Roseburia hominis: a novel guilty player in ulcerative colitis pathogenesis?

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Inflammatory bowel diseases (IBD) such as Crohn’s disease (CD) or ulcerative colitis (UC) comprise the two most common forms of intestinal inflammation characterised by a chronic relapsing disease course. The aetiology of both disorders has still not yet been identified. Whereas it has been elegantly demonstrated in many studies in the last years that genetic factors are crucially involved, other so-called environmental factors are much less well defined. 3 In recent years evidence was accumulating that the gut microbiota and its manipulation might constitute one of those relevant ‘environmental’ factors. Trillions of microbes compose the intestinal microbiota of healthy individuals and several studies have demonstrated in the past that IBD patients exhibit a pronounced dysbiosis. It remains, however, speculative whether observed changes are causally involved in IBD pathogenesis or reflect simply epiphenomena due to inflammation. 4

Whereas several clinical aspects strongly support a role for intestinal bacteria in CD such as improvement of inflammation after diversion of the faecal stream or improvement of disease during antibiotic therapy, similar observations are mostly not available for UC. However, other aspects are suggesting a role for bacteria in the pathogenesis of UC as, for example, abnormal mucosal secretion of IgG antibodies against certain commensals. Several preclinical and clinical studies have recently supported the notion that some bacterial strains such as Lactobacillus casei, Lactobacillus plantarum or Faecalibacterium prausnitzii are able to suppress the production of potent proinflammatory cytokines or even induce anti-inflammatory cytokines such as interleukin 10, whereas others such as non-pathogenic Escherichia coli strongly stimulate the synthesis of proinflammatory cytokines such as interleukin 12, interferon-gamma, interleukin 2 or tumour necrosis factor-alpha. 5 Whereas earlier studies demonstrated no major differences in the gut’s microbiota between healthy individuals and patients with UC in remission, 6 others observed marked differences between healthy subjects and UC patients, especially at the mucosal level. 7 Besides the rather well-established reduction of microbiota diversity in IBD patients, recent studies have proposed a potential role for certain bacteria such as Faecalibacterium prausnitzii strains as rather proinflammatory and detrimental, whereas other bacteria such as F prausnitzii exert protective properties. Indeed, F prausnitzii, a commensal under-represented in UC patients both during active disease and in remission, shows prominent anti-inflammatory activities in vitro and in certain in vivo models. 8 Importantly, it has been recently demonstrated that the recovery of F prausnitzii after disease relapse in UC patients was associated with maintenance of clinical remission. 9 Overall, so far only a very few strains of the gut’s microbiota have been linked with a potential role in the pathogenesis of UC. Machiels et al 10 propose that another member of the microbiota, that is, Roseburia hominis, might play a role in UC. In this large clinical trial where 127 UC patients and 87 age-matched and sex-matched controls were studied, the main microbial signature consisted of a decrease in the butyrate-producing species R hominis and F prausnitzii, both members of the Firmicutes phylum, as assessed by denaturing gradient gel electrophoresis and PCR confirmation, whereas other species typically being altered in CD remained unaffected. Interestingly, both R hominis and F prausnitzii were inversely correlated with disease activity suggesting that their depletion might negatively influence intestinal inflammation. It remains, however, unclear whether other environmental factors such as dietary factors, certain medications and others might have affected obtained results. Overall, R hominis might be added as another member of the microflora playing potentially a role in UC.

Butyrate-producing commensals are assumed to play a major role in gut health and maintenance of immunity such as regulatory T cell homeostasis. 9 Although the concentrations of short-chain fatty acids (SCFA) were not significantly lower in the Machiels study in UC patients compared with healthy controls, several other studies have shown that SCFA concentrations are impaired in IBD patients. Surprisingly, the current knowledge of R hominis and especially its role in immunity and inflammation is very sparse and its potential role in intestinal inflammation can only be speculated from one of its main properties, namely butyrate production. Interestingly, iron availability might affect Roseburia spp. concentrations as very low iron concentrations resulted in a decrease in Roseburia spp. in an in vitro colonic fermentation model after inoculation with immobilised faecal microbiota. 10 Intestinal iron availability is commonly impaired in IBD patients and the relationship between iron stores and concentrations of R hominis in IBD patients would be another major interest of further studies.

Even though Machiels et al 10 have replicated their findings of decreased R hominis concentrations in UC patients in a second cohort, 3 other studies so far have failed to show this type of dysbiosis in UC patients. 4, 5 Only a small study described a reduction in Roseburia spp. in UC patients. 11 Despite these challenging and exciting data introducing a ‘potentially new player in UC’, several questions have to be addressed in the near future: first of all, further clinical studies have to confirm this association. In vitro studies should mechanistically demonstrate how R hominis might affect mucosal cytokine cascades. Does R hominis also exert mainly anti-inflammatory activities similar to F prausnitzii? Is the whole R hominis necessary or a simple antigen needed? Preclinical animal experiments must investigate their effects in various established models of experimental colitis and finally if all these studies reveal promising results the final ‘human proof’ for a role of this interesting commensal in UC warrants prospective clinical trials using a ‘R hominis probiotic’ as a novel potential treatment option.

Overall, evidence is increasing that a microbial signature exists differentiating the two forms of IBD from each other and from healthy individuals. Whether these findings have any implications in understanding disease pathogenesis or even affect treatment strategies remains to be investigated. Commensals and IBD are currently a fascinating and exciting topic, whether this promise will hold its...
expectations will be clarified hopefully in the next years.

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