

Conclusion In the setting of acute severe ulcerative colitis, serum calprotectin is comparable with serum CRP in predicting outcome. Further work is needed to establish if it may be a useful predictor of outcome in patients with ulcerative colitis who fail to mount a high CRP response despite endoscopic assessment confirming severe active inflammation. Work is also ongoing to establish its utility in the outpatient setting both in Crohn's disease and ulcerative colitis.

Disclosure of Interest None Declared.

PTH-083 METHYLATION SIGNATURES OF NON-EXPRESSED GENES REVEAL INSIGHTS INTO THE EFFECTS OF INFLAMMATION ON STEM CELL DYNAMICS AND CRYPT FISSION IN INFLAMMATORY BOWEL DISEASE

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Introduction Inflammatory bowel disease (IBD) confers a high risk of development of colitis-associated colorectal cancer (CACRC) in patients with extensive colitis. Crypt fission (a crypt bifurcating into two) has been shown to be a mechanism of clonal expansion in the intestinal epithelium. Although fission is rare in normal colon, many crypts in patients with colitis appear to be in the process of fission. A recent study from the host laboratory demonstrated that protumourigenic mutations can spread through the entire inflamed colon suggesting that this occurs at a considerable rate indicating stem cell dynamics are altered in IBD¹.

Methods Somatic mitochondrial DNA (mtDNA) mutations are a reliable marker of clonal expansion in human colon. Combining mtDNA mutations with additional markers of clonal expansion that change over time, such as methylation patterns of non-expressed genes, reveals whether populations of cells show a recent ancestry. This is measured by evaluating methylation pattern diversity between samples. Methylation patterns of *CSX* and *MYOD1* genes were examined in clonally related and unrelated crypts from multiple areas in IBD patients by laser capture microdissection bisulphite sequencing. Clonality was demonstrated by cytochrome *c* oxidase deficient (CCO-) cells sharing an identical somatic mtDNA mutation.

Results In active inflammation, both adjacent clonally related CCO- crypts and adjacent unrelated crypts had similar methylation patterns, indicating recent crypt fission. In contrast, adjacent unrelated crypts in quiescent disease had dissimilar methylation patterns, indicating that crypt fission rates are slow and resemble that of normal colon. The number of unique methylation patterns in crypts from active IBD were significantly less than those obtained from normal patients suggesting that niche succession (a stem cell populating the niche) is elevated in IBD.

Conclusion Elevated crypt fission in active IBD may explain the extensive dispersion of protumourigenic clones previously observed in IBD. Subsequent cycles of crypt atrophy and mucosal healing by crypt fission, may provide a key growth stimulus in the inflamed colon. Furthermore, there appears to be an increased rate at which a single stem cell populates the niche within IBD crypts. Such expansion facilitates the establishment of protumourigenic mutations within crypts.

Disclosure of Interest None Declared.

REFERENCE

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PTH-084 ENDOSCOPIC AND HISTOLOGICAL ACTIVITY AS PREDICTORS OF RELAPSE IN PATIENTS UNDERGOING SURVEILLANCE COLONOSCOPY FOR ULCERATIVE COLITIS

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Introduction Mucosal healing has shown to correlate with improved long term outcomes in patients with inflammatory bowel disease. Histological inflammation is often noted in endoscopically normal mucosa. We aimed to investigate the predictive role of endoscopic and histological inflammation on disease relapse in UC patients in clinical remission

Methods We conducted a retrospective review of adult patients in clinical remission who underwent surveillance colonoscopies in our institution from January 2008 to December 2011. Electronic records were reviewed for endoscopy reports and subsequent clinical care. Data was recorded on age, gender, duration and extent of the disease, medications, steroid use in the last 6 months, Mayo endoscopic score, Geboes histological activity index and follow up data for any flares till date. Patients were deemed to have a relapse if they required steroids or an increase in their medication dose for symptom control in the subsequent 12 months following their index colonoscopy.

Statistical analysis: Rate of clinical relapse and the predictive value of the variables of interest were assessed using SPSS version 17. All variable analysed in univariate fashion and included in multivariate analysis if *p* was less than ≤ 0.3 . Multivariate analysis was based on an automated backward logistic selection process. *P* values < 0.05 were considered significant.

Results 406 patients underwent surveillance colonoscopy during the study period of which 317 (Male: 172 Females: 145) met the inclusion criteria. 57 patients (Males 29, females 28) relapsed within 12 months (Table 1 provides the baseline characteristics). On univariate analysis age (OR 0.96 95%CI 0.94–0.98), Geboes score ≥ 2 (4.53, 2.40–8.52) and Mayo score ≥ 1 (3.72, 2.05–6.73) were significantly associated with relapse. Duration of disease (*p* = 0.09), use of immunomodulators (*p* = 0.29) and recent steroid use (*p* = 0.3) were included in the multivariate analysis. On multivariate analysis Geboes score of ≥ 2 (5.11, 2.73–9.59) and age (0.97, 0.97–0.99) were predictive of clinical relapse.

Abstract PTH-084 Table 1

| Variables | Flare up | No flare |
|---------------------------|-----------------|-----------------|
| Age (mean \pm SD) | 51.2 \pm 14.6 | 57.9 \pm 12.5 |
| Endoscopic score ≤ 1 | 22 | 182 |
| Endoscopic score ≥ 2 | 35 | 78 |
| Geboes score < 2 | 33 | 224 |
| Geboes score > 2 | 24 | 36 |

Conclusion Histological activity and younger age are significant predictors of disease relapse in patients undergoing surveillance endoscopy. Endoscopic activity with standard white light endoscopy did not predict clinical relapse. Better non-invasive markers of disease relapse are required for patients with ulcerative colitis

Disclosure of Interest None Declared.

PTH-085 MONOCLONAL ANTIBODY THERAPY IN CROHN'S DISEASE: DOES SERIAL FAECAL CALPROTECTIN PLAY A ROLE?

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Introduction Background Mucosal healing (MH) is an increasingly important therapeutic goal in inflammatory bowel disease. Monoclonal antibody (MA) therapy aims to achieve this and faecal calprotectin (FC) concentration has been shown as a surrogate marker for MH.

Aims Our aim was to study the profile of Crohn's disease (CD) patients on MA therapy and evaluate whether FC levels after induction therapy with MA predicts the medium-term outcome.

Methods Thirty-two CD patients: infliximab n = 11, adalimumab n = 21 were identified from our MA database. Data on demography and disease characteristics were extracted from case records. A subset of CD patients with FC levels measured both at baseline and after induction therapy were analysed further for response to therapy and disease course during follow-up (n = 10). Disease activity was evaluated by modified Harvey-Bradshaw index at baseline, after induction, and at 6 and 12 months during maintenance therapy.

Results Of 32 patients, 22 patients were female, medium age 39.5 (range: 19–65 year), medium age at diagnosis 30.2 (range: 16–61 year), mean disease duration prior to MA was 6.1 (range: 10–22 year) and 21.8% has family history of inflammatory bowel disease. Of these, 56.2% had history of surgery prior to MA and 71.7% had concurrent immunomodulation. Disease phenotypes are shown in table. Of the 10 patients with full FC data, 6 patients normalised FC after induction (median levels 67 mg/kg, median 64 mg/ks, range 30–72). All remained in remission during follow-up median- 22 months (range 13–33 months). Four patients failed to normalise FC levels with induction therapy (median 11 months, range 6–39). Of these, 2 had operation, 2 had multiple relapses (1 treated with prolonged enteral therapy and 1 with additional oral corticosteroid courses).

Abstract PTH-085 Table 1

| | |
|------------------------------------|---------------|
| % ileal disease | 3.1% (1/32) |
| % colonic | 34.3% (11/32) |
| % ileocolonic | 59.3% (19/32) |
| % isolated upper GI | 3.1% (1/32) |
| % B1 (non stricturing/penetrating) | 50% (16/32) |
| % B2 (stricturing) | 15.6% (5/32) |
| % B3 (penetrating) | 34.3% (11/32) |
| % P (perianal) | 53.1% (17/32) |

Conclusion MA therapy is used in CD patients with aggressive disease course who are treated/intolerant to immunomodulatory therapy. Normalisation of FC after induction therapy with MA is a useful marker to predict sustained clinical remission.

Disclosure of Interest None Declared.

PTH-086 INVESTIGATION OF THE ANTIMICROBIAL ACTIVITY OF ESSENTIAL OILS OF CULINARY AND MEDICINAL HERBS AND SPICES AGAINST SELECTED GASTROINTESTINAL PATHOGENS

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Introduction Pathogenic gut microorganisms, and dysbiosis of the gastrointestinal microbiota are a significant cause of mortality and morbidity worldwide, for instance infection with *Clostridium difficile* or *Salmonella* species can prove fatal, whereas alteration of the gastrointestinal microbiota has been implicated in irritable bowel syndrome. Due to increasing resistance of gastrointestinal pathogens to conventional antibiotics, alternative antimicrobial agents

are urgently needed. The aim of this study is to investigate whether essential oils (concentrated mixtures of aromatic compounds obtained by the distillation of plant tissues) have antimicrobial activity against selected gastrointestinal pathogens.

Methods We have investigated the antimicrobial activity of essential oils of a wide range of culinary and medicinal herbs against type strains of selected gastrointestinal pathogens, namely *Salmonella enterica*, *Clostridium difficile*, two strains of *Escherichia coli*, and *Candida albicans* by disc diffusion assays. Grape seed oil was the negative control. If the essential oils inhibited the growth of the organisms, a clear halo was seen around the test discs. This was measured. The experiments were performed three times and results were analysed by two sample T Tests. Essential oils were analysed by thermal desorption gas chromatography with mass spectrometry to identify the compounds present.

Results Seven of the essential oils (aniseed, asafoetida, cinnamon, clove, oregano, thyme and winter savoury) produced a strong and statistically significant inhibition of the growth of all five of the organisms tested whereas a further seven essential oils (coriander, garlic, lemon balm, lemon grass, May Chang, peppermint and rosemary) markedly inhibited the growth of three or four of the organisms (and these results were also statistically significant). Batch to batch variation was evident in the antimicrobial activity of some of the essential oils. This might correlate with variations in the profile of compounds present in the essential oils.

Conclusion Some of the essential oils studied might be therapeutically useful against gastrointestinal pathogens. Quality control of the oils would be necessary and further work is needed to identify the active antimicrobial compounds in the oils.

Disclosure of Interest None Declared.

PTH-087 FAM5C, A POSSIBLE CAUSAL MOLECULE IN ULCERATIVE COLITIS REVEALED THROUGH A TRANSCRIPTOMIC ANALYSIS OF THE BOWEL MUCOSA

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Introduction Abnormalities of the colonic mucosa have been implicated in the pathogenesis of ulcerative colitis (UC). We investigated mRNA profiles of macroscopically non-inflamed mucosal biopsies from the colon in patients with UC, Crohn's disease (CD) and control subjects without gastrointestinal disease (HC), to identify genes that might be involved in the aetiology of the disease.

Methods Paired biopsies were taken for histology and mRNA extraction from macroscopically non-inflamed mucosa in the ascending and descending colon, and the rectum, from 24 patients with UC, 14 with CD and 27 HCs undergoing routine colonoscopy. Patients were in complete clinical remission and were either on no treatment or on 5-aminosalicylates ± azathioprine. rRNA was hybridised to Illumina HumanHT-12 v4 Expression Beadchips. Array expression data were log transformed and normalised. Only probes with a detection p-value < 0.01 were analysed. Differential gene expression analysis between groups (using p < 0.05 FDR correction) and outlier analysis (p < 0.005, fold change (FC) ≥ 1.5) were performed at each location using customised software. Results were verified by qPCR and candidate molecules were examined in an independent cohort of UC patients.

Results In group comparisons, of the 26,261 expressed probes, Family with Sequence Similarity 5, member C (*FAM5C*) was the only gene to be significantly under-expressed in UC, both in the rectum (FC = -1.58, p = 0.0008) and the descending colon