Chronic inflammatory diseases, such as atherosclerosis and nonalcoholic fatty liver disease are a worldwide public health problem and one of the frequent causes of death in the Western countries. Furthermore, currently used pharmacotherapy is not fully effective in the treatment of these conditions. Importantly, low-grade chronic inflammation associated with oxidative stress and dysfunction of mitochondria – organelles, which are responsible for the production of energy in the cell - plays an important role in the pathogenesis of both diseases. The cells of immune system: macrophages derived from monocytes are engaged in the development of atherosclerosis and nonalcoholic fatty liver disease. We distinguish two main phenotypes of macrophages: "proinflammatory" M1, which are responsible for the clearance of pathogens and "anti-inflammatory" M2, which play a role in the resolution of inflammation, tissue repair and wound healing. In chronic inflammatory diseases, such as atherosclerosis and nonalcoholic fatty liver disease, the mechanisms involved in the resolution of inflammation associated with the activity of M2 macrophages are impaired. Interestingly, M1 and M2 macrophages can be characterized by distinct metabolic features in mitochondria. M1 macrophages mainly rely on glycolysis, whereas M2 macrophages exhibit high levels of oxidative phosphorylation. Recent studies have shown that the reprogramming of mitochondrial metabolism in macrophages, such as boosting oxidative phosphorylation and/or mitochondrial biogenesis might lead to macrophage class switching from M1 to M2 and could be of potential therapeutic benefit in the treatment of chronic inflammatory diseases.

Hydrogen sulfide (H_2S) is a small gaseous signaling molecule, which is partially responsible for the regulation of vascular tone. At high concentrations H_2S is toxic, while at low concentrations it can support cellular bioenergetics. It has been demonstrated, that H_2S derived from mitochondrial enzyme: 3-mercaptopyruvate sulfurtransferase (3-MST) may be an alternative source of electrons for oxidative phosphorylation and energy production. We are tempting to speculate that mitochondria – targeted H_2S could induce the metabolic reprogramming of mitochondrial metabolism and consequently macrophage polarization to M2. **Thus, the goal of our study is to comprehensively investigate the influence of mitochondria-targeted H_2S on the reprogramming of mitochondrial metabolism in macrophages in chronic inflammatory diseases: atherosclerosis and nonalcoholic fatty liver disease.** The experiments will be carried out *in vitro* using different cell lines as well as peritoneal macrophages, and *in vivo* using a mouse model of atherosclerosis – apoE-knockout mice and a mouse model of nonalcoholic fatty liver disease – high fat diet – induced obese mice. To investigate the influence of mitochondria-targeted H_2S on the reprogramming of macrophages we will use different methods: morphological, biochemical, molecular and proteomic.

We believe that our study may shed a new light on role of H_2S and mitochondrial metabolism in macrophage class switching as well as may broaden the knowledge on the pathogenesis of atherosclerosis and nonalcoholic fatty liver disease. Furthermore we believe that our research could help to develop a new pharmacological approach to induce macrophage polarization with its possible role in the treatment of chronic inflammatory diseases.