

Inflammatory bowel disease (IBD) primarily includes ulcerative colitis and Crohn's disease (CD). Both usually involve severe diarrhea, pain, fatigue and weight loss and can be debilitating and sometimes leads to life-threatening complications. The exact cause of inflammatory bowel disease remains unknown and while heredity seems to play a role in IBD, the probability of disease development is modified by diet, lifestyle, and endogenous factors, including the gut microbiota. We are witnessing an increase in the number of cases of IBD in last years in developed countries and the rise witnessed in the rest of the world closely correlates with adopting a Western lifestyle. These observations show an increasing role of environmental factors in the pathogenesis of the disease. In developed countries, peoples' lifestyle changed significantly leading to serious modifications in dietary habits and physical inactivity. Gut microbiota, consists of a complex community of microorganism species that live in the digestive tracts of animals and is the largest reservoir of microorganisms mutual to humans. Westernized diet, particularly high-fat diet can affect the composition of gut microbiota in humans and in an experimental mouse model, leading to a “dysbiotic” microbiome, the increased plasma bacterial cytotoxin lipopolysaccharide (LPS) levels and impaired intestinal integrity. As was shown recently sedentary style of life could also influence composition of gut microbiota in humans. Although malnutrition is serious problem in CD patients and most are underweight, the hypertrophy of the mesenteric fat tissue located around the inflamed parts of the intestine is observed, and recent research suggests that this fat wrapping actively contributes to disease severity releasing proinflammatory cytokines and may influence the onset of complications. The intestinal alkaline phosphatase (IAP) has been shown to function as a endogenous gut mucosal defence factor which plays an important role in maintenance of gut homeostasis. Previous studies have demonstrated the promising therapeutic effect of IAP against several LPS-mediated diseases. Our present project is aimed to determine the hypothesis that high fat diet influences the macroscopic, microscopic and functional status of the intestinal mucosa in mice with experimental, trinitrobenzene sulfonic acid (TNBS)-induced colitis, endogenous IAP plays a crucial role as an important mucosal defense factor and that treatment with exogenous IAP exerts a protective influence on the extent and severity of experimental colitis particularly in high fat diet-fed animals. We also plan to test hypothesis that protective effects of IAP administration could be augmented by voluntary physical activity in mice fed with HFD and ND with or without TNBS-induced colitis. The beneficial effects of exercise in IBD may be also mediated by the anti-inflammatory action of myokines released from active skeletal muscles. Because the hypertrophy of mesenteric fat is, at least partially LPS induced it is possible that could be decreased by IAP administration but also exercise could help by stimulating secretion of myokines from active muscles and influence muscle-fat crosstalk.

IBD places a heavy burden on populations because its symptoms can greatly affect a person's quality of life and capacity for work and this may finally lead to increase disability. The increasing prevalence particularly of CD, has a major impact on health care resources. Although IBD treatments are available, there is still a significant and unmet medical need for moderate to severe IBD patients, due to the poor prognosis and efficacy, significant side effects and very high costs of current treatments for the chronic disease. Altogether, the above considerations clearly imply that, by responding to the great social challenges posed by IBD the potential impact of any action targeting this disease is very high. The project's result will expand the knowledge base of intestinal mucosal defence factors and pathomechanism of IBD, including the possible role of the “westernized” diet in this disease. Our intention is that data generated by project could possibly be translated into clinical practice and help to understand of human “scenario” of IBD in human subjects.