"Understanding the regulation of GDF11 signaling in the context of the gastrointestinal diseases"

Inflammatory bowel diseases (IBD) are chronic relapsing disorders, which affect the gastrointestinal (GI) tract. The major symptoms of IBD include abdominal pain, loss of body weight, fever, diarrhea and rectal bleeding due to the intestinal inflammation. IBD pathogenesis is not fully understood, numerous genetic, environmental and immunological factors as well as disturbances in gut microbiota are listed as potential causes of IBD. The efficiency of therapy is not satisfying, as IBD patients complain due to relapsing periods and side effects. Moreover, it was assessed that 25% of IBD patients may develop colitis-associated colorectal cancer in next 20 years after diagnosis. Interestingly, inflammation, which occurs in the liver is combined with liver failure, in consequence it leads to coagulopathies, digestive processes, xenobiotics metabolism, in further perspective to death.

GDF11 is a protein belonging to TGF-β family, which participates in embryogenesis. Recently, it was revealed that GDF11 is expressed in kidneys, liver, intestine, brain and pancreas. The action of GDF11 is no well described, currently available data are conflicting.
It was indicated that GDF11 possesses pro- or anti-inflammatory action depending on the affected organ. Additionally, disturbances in GDF11 action was determined in carcinogenesis, it was evidenced in colorectal, pancreatic, kidney or liver cancer.

The aim of this proposal is to assess activity of GDF11 in the course of hepatic and colonic inflammation as well as colitis-associated colorectal cancer. GDF11 role in these disorders will be determined regarding to the proteins involved in the maintenance of the mucosal integrity and fibrosis occurring during inflammation and cancer.