DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Breast cancer, the most common cancer type in women, is still considered a clinical challenge as it often comes back after treatment and results in high level of morbidity. Therefore, new therapies need to be considered. However, breast cancer is a complex disease, which needs to be classed into different types, before decision on patient's treatment, based not only on clinical information but often also on a presence of specific proteins, mainly receptors for steroid hormones, estrogen and progesterone, as well HER2 protein. Such diversity in breast cancer types results in different treatment outcomes, and should be taken under consideration when new, potential therapies are considered.

One of emerging targets for therapy in cancer is CD73 (ecto-5'-nucleotidase), a cell surface protein, with a dual activity as cell adhesion molecule and an enzyme producing extracellular adenosine. Its inhibition in animal models was demonstrated to inhibit tumor growth of many cancer types as well their dissemination as metastases. In clinical patients, high amount of CD73 in cancer correlated with their poor overall survival and a worse outcome for many cancer types. However, for breast cancer, the results were controversial, and CD73 dependence on other aspects, e.g., cancer type, was suggested. **Therefore, in depth analysis of CD73 role in breast cancer is needed. First, to analyze CD73 multi-faceted function in breast cancer and its potential correlation with a specific tumor type. Second, to find a reason for a lack of consistency between the data obtained from animal models and from clinical samples to asses, which functions of CD73 in breast cancer development could possibly limit its usefulness in the anti-cancer therapy.**

However, for successful translation of a new data from mouse model to the clinic, animal model should reflect similar diversity as well develop similarly as human disease. This could be obtained by stimulation of animals with a synthetic analogue of progesterone, steroid hormone important for breast development and lactation, and later with chemical carcinogen to induce cancer formation in mammary gland. Such tumors will represent different types of breast cancer. The use of mice lacking CD73 due to the genetic modification for breast cancer induction will allow to analyze CD73 role in changes in breast cancer development before the growth of tumor and at the stage of tumor growth and late metastasis formation. The changes in tumors growth rate, amount of tumors, as well how quickly they developed and in how many animals will be analyzed and correlated with cancer type. Breast cancer classification will be assessed by veterinary pathologist using standard staining of tumor tissues with histological stains as well by assessment of ER, PR and HER2 presence. CD73 was demonstrated to stimulate formation of blood vessels in tumors, change the amount of immune cells present in tumor, including macrophages as well pro- and anti-tumor lymphocytes T. It was also suggested, that CD take part in processes of important for development of metastatic phenotype by breast cancer, involving the change from cells with epithelial to mesenchymal phenotype, as well in development of cancer resistance to chemotherapy due to the presence of cancer stem cells. The presence of specific markers, proteins characteristic for these processes will be analyzed in histological slides of cancer tissues using specific antibodies. Also a changes in RNA production for all active genes will be analyzed both in mammary gland and tumor tissues. Changes in immune system will be analyzed in lungs and spleen through analysis of a presence of anti- and pro-tumor lymphocytes T. The metastatic spread of breast cancer cells and the presence of breast cancer stem cells will be analyzed in blood, bone marrow and lungs at both stages of tumor development to check for their early and late dissemination.

Obtained results will allow to assess CD73 role in breast cancer development both at its early stage, before tumor formation and later, when solid tumor is formed and late metastases are developing. It will also allow to asses its role in aspects important for cancer dissemination and resistance to chemotherapy, and as a result, define its potential as a therapeutic target in breast cancer. It will also allow to determine, if there exist any correlation between CD73 role in breast cancer and its type according to the presence of ER, PR and HER2.