

The main goal of our project is to determine role of RNase called MCPIP1 (Monocyte Chemoattractant Protein-Induced Protein 1) in paracrine activation of endothelial cells.

MCPIP1 is one of the protein involved in a negative regulation of inflammation. MCPIP1 binds to mRNAs and digests it – in the similar way to ‘Pacman’ from the classic PC computer game. Such activity of MCPIP1 defines it as an enzyme called “endoribonuclease”. MCPIP1 shortens life of selected transcripts leading, as a result, to reduced protein amount of IL-1 β and IL-6 for example. Both of above-mentioned proteins are important in the development of inflammation.

Development of inflammation is tightly linked to the function of endothelial cells. Endothelium plays a pivotal role in maintaining homeostatic balance of the organism. In normal conditions it acts like a selective permeable barrier between organs, blood and immune cells. However, under pathological state, e.g. exaggerated inflammation, endothelium becomes activated or damaged what leads to its loss of function: i) increased expression of adhesion molecules, ii) enhanced permeability, iii) diminished production of NO, iv) migration of leukocytes to the surrounding tissue. In this project we want to test what impact will have proinflammatory activation of hepatocytes and leucocytes, related to Mccpip1 depletion in these cells. We hypothesize, that lack of Mccpip1 in hepatocytes and leukocytes of the myeloid lineage will lead to enhanced production of proinflammatory mediators by this cells. As a result, we will be able to demonstrate activation or damage of endothelium by Mccpip1 acting in a cells’ extrinsic way.

For analysis of Mccpip1 in activation of hepatocytes and myeloid leukocytes leading to altered paracrine stimulation of endothelium we will use genetically modified mice that do not have Mccpip1 protein in hepatocytes and in leukocytes of myeloid origin. Such mice will be kept in Animal House of our Faculty according to the regulations of Local Ethical Committee.

In our opinion, demonstration of Mccpip1 involvement in regulation of endothelial cell biology in a cells’ extrinsic way can contribute to the discovery of new medical therapies. Compounds that inhibit degradation of Mccpip1 might be used in the future for designing new drugs used in the treatment of chronic inflammation. Since Mccpip1 inhibits inflammation, its local activation should help to restore homeostasis unbalanced by unresolved or untamed inflammatory processes.