3% (1–5) in IBD (4% of total CD4+ T cells) and 5%, (5–7) in HC (11% of total CD4+ T cells, p = 0.007). The %CD3+CD103+CD8+ in IBD was 9% (4–15, 33% of total CD8+ T cells) and in HC 42% (23–57, 83% of total CD8+ T cells, p = 0.001). The majority of CD3+CD103- T-cell subsets in active IBD at baseline was represented by CD103-CD4+ T cells (65% [52–74], in HC 30% [21–50], p = 0.001), while CD103-CD8+ in IBD was 22% (15–27) and in HC 13% (10–20), p = 0.001. When endoscopic remission is seen in IBD patients during follow-up, all frequencies of CD103+ T-cell subsets approach percentages comparable to HC.

Conclusions: Active mucosal inflammation in IBD patients is associated with decreased percentages CD3+CD103+ T-cell subsets. The CD103+ CD8+ T-cell subset is lower in active disease compared with healthy controls. Endoscopic remission in IBD is associated with normalisation of the mucosal T-cell profiles, also the CD103+CD8+ T-cell subset. The suggested pro-inflammatory CD103+ CD4+ T cells represented only a minority of the total mucosal (CD103+) T-cell subset. It is mainly the CD4+CD103-T-cell subset that infiltrates the inflamed colon in IBD. These results challenge the pro-inflammatory role of these CD103+CD4+ T cells in IBD patients.

P009
Adalimumab and infliximab biosimilar ameliorated cachexic syndrome of Crohn Disease
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Background: Crohn disease in some paediatric and adolescent patients is presented with cachexic status manifested with malabsorption, nutritional deficiencies, osteopenia, sarcopenia, and growth failure. Though different with cancer cachexia, underlying pathogenic mechanisms share similarity. Stimulated with cancer cachexia pathogenesis, we have challenged TNF-alpha antibodies, adalimumab and biosimilar of infliximab, Remsima, in animal model with cancer cachexia because significant surge up in TNF-α and IL-6 was prevailing condition in cachexia.

Methods: Humira and its biosimilar Remsia were administered three times per week in mice xenografted with C26 adenocarcinoma cells up to 3 weeks of cachexia condition.

Results: As results, adalimumab and Remsima significantly ameliorated cancer cachexia, presenting with significantly lowered mice survival, attenuated weight loss, appetite preservation as well as preserved skeletal muscle and abdominal fats (p < 0.01). Genes including PAX7, muscle related genes such as Murf-1, antrogin-1, and Mul-1 were significantly attenuated along with significant decreased TNF-α serum levels (p < 0.01). Experiments were repeated in Min mice model, which showed cachexic status as intestinal polyposis progressed, administered with DSS to simulate CD manifestation. As results, cachexic status was significantly ameliorated in group treated with either adalimumab or infliximab biosimilar.

Conclusions: In conclusion, top-down administration of biologics targeting TNF-α should be considered in paediatric or adolescent CD patients presenting with severe wasting conditions.

P090
Is Epstein–Barr virus infection associated with the pathogenesis of microscopic colitis?
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Background: Epstein–Barr virus (EBV) has been associated with inflammation in the colon, particularly in patients with inflammatory bowel diseases, even if its potential impact on pathophysiology and course of the disease is still unclear. Conversely, no data are available on the association between EBV and microscopic colitis (MC). We aimed to compare the frequency of colonic EBV infection in patients with MC, ulcerative colitis (UC), and irritable bowel syndrome (IBS).

Methods: The frequency of colonic EBV infection in biopsies of 30 patients with MC, 30 patients with UC, and 30 controls with IBS was retrospectively assessed. PCR was performed to detect viral EBV DNA in colonic biopsies. In situ hybridisation was also performed to identify and localise EBV-encoded small RNAs (EBERs) within cells, which are known to play a role in inhibition of apoptosis, increase of cell proliferation, and induction of pro-inflammatory cytokines.

Results: The presence of EBV DNA was detected in 27 of 30 MC patients, in 20 of 30 UC cases, and in none of the IBS group. The frequency of EBV DNA in MC was significantly higher compared with that reported in UC (90.0% vs. 66.7%, p = 0.03). EBERs+ cells were observed in 18 of 30 MC patients, who also displayed the presence of EBV DNA, in only 3 of 30 UC patients (60.0% vs. 10.0%, p < 0.001), and in none of the IBS group.

Clinical and histological characteristics of patients with microscopic colitis (MC), ulcerative colitis (UC), and irritable bowel syndrome (IBS).

<table>
<thead>
<tr>
<th>Variables</th>
<th>MC (n = 30)</th>
<th>UC (n = 30)</th>
<th>IBS (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (range)</td>
<td>47 (20–78)</td>
<td>48.7 (17–88)</td>
<td>44.5 (20–64)</td>
</tr>
<tr>
<td>Males</td>
<td>23 (76.7%)</td>
<td>15 (50.0%)</td>
<td>15 (50.0%)</td>
</tr>
<tr>
<td>Collagenous/lymphocytic colitis</td>
<td>18 (60.0%)/12 (40.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe colitis</td>
<td>4 (14.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colonic EBV/DNA +</td>
<td>27 (90.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EBERs+ cells</td>
<td>18 (60.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: This study shows for the first time that EBV infection is almost always detectable in patients with MC. The high frequency of EBERs+ cells observed in MC suggests that EBV may act as an innocent bystander, as it could play a causative role in the pathogenesis of the disease. Further studies are necessary to confirm this association and to clarify the role of EBV in MC and, more generally, in colonic inflammation.

P091
Inflammation in relation to mucosal barrier function in chronic colitis: a study in time
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Abstract: The pathogenesis of inflammatory bowel diseases (IBD) is multifactorial. Midst in the complex interaction between genetic, environmental and immunological factors is the intestinal barrier. IBD patients have been observed to have increased intestinal permeability which can partially explain the exaggerated immune response towards luminal antigens. Inflammatory mediators perpetuate this barrier defect by causing further damage to the intestinal barrier. Our aim is to investigate the interaction between permeability and inflammation in a chronic colitis mouse model.

Methods: Colitis was induced in immunodeficient SCID mice by the adoptive transfer of naive T cells, isolated from BALB/c mice. Mice were sacrificed at fixed time points to study disease progression resulting in five groups: control mice (Week 0); colitis mice in week 1, 2, 4 and 6 of the experimental protocol (Week 1; Week 2; Week 4; Week 6; all n = 10). FITC-dextran was used to assess intestinal permeability, next to the messenger RNA of the tight junction proteins Claudin-1 and Occludin. After sacrifice, colonic inflammation was assessed by macro- and microscopic scoring, myeloperoxidase (MPO) activity and cytometric bead array (CBA) for TNF-α and IL-1β. Messenger RNA of transcription factors that regulate T helper (Th) cell differentiation including T-bet (Th1), GATA-3 (Th2), ROR-γt (Th17) were quantified using RT-qPCR technique.

Results: Mucosal inflammation appeared gradually in the colon of the diseased mice. Macroscopically there was a significant increase starting from Week 2 on, gradually increasing until Week 6. The same was true for the MPO activity. Microscopically, however, the first significant signs of inflammation were observed at Week 1, which then also gradually increased with the highest score at Week 6. The colonic inflammation was mainly Th1/Th2 driven, since the transcription factors T-bet and GATA-3 were significantly upregulated from respectively Week 2 and Week 4 on. TNF-α and IL-1β were significantly elevated starting from Week 1. Intestinal permeability was significantly elevated at Week 1 and remained elevated at Week 2, 4 and 6.

Data are presented as mean±SEM and analysed by one-way ANOVA with multiple comparisons SNK posthoc testing. *<0.05 vs. WEEK 0 # <0.05 vs. WEEK 1.

Conclusions: Our results show a gradual increase of intestinal inflammation over time which, for most parameters, started at Week 2. However, we observed an unexpectedly early increase in intestinal permeability at Week 1. This shows that the mucosal barrier function is of great importance in disease onset and could be an interesting therapeutic target or biomarker predicting flares.

P092
Serological assessment of wound healing in Crohn’s disease

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