Description for the general public

Cancer cells are characterized by fast growth and proliferation, the processes demanding a high supply of nutrients. Uptake and exchange of such compounds is possible due to the activity of transmembrane proteins called transporters. This project is focused on two plasma membrane proteins (SLC22A5 and SLC6A14) transporting carnitine – a compound necessary for oxidation of fatty acids. This energy-delivering process, beside glucose metabolism, plays an important role in quickly proliferating cancer cells. Interestingly, both carnitine transporters are present in estrogen receptor-positive breast cancer cells.

As all plasma membrane proteins, both carnitine transporters are inserted during their synthesis to the membrane of endoplasmic reticulum (ER) and reach the cell surface in the process of vesicles budding and fusion. The first step – transport between ER and Golgi apparatus demands formation of a vesicle coat, so called coatomer II (COPII). Among COPII components four isoforms of SEC24 protein are responsible for recognition of cargo (in our case the carnitine transporter). Two of these isoforms, SEC24C and SEC24D were shown previously to be phosphorylated by a protein kinase AKT, known to be hiperactivated in cancer and to control cell death and survival, cell metabolism, cell growth and division.

We detected an exclusive interaction of SLC6A14 with SEC24C, while identification of SLC22A5 – recognizing SEC24 isoform is a part of this study. Since the role of SEC24 phosphorylation in vesicle trafficking is not known, the main aim is to find-out how modulation of AKT activity leading to differences in SEC24 phosphorylation, can influence surface presence of both carnitine transporters. We will apply AKT inhibitors and activators, AKT will be as well activated by growth factors, e.g. Insulin-like growth factor I. The experiments will be performed in a model system, after expression of the genes coding both studied transporters in human HEK293 cells. They will be performed also in human breast cancer lines. The far-reaching goal is to find conditions resulting in retardation of both transporters within the cell, what, in consequence, should diminish the uptake of carnitine, leading to a decrease in cancer cell viability.