ABSTRACT

Although the etiology and pathogenesis of inflammatory bowel disease (IBD) is not fully understood, it is generally accepted that the inflammation results from aberrant immune responses to antigens of gut microbiota in genetically susceptible individuals (Sartor et al., 2006). Alteration in intestinal microbiota has been found in IBD patients with increased abundance of certain bacteria and decreased abundance of others. Due to the complexity of the disease, multifaceted interactions between genetic factors, host immune response, gut microbiota and environment factors need to be taken into account.

In this thesis, the pathogenesis of IBD was first reviewed in respect with the four factors mentioned above. Then we concentrated on the interaction between IBD-associated bacteria and mucosal immune system. We investigated the ability of mucosal-associated bacteria (MAB) from IBD patients to induce spontaneous colitis in germ-free (GF) mice and the impact of those bacteria on the development of dextran sulfate sodium (DSS)-colitis. Together with the analysis of the composition of gut microbiota of MAB colonized mice, we demonstrated the potential deleterious microbes were able to increase the susceptibility to DSS-colitis once they found a suitable niche. We revealed the mechanism of an *E.coli* strain which were reported to be more frequently isolated from IBD patients to damage the integrity of the intestinal epithelium by its hemolytic activity. Not only focusing on the “bad guys”, we also elucidated the protective effect of the probiotic strain *Clostridium tyrobutyricum* against acute colitis by promoting the mucosal immune homeostasis and we found butyrate produced by the bacterium as a key component to elicit the anti-inflammatory capacity.

Gut microbiota has a profound impact on immune response with subsequently affecting the total health of a host. This thesis provides us better knowledge of bacteria interacting with the immune system and may bring new insights to treatment of IBD.