Melanoma is one of the most malignant types of skin cancer. Currently, the treatment of this cancer mainly involves immunotherapies and targeted therapies. Although more and more advanced forms of therapy are being used, drug resistance remains a significant problem that limits their effectiveness. One of the factors influencing the development of drug resistance in melanoma patients is the tumor microenvironment. The cancer niche consists not only of malignant cells, but also of accompanying cells among others fibroblasts, adipocytes and keratinocytes that, under the influence of melanoma, change from normal cells to cancer-related cells that promote progression.

Taking into account the significant impact that the melanoma microenvironment has on cancer progression and the development of drug resistance in patients, it was decided to investigate the interactions between cancer cells and cancer-associated cells. For this purpose, the modifications occurring in cancer-associated cells under the influence of melanoma cells and the changes in the biology of cancer cells cultured in the presence of cancer-associated cells were characterized. Two research models were selected for the study, one of them was the culture of normal cells with conditioned medium collected from melanoma cell culture, the other was based on the co-culture of normal cells with cancer cells using Transwell inserts. A number of analyzes were performed, mainly focusing on the study of features influencing melanoma progression, such as proteolysis, migration, invasion, activation of signaling pathways, and proliferation.

We have established that in all examined melanoma-associated cells occur changes in proteolytic activity under influence of cancer cells. The main role in this process within the melanoma microenvironment seems to be played by keratinocytes, which have so far been assigned the function of inhibiting the development of this cancer rather than supporting its progression. Moreover, both activated fibroblasts and keratinocytes were characterized by increased migration and invasion compared to control cells. Taking into account the fact that cancer cells can move together with accompanying cells as a result of the so-called collective migration, it can be assumed that the intensification of these processes in cancer-associated cells probably results in the induction of these functions in melanoma cells. Additionally, changes in the morphology of adipocytes due to co-culture with cancer cells were demonstrated. As a result of culture with melanoma cells, fat cells from rounded, with a high lipid content, became spindle-shaped, resembling fibroblasts in shape with a much smaller number and surface area of lipid drops. Moreover, CAAs cells were characterized by increased production of proteins specific for fibroblasts. In turn, in melanoma cells, under the influence of CAFs and

CAKs, epithelial-mesenchymal transition is induced, which may contribute to the formation of metastases. Additionally, culturing adipocytes with melanoma cells leads to the accumulation of lipids in cancer cells.

To sum up, it has been shown that both fibroblasts, adipocytes and keratinocytes undergo significant changes under the influence of melanoma cells, which may contribute to the progression of the disease. Moreover, melanoma cells cultured in the presence of the examined cellular elements of the tumor niche showed metabolic changes, induction of epithelial-mesenchymal transition and, in the case of co-culture with adipocytes, lipid accumulation. Understanding the interactions between cancer cells and the melanoma microenvironment may in the future be the basis for developing a therapy targeting both cancer cells and those promoting disease progression.