According to World Health Organization (WHO) reports cancer remains a major cause of deaths worldwide with estimated in 2022 over 20 mln new case and 9.7 mln deaths. Extensive research on molecular mechanisms of tumor growth, differentiation, invasion, and metastasis constantly brings novel diagnostic and therapeutic strategies. However, current knowledge is still insufficient to prevent cancer-related mortality. It is vital to understand the biology of cells in tumor microenvironment in more details to improve effectiveness of new therapies. Learning about relevant factors regulating anti-cancer immune response, angiogenesis, and signaling events induced through cellular receptors controlling carcinogenesis are key for identification of specific diagnostic targets that will guarantee better outcome of the treatment.

One of the factors that impact tumor immune status are advanced glycation end-products (AGEs), associated with oxidative stress, chronic inflammation, angiogenesis, and immune suppression. This is a very heterogeneous group of products formed during nonenzymatic reaction of biomolecules containing free amine groups with reducing sugars or aldehydes. In the previous research our group have identified the novel AGE called MAGE, formed from melibiose. We have established the immunomodulatory role of MAGE *in vitro* on immune cells. However, the biological role of MAGE is still not fully understood and needs further research. Our goal in this project is to study activity of MAGE accumulating in tumor environment by identification of the molecular pathways and engaging receptors that regulate cellular response, along with paving a way to future diagnostic and therapeutic strategies using novel tools targeting MAGE.

This project includes 3 specific aims that will answer the questions on MAGE role in cancer microenvironment by studying:

1) interaction with extracellular receptors – using confocal microscopy we will test MAGE interaction with the common AGE receptors including AGEs-specific receptor RAGE, Galectin-3, and elastin-laminin receptor ELR that are expressed on cancer, endothelial, as well as on immune cells; the synthetic MAGE product will be used in a labeled form or loaded on multimodal biocompatible nanoparticles developed for this purpose;

2) cellular effects – toxic effects, metastatic activity and signaling pathways will be tested on cancer while MAGE impact on angiogenesis will be tested on endothelial cells using appropriate model cell lines and molecular functional assays in connection with the biochemical binding assays;

3) generation of nanoparticles loaded with MAGE, fluorescent dye, and anti-cancer drugs to test MAGE-driven imaging and therapeutics delivery approach – novel multifunctional nanoparticles will be generated and characterized to function as probes and carrier of the targeted drugs based on affinity to MAGE that accumulate in tumor microenvironment.

The results of our project will deliver new insight about MAGE within tumor microenvironment and will answer the question on the role of this unusual AGE in cancer biology, especially will inform about activation of cellular signaling, metastatic and angiogenic potential of this novel cancer factor. Finally, it will bring potential tools for diagnostic or therapeutic strategies based on the developed analytical assay or multifunctional nanoparticles, respectively.