Metastatic melanoma (MM) is one of the most malignant skin cancers that responds poorly to treatment despite significant advances in targeted therapies and immunotherapy. The 5-year survival rate for patients diagnosed with stage III melanoma is about 68%, while it drops to only about 30% in stage IV, so new therapeutic approaches are being investigated. Our research focuses on receptor-interacting protein kinase (RIPK4), which regulates the NFκB, Wnt/β-catenin signaling pathways important for melanoma cell survival. As our previous studies have shown, that RIPK4 level is significantly increased in various melanoma cells compared to normal melanocytes. Interestingly, diminishing of RIPK4 expression inhibits melanoma cell proliferation and invasive potential *in vitro* by impairing signal transduction through the NFκB and Wnt/β-catenin pathways. However, data illustrating the function of this kinase in melanoma development and metastasis under *in vivo* conditions are lacking. Therefore, in the present project, we plan to investigate whether RIPK4 affects metabolic reprogramming, adhesion, angiogenesis and metastasis because, as indicated by many scientists, these processes are closely related.

In our study, we want to use spheroids, which better mimic *in vivo* conditions due to the three-dimensionality of the tumors and the natural spatial intercellular contacts, the availability of various factors, including oxygen, which is compromised in the 2D culture model. We will use two *in vivo* models to study vascularization: the chicken embryo model and the NOD/SCID mouse metastatic model, in which cells will be injected into the interlobar fat pad, as blood vessel formation in this model can be monitored by ultrasound. Additionally, the mouse model will be used to study metastasis and the tumor microenvironment, including hypoxia and redox status.

We would like to use the results obtained as a basis for further research into the therapeutic potential of RIPK4 in melanoma therapy and publish them in international journals.