PWE-021

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Colon and Anorectum

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OTH-08

CIRCULATING MICRORNAS LINKED TO IMMUNOMETABOLIC TRAITS ASSOCIATE WITH FAECAL MICROBIOTA TRANSPLANTATION FOR CLOSTRIDIODES DIFFICILE INFECTION

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Introduction The molecular mechanisms underlying successful faecal microbiota transplantation (FMT) for recurrent *C. difficile* infection (rCDI) remain poorly understood. The aim of this study was to characterise alterations in circulating microRNAs and immunometabolic traits following FMT for rCDI.

Methods We analysed a subset of serum samples previously acquired from a prospective multicentre, randomized trial of FMT delivered by capsule vs colonoscopy in the management of rCDI [NCT02254811]. 126 sera from 42 patients at screening, 4 and 12 weeks post FMT [12M, median age 68.5 yrs (2–1); 30 F, 53 yrs (2–1)] were included. MicroRNA panel v3 and the nCounter platform (Nanostring Tech) were used for the analysis of 800 microRNAs. Quantitative PCR and 3'UTR reporter assays were employed to verify microRNA inflammatory protein targets in colonic epithelial and peripheral blood mononuclear cells. Biometal levels were

assessed using inductively coupled plasma mass spectrometry (ICP-MS). Hydrophilic interaction ultra-performance liquid chromatography (HILIC-UPLC) and nano-liquid chromatography coupled with electrospray mass spectrometry (nanoLC-ESI-MS) were utilised to profile the total serum and IgG Fc N-glycome. Pathway analysis was performed using Metacore software. All statistical analyses including non-parametric longitudinal method (nparLD) followed by Wilcoxon signed-rank test for pairwise comparisons and linear mixed modelling were performed in SPSS v.24 and R 3.5.1.

Results MicroRNA profiling revealed an upregulation in the levels of 64 circulating microRNAs 4 and 12 weeks following successful FMT for rCDI compared to screening time point. MicroRNA signatures coincide with a reduction in circulating selenium and copper, and regulate levels of interleukin-12B, (IL-12B), IL-18 and fibroblast growth factor-21 (FGF21) as well as serum protein N-glycosylation traits. MicroRNA alterations reveal commonalities with several types of cancer and multiple sclerosis, and link metabolic traits to immune cell survival and differentiation.

Conclusions These findings contribute to a greater understanding of the molecular mechanisms underlying FMT and identify new potential targets for therapeutic intervention.

OTH-09

FERROUS SULPHATE SUPPLEMENTATION IS ASSOCIATED WITH A CHANGE IN THE FAECAL METABOLOME

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Introduction Oral iron supplementation treats iron deficiency anaemia, but it may cause GI side effects. Iron influences the growth of specific gut bacteria and may lead to dysbiosis, which may contribute to the side effects. Previously, we have shown that oral iron worsens colitis in mice and causes a dysbiosis. Here we report the effect of ferrous sulphate supplementation on the human metabolome by quantifying changes in faecal volatile organic compounds (VOCs), for the first time. VOCs are part of the metabolome and reflect gut

Abstract OTH-09 Figure 1 (A) Pre- and post-iron (Fe) concentrations of 2-pentylfuran. (B) Partial least squares – discriminant analysis (PLS-DA) plot of pre- and post-iron samples.

bacterial metabolism. We aimed to compare the faecal metabolome before and after ferrous sulphate supplementation.

Methods 77 faecal samples were collected from patients with iron deficiency anaemia, before treatment and after two months of therapy. Faecal headspace gases were analysed using gas chromatography–mass spectrometry: VOC identification involved matching mass spectra against the NIST Library. Univariate and multivariate analysis was performed on the VOCs found, including partial least squares regression (PLS-DA).

Results A significant change in abundance of 17 VOCs was found. Adjustment was made for the number of comparisons: one VOC was then shown to increase significantly. The median abundance of 2-pentylfuran changed four-fold (FDR adjusted $P = 0.006$) in patients taking ferrous sulphate for two months (Fig. 1A). Overall, a plot to illustrate the PLS-DA shows how the pre- and post-treatment samples differ (Fig. 1B). Though the abundance changed in 16 other VOCs—which included aldehydes, esters and ketones—their significance was lost after correction for multiple testing, which indicates that the study may be underpowered.

Conclusions The abundance of faecal 2-pentylfuran increases significantly during ferrous sulphate therapy. 2-pentylfuran is a metabolite of fungi. It remains to be seen whether ferrous sulphate directly acts on fungi or whether there is an interaction between iron and bacteria, and then between bacteria and fungi. It is very clear that faecal metabolites are influenced by ferrous sulphate supplementation.

OWE-22 ROLE OF LOW GRADE DYSPLASIA SMALL POLYPS DURING SCREENING COLONOSCOPIES SURVEILLANCE: A PROSPECTIVE COHORT STUDY

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Background The role diminutive polyps and small polyps play in the development of advanced neoplasia (AN) or cancer during follow-up (FU) continues to be debated. Recent studies have shown that the risk of AN development during FU is higher in patients with > 5 small polyps but similar in patients with – or – small polyps^{2,3}. Given these findings, the current study aimed to evaluate if current European FU guidelines¹ at first screening colonoscopy according to the number of low-grade dysplasia tubular adenoma < 1 cm (“micropolyps”, MP) are too strict.

Methods A longitudinal cohort study was carried out on a representative sample (50%) of patients who underwent a screening colonoscopy (clean colon) in 2010 showing at least 1 polyp. Patients with AN or cancers were excluded. Polyps > 1 cm or villous or high grade dysplasia/carcinoma in situ were considered AN. These patients made a FU colonoscopy according to UE screening CCR guidelines. Patients were split up according to European guidelines in Low risk (– MP), Intermediate risk (– MP) and High risk (>5 MP). Data were analyzed by SPSS program.

Results Of 640 patients included in the sample 172 (27%) were included in the surveillance program (mean age 62,2±5,7 yr, 5–90), 120 male (69,8%). During first colonoscopy (2010) 370 MP were detected (M±SD 2,1±1,5, range –3 polyps for each patient). During FU (median 5.5 years), 315 colonoscopies were performed (mean 1.8; range –) and an

AN was detected in 23 patients (13.4%): 20/23 tubulovillous microadenoma, 1/23 high grade dysplasia, 2/23 tubular adenoma > 1 cm. The detection of AN among patients in treatment with ASA was non significantly lower than the others. AN detection was lower among Low risk patients (13/108; 10.7%) as compared to Intermediate risk (7/33; 17.5%) and High risk (3/8; 27.3%) ($P=ns$). According to Kaplan-Meier analysis, the cumulative risk of AN among High risk was significantly increased ($p=0.035$) (figure 1). No interval cancers were found during the follow-up.

Abstract OWE-22 Figure 1

Conclusions These findings suggest that EU guidelines for surveillance colonoscopies for > 3 small LGD polyps are excessively strict. We propose extending the time for a repeat colonoscopy FU for these patients to 5 yrs

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OWE-23 VERSATILE ROLE OF SECRETED FRIZZLED RELATED PROTEIN 2 (SFRP2) IN COLON CANCER: POTENTIAL STROMAL TARGET

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Introduction Dysfunctional adipose tissue has emerged as a key contributor to colorectal cancer. However, the role of peritumoral adipose tissue (pAT) in colon cancer has not been widely investigated. Aim of this study is to identify differentially expressed genes (DEGs) associated with cancer pathways in peritumoral adipose tissue compared with adjacent normal adipose tissue in human colon cancer.

Methods Fresh peritumoral and distal adipose tissue samples were collected from 6 patients undergoing surgery for colon cancer stage T3/T4. DEGs were identified employing Nanostring PanCancer Pathway Panel including 770 cancer-associated genes. Criteria for differential expression included p-value