Description for the general public

Each cell has to take up several compounds and release certain metabolites. This process of communication with cellular environment occurs thanks to the activity of transporting proteins localized in the cell membrane. Cancer cells, due to their fast growth and proliferation have a high demand for nutrients and are known for an augmented level and activity of certain transporting proteins, in particular those transporting glucose and amino acids. This project is focused on one of such transporters – SLC6A14, transporting to the cell all but acidic amino acids. Presence of SLC6A14 has been detected in malicious breast cancer cell lines with a high level of estrogen receptor α. Cell membrane transporters are incorporated in the membrane during protein synthesis and delivered in vesicles to the plasma membrane. Before reaching the cell surface they undergo several modifications, due to activity of other proteins. Transporting proteins have to acquire a properly folded structure – a process controlled by so-called chaperone proteins. In this project we assume that knowledge of the mechanism leading SLC6A14 to the cell surface can allow modulation of transporting activity and to decrease the amount of amino acids delivered to the cancer cell. The main aim is an attempt to arrest transporter trafficking to the plasma membrane by chaperone proteins activity modulation.

SLC6A14 has been a subject of our research for many years. In our previous studies we observed interaction of SLC6A14 with several chaperone proteins, in particular those known to be present at higher amount in cancer cells. Therefore, we are going to study the effect of chaperons on SLC6A14 trafficking to the cell surface as well as to verify, how this process could be affected by inhibition of chaperone proteins with compounds being under clinical trials. The experiments will be performed in a model system, after expressing SLC6A14 coding gene in human cells (HEK293), as well as in human breast cancer cell lines known for a high level of SLC6A14. We are also going to check, if modulation of SLC6A14 presence in plasma membrane with a simultaneous treatment with anti-estrogens results in a synergistic effect, what could be important for more and more frequently applied combination therapies. A possibility of arresting SLC6A14 within the cell, resulting in a drastic diminution of the transporter in plasma membrane, should lead to decrease in amino acid amount taken-up by cancer cells, leading to their starvation.