OC-092 ALTERATION IN MUCOSAL KERATIN 8 LEVEL, PHOSPHORYLATION AND RELATIVE RATIO TO VIMENTIN ASSOCIATE WITH DEVELOPMENT OF COLITIS-ASSOCIATED CANCER

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Introduction Intermediate filament(IF) proteins keratin(K) and vimentin(VIM) are cellular cytoskeleton components. Mutations of K8 gene associated with inefficient IF assembly is seen in subset of IBD patients. VIM a marker of epithelial-mesenchymal transformation is associated with aggressive colorectal cancer(CRC). We have previously shown alterations in mucosal IF proteins on mass spectrometry(MS) in UC patients at differing risk of CRC. We aimed to validate changes noted on MS and additionally investigate post-translational modifications in K8.

Methods Rectal biopsies were studied from the following groups of patients with UC: quiescent long standing pancolitis(LSPC-20–40years); inactive recent onset UC(ROUC < 5 years), UC with primary sclerosing cholangitis(PSC), pancolitis with dysplasia (DR), distal active colitis (ACT) & controls(CON). Biopsies were also taken from dysplastic lesions(DT) and un-inflamed proximal colonic mucosa(INACT) in ACT group(to investigate proteomic changes due to inflammation in same group of patients). Western immunoblotting was undertaken using antibodies to K8, K18, K19, VIM, and K8 phosphorylated at Ser23, Ser73 and Ser431. Individual band intensities were quantified by densitometric analyses of the blots.

Results Multiple K8 forms were noted; relative to CON, low K8 levels & molecular weight(MW) forms (37kDa) was seen in ROUC and DT (Fig A). Similar to MS results, in ACT there was reduction in K8, K18, K19 & VIM levels with low MW K8 forms (FigB). Vimentin was increased in LSPC, PSC, DR & DT compared to CON (Fig A); progressive increase in VIM:K8 ratio was noted (DT > DR > PSC > LSPC > ROUC- Fig C). K8 phosphorylation was reduced or absent in ACT and ROUC (Fig A&B), with diminished levels noted in PSC, DR and DT compared to LSPC. K8pS23 levels relative to total K8, was comparable in CON and LSPC but showed a reduced ratio in ROUC & dysplasia(Fig D).

Conclusion K8 levels and phosphorylation are reduced in acute inflammation and restore/overcompensate in longstanding quiescent disease. This restoration is not apparent in recently inflamed mucosa (ROUC) despite endoscopic and histological remission; with similar changes seen in more aggressive disease. Recurrent bouts of acute inflammation in the mucosa with associated failure of restoration of K8 integrity may be associated with increased colon cancer risk. An altered VIM:K8 ratio may in addition be a surrogate mucosal marker of disease progression.

Disclosure of Interest None Declared

OC-093 THE EFFECTS OF FAECAL MICROBIOTA TRANSPLANTATION ON THE INNATE IMMUNE SYSTEM AND EPITHELIAL TIGHT JUNCTION EXPRESSION IN CHRONIC REFRACTORY POUCHITIS

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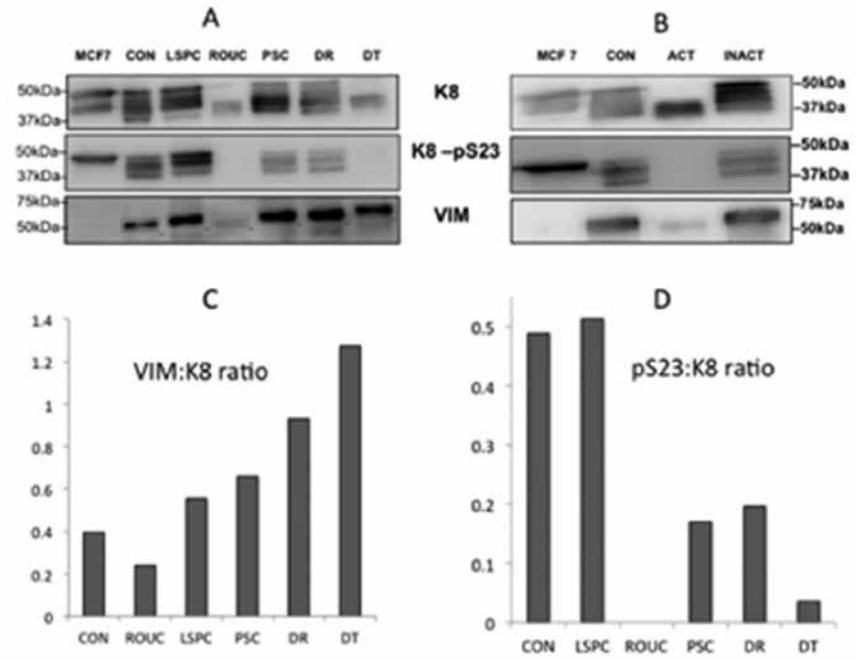
Introduction Faecal microbiota transplantation (FMT) may be beneficial in IBD. A durable change in recipients' microbiota following FMT has been demonstrated. No previous study has assessed the immunological effects of FMT. We aimed to assess the immunological effects of FMT in patients with chronic refractory pouchitis.

Methods FMT was performed via nasogastric tube. Mucosal biopsies samples were collected at pouchoscopy from eight patients with chronic refractory pouchitis before and four weeks after FMT. The epithelium was identified following incubation with EDTA and lamina propria dendritic cells (DCs) were identified following collagenase digestion. Epithelial cells were identified as pancytokeritin positive cells and expression of ZO-1, claudin 1 and claudin 2 were



Abstract OC-092 Figure