

ABSTRACT

Inflammatory bowel disease (IBD) represents a group of multifactorial illnesses with increasing incidence worldwide. Crohn's disease (CD) and ulcerative colitis (UC) are the two most thoroughly defined phenotypes of IBD. IBD associated with primary sclerosing cholangitis (PSC) – a progressive biliary disease leading to cirrhosis and liver failure – is considered as specific IBD phenotype (also referred to as 'PSC – IBD') due to its clinical and pathophysiological characteristics.

The aim of the experimental part of this thesis was to define specific features of PSC – IBD in the key areas of IBD pathogenesis. These are: microbiota composition, gut – barrier failure, genetic predisposition and aberrant cellular and antibody immune response. Furthermore, the other goals were to describe relation of IBD status and activity to liver transplantation (LTx) and carcinogenesis based on thorough analysis of clinical data in patients under surveillance at the liver transplantation unit.

Using the next-generation parallel sequencing technology, we discovered specific bacterial and mycobial features of gut microbiota composition in PSC – IBD which significantly differed from UC and healthy controls recruited from Czech general population. Moreover, we identified numerous seral biomarkers distinguishing CD, UC and PSC – IBD and/or reflecting disease and treatment status. Some of these findings stress out the importance of gut barrier dysfunction in IBD. Additionally, we characterised antibody and cellular immune response showing significant variations among IBD phenotypes. Within the retrospective study analysing the largest Czech set of patients after LTx for PSC up-to-date we revealed that IBD status has a crucial impact on PSC recurrence rate and therefore the liver graft prognosis. After HLA-typing of subject cohort of patients involved, we also demonstrated the genetic predisposition importance regarding this issue. Additionally, we evaluated risk of biliary and colorectal neoplasia development in context of LTx for PSC. Lastly, we revealed a significant correlation between autoimmune pancreatitis (condition significantly associated with IBD) and pancreatic carcinoma in patients resected for focal pancreatic mass.

In future, the data presented in this thesis will be followed by further projects with similar research focus. Our results may significantly contribute to establishing suitable clinical biomarkers and/or therapeutic goals and identifying high – risk patients.