

## **The role of the ABCA1 protein in cholesterol metabolism and the organization of key cell membrane structures in the process of carcinogenesis**

The aim of the project is to determine the role of the cholesterol transporter (ABCA1 protein) in the organization of membranes lipid structures in the development of the cancer process. The study will focus on skin cancer - melanoma, one of the most common skin cancer characterized by a high rate of proliferation and invasion. It is often accompanied by chemoresistance, so the prognosis for patients with this type of cancer remains poor. Melanoma is a significant global health problem with high morbidity and mortality with only a few drugs, often in combination with surgery and radiotherapy, as treatment options.

The latest literature data indicate significant changes in the content of cholesterol and other lipids in the course of neoplastic processes. Changes in cholesterol levels can affect the disruption of membrane structure, which can change cellular communication and trigger the cancer process. One of the proteins regulating the amount of cholesterol in cells is the ABCA1 transporter, which plays an important role in removing cholesterol from cells.

Our preliminary experiments indicate that metastatic melanoma cell lines are characterized by high expression of cholesterol transporter, and inhibition of its activity significantly reduces cell proliferation, migration and invasion (*in vitro* and *in vivo* analyses).

We plan to use probucol, a cholesterol transporter inhibitor, and characterize melanoma cells using 3D organoid cultures. We also want to assess the effect of a high-cholesterol diet on melanoma cell growth in the *Danio reiro* model, and then examine cholesterol levels in the fish and assess lipid-related proteins. We will also check cholesterol transporter activity in the context of key cellular communication pathways.

We believe that our extensive research will allow us to better understand the impact of the cholesterol transporter on the organization of the cell membrane and modulation of cancer cell growth and proliferation.