Research Project objectives

The goal of the project is to learn about the role of different glycation products in modulation of the cancer microenvironment.
Glycation is the non-enzymatic process that generates heterogeneous group of adducts (AGEs) from the reaction between carbohydrates and proteins. Some of the structures have been described, however majority remains unknown, so do they properties and biological effects. Recently we have discovered the unique AGE (called MAGE) with different structural properties from the known products. The developed specific anti-MAGE antibodies did not react with the conventional AGEs. The preliminary data have shown that anti-MAGE antibody recognized products present in some cancer tissue. Also, macrophages cultured in presence of different AGEs, including MAGE expressed different panel of cytokines, thus we hypothesize that different AGEs display diverse biological properties and might modulate phenotype of the cells within cancer microenvironment. We plan to investigate the involvement of different AGEs in cancer disease progression by studying cellular effects related to AGE/RAGE interaction and activation of the anti-cancer immune defense.

Research project methodology

Aim 1. Identification of AGEs in the cancer microenvironment

Task 1. Analysis of cancer tissues for novel AGEs and protein modifications by kynurenines by immunohistochemistry and MALDI-TOF mass spectrometry in cancer tissue from patients and blood samples

Task 2. Comparison of cancer and normal cells for the accumulation of proteins modified by MAGE and kynurenines. The in vitro cultured cells from endometrial cancer and control tissue will be analyzed in MALDI-TOF for MAGE and kynurenine modified proteins

Aim 2. Studying the pro-cancerous effect of different AGE classes on the cancer microenvironment cells

Task 3. Determination of macrophage cytokine production induced by selected AGEs. The model THP1 cells treated with different AGEs will be analyzed for cytokine panel using multiplex method

Task 4. Determination of changes in RAGE expression on macrophage and the in vitro cultured cancer cells treated with selected AGEs. MDA-MB-231 and SK-BR3 cells treated with different AGEs will be analyzed in WB, QPCR for RAGE expression.

Aim 3. Studying the role of different AGEs in modulation of the kynurenine pathway

Task 5. Determination of kynurenine pathway activation in cancer cells upon treatment with selected AGEs. The model cancer cells treated with AGEs will tested for IDO expression (WB, QPCR) and activity as well as for accumulation of kynurenines by HPLC.

Task 6. Effect of secreted by macrophages mediators (as the result of AGEs treatment) on kynurenine pathway metabolism in cancer cells. The kynurenine pathway activation in MDA-MB-231 and SK-BR3 cells treated with conditioned medium from the THP1 cells (cultured with different AGEs) will be tested by WB, QPCR and HPLC.

Expected impact of the research project on development of science

Our project will bring answer to how different AGEs influence cancer progression. The presence of novel AGEs in different cancers will be studied. The new data on AGEs role in modulation of the cancer cells activation and immune response will be generated. We will describe the role of kynurenine pathway in this process.