

Autophagy is a natural process of degradation of damaged organelles and redundant or altered macromolecules, and degradation products can be used to obtain energy or material to build new structures. It is believed that alteration of autophagy may play an important role in cancer, although the role of autophagy in carcinogenesis is ambiguous. Autophagy prevents the formation of tumors by removing of redundant, damaged and harmful cellular elements. On the other hand, in advanced cancers exposed to nutrient deficiencies, it promotes their survival and growth. The precise identification of the mechanisms underlying the autophagy process and its role in cancer is very important for the design of new anticancer therapies. Recent studies indicate that epigenetic factors that influence gene expression through histone chemical modifications may play an important role in the regulation of autophagy process. One of the important epigenetic regulators is the PRC1 complex, which is responsible for inhibiting the expression of many genes by modifying histone H2A. **The aim of the project is to determine the role of BMI-1 and RING proteins, components of the PRC1 complex in autophagy in endometrial and breast cancer cells. In addition, the antitumor efficacy of PRC1 complex inhibitors in combination with other autophagy modulators will be investigated.** Planned research will be carried out using four cell lines. Control cells and cells with inhibited BMI-1 and RING1 expression / activity by RNA interference or chemical inhibitors will be grown under optimal for growth as well as starvation conditions. In these cells expression of genes related to the autophagy will be determined at mRNA and protein levels, and the level of H2A histone modification in the promoter regions of these genes will be checked. The intensity of the autophagy process will be examined via fluorescent confocal microscopy using the presence of the p62 receptor conjugated to the GFP protein and the LysoTracker Red lysosomal fluorescent dye. Suppression of PRC1 complex activity along with autophagy modulators will be checked using the proliferation test as well as by flow cytometry. In addition, the influence of modulators (inducers and inhibitors) of autophagy on the mechanism of apoptosis and necroptosis will be examined by the detection of markers characteristic for these processes. The research planned in this project will help to understand the role of the PRC1 complex in the autophagy process, which in the future may contribute to the development of more effective strategies for anticancer therapies.