Abstract

One of the most common used therapies in inflammatory bowel diseases (IBD) treatment are inhibitors of a cytokine TNF-α. Nevertheless, up to one third of IBD patients stop respond to this therapy for unknown reason. In these days, there are not any ideal biomarkers which could predict patient's long-term response to anti-TNF-α therapy. Because the gut microbiota composition changes are tightly related to the pathogenesis of IBD, my aim in this thesis was to find out if these changes in composition are happening also due the therapy by inhibitors of TNF-α as well. Moreover, I tried to find out if there are changes in production of serum biomarkers related to the gut barrier damage and to the immune response associated with microbial translocation. Also, I focused on the immune response of IBD patients against common gut commensal bacterial antigens during the anti-TNF-α therapy. In our study, we collected for these purposes stool or blood samples from 46 IBD patients before the therapy and at 38th week from the start of the therapy and 39 healthy controls.

I found that IBD patients had higher bacterial diversity (α-diversity) as well as different bacterial composition across observed groups (β-diversity) at 38th week of the anti-TNF-α therapy than before the therapy. When I divided IBD patients according to their therapy response at 38th week, I did not find any differences in α-diversity before and at 38th week of the therapy in IBD patients. Furthermore, I measured blood serum levels of 7 biomarkers before and at 38th week of therapy. In IBD patients, I measured levels of serum calprotectin (sCP), α-defensin (DEFA)1, lipopolysaccharide binding protein (LBP), mannan-binding lectin (MBL), intestinal (I-) and liver fatty acid-binding protein (L-FABP) and sCD14 molecule. After that, I compared the biomarker levels detected in patients with those in healthy controls. Then I compared levels of these biomarkers before and at 38th week of anti-TNF-α therapy in patients with Crohn's disease and with ulcerative colitis according to their therapy response. Compared to healthy controls, IBD patients had significantly higher levels of sCP before the start as well as at 38th week of the therapy and they had also significantly higher levels of DEFA1 before the start of the therapy. The next result of my diploma thesis was that IBD patients responding to the anti-TNF-α therapy had significantly decreased levels of sCD14 and MBL at 38th week of the therapy. Moreover, I used *ex vivo* cultivation of IBD patients' peripheral blood mononuclear cells with bacterial lysates for characterisation of the immune response against antigens of 10 common gut commensal bacteria during the anti-TNF-α therapy.

Despite of the limited number of patients in our study, results in my diploma thesis show that gut microbiota plays an important role in the pathogenesis of IBD, even during the anti-TNF-α therapy.

Key words: inflammatory bowel disease, biological therapy, tumor necrosis factor-α, gut microbiome, serum biomarkers, intestinal barrier