Altered microbiota in microscopic colitis

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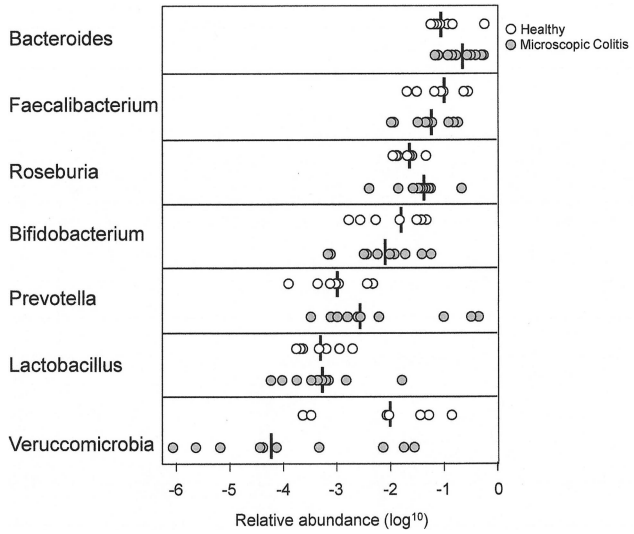

Figure 1 Occurrence of bacterial species in the microbiota in patients with microscopic colitis compared with healthy controls.

Altered microbiota in microscopic colitis

Recently, Shin *et al*[1] reported that *Akkermansia* spp had a beneficial effect on glucose homeostasis in obese mice. Mucin degrading *Akkermansia*—promoting mucin degradation and turnover—is associated with a healthy mucosa. In IBD, a deranged microbiota is reported while findings in microscopic colitis (MC) are lacking. MC is a disorder characterised by chronic non-bloody diarrhoea, predominantly affecting elderly smoking women. Despite frequent diarrhoea, laboratory anomalies are seldom seen.

Since an altered microbiota is reported in several immune mediated diseases and since MC affects the gut, our hypothesis was that the microbiota would be altered in patients with MC.

A group of 10 female patients (mean age 48 years, range 43–68 years) with onset of MC collected as previously described[2] donated faecal samples that were compared with samples from seven healthy control women (mean age 50 years, range 45–65 years) with respect to their faecal microbiota.

The bacterial microbiome was analysed by DNA sequencing (Illumina Hiseq 2000) and sequences were aligned to a catalogue of sequenced genomes from the National Center for Biotechnology Information and hmpdacc.org to determine the composition of the microbiota. Sequences were aligned with Bowtie to the sequenced species catalogue of 2382 genomes. Alignments with the fewest number of mismatches were counted. Relative abundance was calculated by calculating the ratio of aligned reads of each genome to the total number of aligned reads. Details about the bioinformatics methods, MEDUSA pipeline, have been described previously.[3] Patients with MC had a marked reduction of *Veruccomicrobia* (*Akkermansia* spp) compared with healthy individuals (figure 1), with a difference approaching 2–3 log (p=0.02; Wilcoxon rank-sum test). In other species (*Bacteroides* and *Prevotella*), some differences could be noticed although not reaching statistical significance.

The notion that patients with MC had a significantly lower amount of *Akkermansia* was further strengthened with specific *Akkermansia* spp. PCR performed on the 10 patients and 7 controls and on an additional 5 female patients with MC (total mean age 50 years, range 43–65 years) and 7 female controls (total mean age 51 years, range 45–73 years) (figure 2). Although the number of patients with MC was low, it should be noted that the smokers had extremely low levels of *Akkermansia*.

Akkermansia is one of the most prevalent bacterial strains in the large intestine. It has been shown in mice that *Akkermansia* thickens the mucin layer, and thus may protect

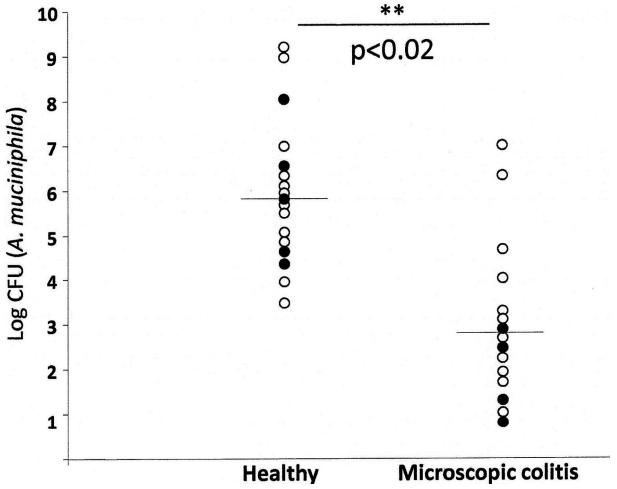

Figure 2 Occurrence of *Akkermansia muciniphila* in the microbiota in patients with microscopic colitis compared with healthy controls. Smokers are marked in black circles and non-smokers are marked in white circles.

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the epithelium against potentially toxic faecal material.[4] The patients with MC were diagnosed because of onset of diarrhoea why chronic disease or continuous medication did not contribute to the alteration. Smoking seems to contribute to the low levels found in MC. The association with smoking is in line with the situation in several types of immune mediated diseases where smoking is detrimental for the disease course, such as Crohn's disease or rheumatoid arthritis. Since smoking has been shown to be a risk factor for MC and since smoking and changed smoking habits have been reported to induce profound changes in the microbiota at least in healthy individuals, it could be speculated that an increased risk for MC could be mediated by changes in the microbiota.

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Competing interests None.

Ethics approval Lund University.

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