DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

The main goal of our project is to determine role of MCPIP1 protein (Monocyte chemoattractant protein-induced protein 1) **in the development and progression of NAFLD** (Nonalcoholic Fatty Liver Disease).

The first stage of NAFLD is called fatty liver disease and is caused by excessive accumulation of triglycerides in hepatocytes and it develops due to impaired hepatocyte metabolism. During next steps in NAFLD progression, besides fat accumulation chronic local inflammation of low intensity plays an important role. Therefore, proteins involved in inhibition of inflammatory response have a very significant impact on this disease. One of the new, very important protein involved in the negative regulation of inflammation is a monocyte chemoattractant protein-induced protein 1 (MCPIP1). MCPIP1 binds to mRNAs' 3'UTR fragments and digested a stem-loop structures. Such endoribonuclease activity of MCPIP1 shortens a half-life of selected transcripts (e. g. IL-1β. IL-6) and reduces amount proteins.

Our project will be carried out based on the in vitro experiments performed on HepG2 cell line and primary murine heaptocytes. Additionally, we will use a human biopsy specimens that will be collected during bariatric surgeries for analysis of NAFLD stage and MCPIP1 expression. Finally, by applying a 'state of the art' Cre-LoxP technology we will be ably specifically knock-out MCPIP1 expression in murine hepatocytes and analyze its role in NAFLD in *in vivo* model.

There is a burning need for development of new medical strategies for NAFLD patients. Patients with early-stage of NAFLD (fatty liver with no signs of inflammation) are advised to change dietary habits and to increase physical activity to gradually reduce weight. Importantly, so far there is no drug used directly for NAFLD therapy. Importantly, between 20% to 30% of general population in the western world suffer nowadays from NAFLD, which makes more than a billion people worldwide. Moreover, meta-analysis performed recently among United States patients undergoing liver transplantation showed that NAFLD is third most common indication for this type of surgery.
We believe, that demonstration of MCPIP1 involvement in development of NAFLD can contribute to the discovery of new medical therapies. Compounds that inhibit degradation of MCPIP1 might be used in the future for designing new drugs used in the treatment of chronic inflammation. Since MCPIP1 inhibits inflammation, its local activation should help to restore homeostasis unbalanced by unresolved or untamed inflammatory processes.