Probiotics and Intestinal Diseases

Philip Rosenstiel^a Eduard F. Stange^b

^aInstitute for Clinical Molecular Biology, Christian-Albrechts-University, University Hospital Schleswig-Holstein, Kiel, and

^bDivision of Internal Medicine 1, Robert-Bosch-Krankenhaus, Stuttgart, Germany

The intestinal tract of higher metazoan organisms is colonized by an indigenous microflora that forms a complex ecosystem including both bacterial and fungal microorganisms [1]. A total number of >1,000 different species are estimated to be present in the human fecal flora at concentrations of up to 10^{12} viable microorganisms per gram stool [2]. It is widely accepted that enteric bacteria are of critical relevance not only to acute gastrointestinal infections but also to the pathophysiology of chronic inflammatory disorders like Crohn's disease or ulcerative colitis. It is well recognized that the close symbiotic relationship between host and resident microflora is an integral part of the homeostasis of intestinal physiology and is crucially involved in diverse processes, such as the metabolism of nutrients and organic substrates, as well as the development of intestinal epithelium, vasculature and lymphoid tissue [3].

This self-healing and self-regenerative capacity of the balanced microflora (resilience phenomenon) seems to be defective in many gastrointestinal diseases, in which reduced microbial diversity is a constant characteristic, e.g. in inflammatory bowel diseases. We therefore think that intestinal inflammation (both during acute and chronic diseases) is promoted by a dysbalance of the microbial community caused by both host and microbial factors and that reconstitution of host micro-

biota homeostasis may be a key factor to guarantee mucosal healing.

A promising option is the therapeutic application of probiotic strains of bacteria that may alter the observed dysbalance of the intestinal flora by both influencing the host side and the associated microbial communities [1]. Probiotics are defined as living microorganisms that – if taken in the appropriate dosage – may result in a health benefit for the human host organism. Several modes of action have been proposed, including antagonistic interactions with other bacterial strains and modification of host-protective immune responses [4]. Among the effects exerted by probiotics the direct competition with other bacteria through microcins, downregulation of inflammatory cytokines and induction of endogenous mucosal peptide antibiotics, most prominently defensins, appear to be the most important [5–7].

In clinical practice, the strongest evidence for the use of probiotics for gastrointestinal diseases has been presented for chronic inflammatory disorders, including pouchitis and ulcerative colitis [4]. In ulcerative colitis the probiotic strain *Escherichia coli* Nissle has been shown to be equivalent to mesalazine in maintaining remission. Probiotics, including lactobacilli and bifidobacteria, administered to children can reduce the incidence and duration of diarrhea, but the benefit may vary upon the na-

ture of the condition. Other promising fields of therapy may include adult traveler's diarrhea, postinfectious irritable bowel syndrome and *Helicobacter pylori* infection. However, rigorous clinical studies are needed to completely understand the effects of probiotics in these disorders [4]. Despite promising data from animal studies, the effects of probiotics in radiation-induced enteritis in first clinical observations have been discouraging.

It must be noted that not all probiotics are created equal and that the term subsumes different commercially available preparations ranging from single defined strains (e.g. *E. coli* Nissle) to complex mixtures (e.g. VSL#3). Future studies must also take into account that different preparations may have completely different therapeutic activities according to the site and modes of action. Thus, deeper insights into the genomic architec-

ture and physiological capacities of the probiotic microorganisms will be needed to develop a rational therapeutic algorithm for each indication area.

We hypothesize that the specialty of gastroenterology may be profoundly affected by the ability to modify the host's gastrointestinal immune responses and gut-associated microbiota through the use of probiotics as rational therapies for gastrointestinal diseases.

Disclosure Statement

P.R. does not have any relationship to disclose.

E.S. has received honoraria for consulting on the topic of probiotics.

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