**Aims** Delineate the genetic, immune and microbial phenotype of patients, siblings and healthy controls (HC); identify factors associated with CD that discriminate siblings from HC.

**Methods** Faecal microbiota, FC, blood T-cell phenotype, IP and genotype risk over 72 CD risk loci, were measured by qPCR, ELISA, flow cytometry, sugar permeability and Illumina Bead Array respectively, in 22 patients with inactive CD, 21 of their healthy siblings and 25 HC.

**Results** In addition to genotype risk, siblings shared aspects of the phenotype of CD patients, distinct from HC, as previously reported. Direct discriminant function analysis revealed that the variables maximally separating siblings from HC (Function 2) were: increased β7 integrin expression by circulating naïve CD4+ T-cells and an increased proportion of memory CD4+ T-cells as well as reduced faecal Roseburia spp. (Image 1). In contrast, the variables differentiating CD patients from HC (Function 1) were: elevated FC and altered faecal microbiota (reduced Faecalibacterium prausnitzii, Cluster IV Ruminococcus spp. Bacteroides-Prevotella and Clostridial cluster IV).

**Conclusion** Healthy siblings of CD patients manifest immune and microbiological abnormalities associated with CD, distinct from their genetic risk. Unaffected siblings of CD patients are an excellent model in which to investigate early CD pathogenesis.

**Disclosure of Interest** None Declared

**REFERENCE**


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**OC-019 ADAMDEC1: A NOVEL MOLECULE LINKED TO CROHN’S DISEASE, IS ASSOCIATED WITH AN INCREASED SUSCEPTIBILITY TO CITROBACTER RODENTIUM COLITIS IN THE KNOCK OUT MOUSE**

**Introduction** Innate immunity is attenuated in patients with Crohn’s disease (CD), with impaired neutrophil recruitment, delayed clearance of E. coli, and defective secretion of pro-inflammatory cytokines from macrophages. This primary macrophage defect may result in failure to eradicate bacterial flora entering the tissues and lead to the chronic granulomatous inflammation characteristic of CD. To discover the molecules responsible, transcriptomic profiles were obtained from cultured human macrophages from CD patients and controls. ADAMDEC1 a Disintegrin and Metalloproteinase was under-expressed in ~10% of CD patients. This protein is almost exclusively found in macrophages and dendritic cells in the small and large bowel lamina propria. Here we describe the response of Adamdec1-/- mice to an enteric bacterial infection with Citrobacter rodentium.

**Methods** Adamdec1-/- and wild type mice were administered ~10^8 or 10^9 C. rodentium by oral gavage and body weight monitored for three weeks. At intervals mice were sacrificed and samples of serum, stool, colon and spleen were collected. Serum cytokine levels were measured and bacteria counted, in stool and spleen. Bowel inflammation was assessed histologically. Neutrophil and immune cell recruitment to the colon were measured by MPO assay and qPCR respectively.

**Disclosure of Interest** None Declared
**Results** During infection, control mice experienced a mild self-limiting colitis, with minimal weight loss. Expression of Adamdec1 was up-regulated in the colon and this normalised with resolution. Adamdec1+ mice were more susceptible to C. rodentium infection: they demonstrated dramatic weight loss (p < 0.001), a more severe colitis and a reduced survival at the higher dose (67% vs 0%, p = 0.009). Serum levels of TNE, IL-1β and IL-6 were significantly lower in the knock-out mice (p < 0.05). Impaired survival was associated with positive cultures of the organisms from the spleen (p = 0.02).

**Conclusion** By analysing the transcriptome of macrophages from CD patients we have identified a novel molecule involved in mucosal immunity. Further work is underway to elucidate the precise role of ADAMDEC1 in the immune response. Individuals with grossly attenuated expression levels may be at an increased risk of developing CD as a consequence of an impaired ability to handle enteric bacterial pathogens.

**Disclosure of Interest** None Declared

**REFERENCES**

**Gastroduodenal free papers**

**OC-020**
**THE MURINE GASTRIC MICROBIOME IS INFLUENCED BOTH BY HELICOBACTER FELIS INFECTION AND SOMATIC DELETION OF NF-KAPPA FAMILY MEMBERS**

doi:10.1136/gutjnl-2013-304907.020

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**Introduction** The development of gastric atrophy in C57BL/6 mice infected with *Helicobacter felis* is differentially regulated by signalling involving NF-κB1 and NF-κB2. After infection, more severe atrophy developed in Nfkb-/- mice than wild-type (WT), whilst Nfkb2-/- mice were protected from atrophic gastritis. Previous studies have also shown that the development of *H. pylori* induced gastric pathology was delayed in INS-Gas mice maintained in germ free, compared to conventional animal house conditions. Consequently we hypothesised that the different phenotypes observed in *H. felis* infected mice lacking specific NF-κB proteins may be influenced by altered gastric microbiomes. We have therefore quantified the abundance of specific bacterial phyla in *H. felis* infected WT, cfα-Proteobacteria, γ-Proteobacteria, Firmicutes and Actinobacteria were determined by qPCR of 16S rDNA. *H. felis* colonisation was quantified by qPCR for Flaα, samples were normalised to murine Gapdh.

**Methods** Groups of 3 C57BL/6, Nfkb1-/- and Nfkb2-/- mice aged 6 weeks were infected with *H. felis* by gavage. Animals were euthanased at 12 weeks and gastric antral DNA was extracted. Total bacterial load and relative abundance of α-Proteobacteria, γ-Proteobacteria, Bacteroidetes, Firmicutes and Actinobacteria were determined by qPCR of 16S rDNA. *H. felis* colonisation was quantified by qPCR for Flaα, results were expressed as a percentage of input DNA.

**Results** Untreated WT mice had 3.4 and 2.6 fold greater universal bacterial transcripts than Nfkb1-/- and Nfkb2-/- mice respectively. Actinobacteria abundance was 6.0 fold greater in untreated Nfkb2-/- mice of WT and 7.0 times greater in Nfkb2-/- mice. α-Proteobacteria were 9.0 times more abundant in untreated Nfkb1-/- mice of WT. *H. felis* infection of WT mice resulted in 5.6 and 16.7 fold increases in α-Proteobacteria and γ-Proteobacteria respectively of untreated mice. γ-Proteobacteria were more abundant in all infected groups, but significantly more so in Nfkb2-/- mice than others. This correlated with a 50 fold higher abundance of *H. felis* (Phylum: γ-Proteobacteria) in infected Nfkb2-/- compared to WT mice. Infected Nfkb2-/- mice also had a 3.3 fold greater abundance of Actinobacteria of infected WT mice. No statistically significant differences were observed in the abundance of Firmicutes or Bacteroidetes.

**Conclusion** Constitution of the murine gastric antral microbiome is influenced both by *Helicobacter felis* infection and somatic deletion of NF-κB family members. Since deletion of NF-κB1 and NF-κB2 have been reported to alter susceptibility to *H. felis* induced gastric atrophy, these data support the hypothesis that specific differences in microbiota may be responsible for, or reflect this altered susceptibility. Further studies are needed to determine whether specific organisms influence the development of gastric pathology either individually or within complex communities.

**Disclosure of Interest** None Declared

**OC-021**
**A RETROSPECTIVE AUDIT OF PNEUMOCOCCAL & INFLUENZA VACCINATION IN COELIAC DISEASE**
doi:10.1136/gutjnl-2013-304907.021

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**Introduction** Patients with coeliac disease (CD) are at increased risk of mortality from sepsis. In particular, the risk of sepsis with encapsulated organisms such as Pneumococci is higher. This may be a consequence of hyposplenism. Current Department of Health Green Book guidelines as well as Coeliac UK recommend vaccination against Pneumococci and influenza. We aimed to investigate whether or not patients with CD received vaccination against Pneumococci and influenza.

**Methods** CD patients were identified through a register of 1000-ID-10 classified patients currently under follow up at Royal Liverpool and Broadgreen University Hospitals NHS Trust. A random sample of 250 patients was selected from the register. Electronic case notes were interrogated for demographic details as well as the most recently confirmed comorbidities. Patients of all ages were included in the study. Patients aged over 65 and patients with certain comorbidities (e.g. chronic obstructive airways disease, ischaemic heart disease, liver cirrhosis etc) were analysed separately as these patients should already be immunised against pneumococci and influenza regardless of their coeliac disease diagnosis. Immunisation status was obtained by contacting individual patient’s general practitioners. The proportion of vaccinated patients were analysed according to the age groups < or > 65.

**Results** A total of 250 patients were included out of which we were able to obtain records for 198 patients. Of the 198 patients, 32% of patients had osteoporosis and 13% of patients had one or more concurrent autoimmune illness (e.g. thyroid disease, pernicious anaemia, Sjogren’s syndrome). 129 patients were < 65 years of age (M: F ratio 1: 2, median age-50, range 19–64) and 69 were > 65 (M: F ratio 1: 2, median age-73, range 65–84). In the < 65 category, we found 10 with no comorbidities necessitating vaccination which left 119 patients in the main study arm; 23 (19.3%) were vaccinated against Pneumococci and 42 (35%) against influenza.

**Abstract OC-021 Table 1** Vaccination uptake in < and > 65 age groups.

<table>
<thead>
<tr>
<th>Age</th>
<th>Pneumococcal vaccine</th>
<th>Influenza vaccine</th>
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<tbody>
<tr>
<td>&lt; 65</td>
<td>19.3%</td>
<td>35%</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>72.5%</td>
<td>82.6%</td>
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</tbody>
</table>

**Conclusion** Very few patients with CD are vaccinated against preventable causes of sepsis such as Pneumococci. Gastroenterologists, GPs and patients need to be aware of the increased risk of sepsis and the need to administer vaccines against preventable infections in CD patients. Vaccination status should be routinely obtained during follow up visits. Due to the lack of a simple clinical test for