Increased abundance of bacteria producing hydrogen sulfide in the colonic mucosa of patients with ulcerative colitis and Crohn’s disease

Franck Carbonero¹, Ann C. Benefiel¹, Jona Kristo¹, Jenna K. Leinberger¹, Maeve M. Leurck¹, Eugene Greenberg², H. Rex Gaskins¹

¹University of Illinois at Urbana-Champaign
²Carle Foundation Hospital, Center for Digestive Health, Urbana, Illinois

The gut microbiota is increasingly suspected as a key factor in the etiology of inflammatory bowel disease (IBD). However, it is most often characterized in stool samples, which are only partially representative of the mucosal micro-environment where the inflammation originates. Here, a molecular-based approach was used to examine mucosa-associated microbiota in ileal, ascending and descending colon and rectal biopsies from ulcerative colitis (UC) and Crohn’s disease (CD) patients, and healthy control subjects. We focused on sulfidogenic bacteria producing hydrogen sulfide, which is proinflammatory and a potent genotoxic agent. Targets included sulfate-reducing bacteria (SRB: dissimilatory sulfite reductase (dsrAB) gene of SRB and 16S rRNA genes of Desulfovibrio, Desulfobulbus, Desulfobacter and Desulfotomaculum), Bilophila wadsworthia (taurine:pyruvate aminotransferase (tpA)) and Fusobacterium nucleatum (Fn1419 and Fn1055 encoding enzymes that convert cysteine to hydrogen sulfide). These targets were quantified through qPCR targeting 16S rRNA genes and functional genes. A total of 321 biopsies, in some instances taken from inflamed and adjacent non-inflamed tissue, from 28 CD and 19 UC patients as well as 40 healthy subjects were quantified for the abundance of sulfidogenic microbes. A 10-fold greater abundance of SRB, in particular the genus Desulfotomaculum, was detected in inflamed tissue of CD and UC. Strikingly, all functional genes for sulfidogenic bacteria and SRB genera except Desulfobulbus were significantly more abundant in biopsies from IBD patients compared to healthy controls (at least 10 times more abundant for the more abundant genes). In addition, Bilophila wadsworthia was ubiquitous in IBD patients (99.5%) but much less prevalent for healthy controls (48%). This increased prevalence of SRB and genes mediating sulfide production from organic sulfur sources in IBD patients is consistent with the proinflammatory properties of hydrogen sulfide, which may contribute to chronic inflammation. As many of the patients examined were in remission, it can be hypothesized that they may be deficient in sulfide detoxification or other host pathways that provide tolerance to bacterial-produced sulfide. Together the data indicate an urgent need for systematic study of the various microbial and host metabolic pathways involved.