the same. The V3-V4 region of 16S rRNA was sequenced by Illumina sequencer. Among the 112 pairs of UC patients and their healthy spouses, feces of 28 pairs of UC patients and their healthy spouses and mucosa of 56 pairs of UC patients and their healthy spouses were randomly selected and sequenced by Metagenomic Sequencing.

Results Alpha diversity of intestinal microflora was significantly different between UC and HC, and also between Mucosa-associated microbiota (MAM) and Lumen-associated microbiota (LAM). Compared with healthy spouses, the ulcerative colitis, oxidative stress, flagellum assembly, peptidoglycan, lipopolysaccharide and other metabolic pathways of intestinal microflora function in UC patients is significantly enriched in. Metabolic pathways involved in carbohydrate, amino acid, cofactor synthesis and nucleotide for nutrient transport and intake are significantly down-regulated.

Conclusions Significant gut microbiome structural and functional disorder were found in UC patients. Compared with LAM, MAM can more precisely reflect the imbalance of gut microbiome of UC. The imbalance of gut microbiome in UC patients leads to increased abundance of oxidative stress pathway and decreased abundance of nutrient delivery and uptake pathway. Enriched bacteria in further UC may be involved in the synthesis of peptidoglycan and lipopolysaccharide, triggering an abnormal immune response. Ultimately, it resulted in persistent, excessive and irreversible immune damage, leading to dysfunction of the intestinal mucosal barrier.

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DYSBIOSIS OF GUT FUNGAL MICROBIOTA IN COLORECTAL CANCER: AN ASSESSMENT FROM FAECAL MICROBIOME SECRETOME

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Background Fungal microbiota may play important roles in maintaining human gut health but to date, the available data are scarce. The intricate crosstalks between these microbiotas and host possibly via protein secretions may contribute to the pathophysiology of Colorectal Cancer (CRC). Therefore, we

aim to identify the faecal fungal secretome in patients with CRC-stricken gut.

Methods Faecal samples from 26 clinically-diagnosed patients with CRC and 20 non-CRC control individuals were collected, homogenized and filtered followed by protein extraction and profiling by quantitative label-free proteomics using Nano-Liquid Chromatography TripleTOF Mass Spectrometry. The mass spectra datasets were searched using MaxQuant against the fungi's Uniprot Fasta databases. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 22. Fungal taxa associated with clinical parameters were identified using multivariate association with linear models.

Results We identified 570 fungal proteins secreted into the human gut. A distinct alteration in the diversity and composition of the fungal microbiota was observed in the CRC, with tremendous reductions of the overall fungal proteins, the diversity and composition of fungal microbiota as compared to the control ($p < 0.05$). Interestingly, the proportion of candida was increased in the CRC, indicating a modified gut microenvironment that favours the fungi. However, the discriminative distributions of the fungi secretome proteins in both CRC and non-CRC were observed with great individual variation.

Conclusions The distinct alteration of fungal proteins observed in CRC may suggest a possible CRC-specific gut microenvironment for fungi. This knowledge may be exploited for new therapeutic approaches for gut-related issues.

Basic Hepatology

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TARGETING MONOCYTE-INTRINSIC ENHANCER REPROGRAMMING IMPROVES IMMUNOTHERAPY EFFICACY IN HEPATOCELLULAR CARCINOMA

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Background Hepatocellular carcinoma (HCC), mostly developed in fibrotic/cirrhotic liver, exhibits relatively low responsiveness to immune-checkpoint blockade (ICB) therapy. As

Abstract IDDF2019-ABS-0174 Figure 1 BET and PD-L1 co-blockade synergistically enhanced TILs and eradicated HCC