The aim of this project is to estimate the character of interaction between gelsolin, an actin cytoskeleton protein and LamR or ILK. We want also to check, how these interactions influence adhesion to laminin of human melanocytes and melanoma cells. Additionally, we are interested in elucidation, if gelsolin interactions with LamR and ILK are important for migration and invasion of studied cells, because alterations in adhesion abilities influence invasion potential of cells.

Normal and tumor cells have **the ability to transmigrate within tissues**. An extremely important issue is a full understanding of processes, which enable tumor cells to move and thus to form metastases. Cytoskeletal proteins can be divided into three groups: microfilaments, intermediate filamenst and microtubules. Microtubules are mainly responsible for intracellular organelle transport and correct cell division. Intermediate filaments are responsible for cell's shape and microfilaments for cell's motility. These last structures are built from actin, which has an unique ability to form polymers. Over 200 proteins directly control formation, fragmentation and depolymerization of actin filaments. These dynamic changes are responsible among other processes for cell's movement. **Gelsolin** is one of actin binding proteins. It severs, caps free ends of microfilaments and under certain circumstances nucleates actin monomers. Apart from these canonical functions gelsolin plays important roles in other processes such as apoptosis or steroid hormones transport to the cel nucleus. Several published data suggest that gelsolin is a player in pathological conditions e.g. Alzheimer disease, heart conditions or tumors emerging from different types of tissues.

Gelsolin is also actively involved in cells' adhesion, although the mechanism of this action is still unknown. It was shown that in leucocytes gelsolin is responsible for localization and activity of β1 integrin, a protein taking part in cells' adhesion.

Our previous published results showed that **gelsolin interacts with non-integrin laminin receptor** (**LamR** aka 37LRP, 67LR, Rpsa) and **integrin-linked kinase** (**ILK**). These proteins are involved in cells' adhesion.

LamR is observed in cell nucleus, cytoplasm and on the surface of a cell. Increased amount of this protein is observed in several tumors and it influences invasion and metastasis of tumor cells. One of the most important proteins responsible for adhesion to laminin and located on the cell's surface are integrins. As it was already mentioned, LamR is a non-integrin laminin receptor, but it was also shown that it supports binding of laminin to integrins. **ILK** on the other hand intracellularly binds integrins within focal adhesion sites.

We want to check, what are the mutual interactions between gelsolin and LamR or ILK, because all these proteins are important for adhesion to laminin. Our studies will be conducted on human melanocytes and melanoma cells (*in vitro* model) and chicken embryos (*in vivo* model). We want to estimate, if these interactions are important for migration and invasion of tested cells. We will also check, which gelsolin isoform (there are at least three) forms complexes with LamR and ILK and modulates adhesion and invasion of tested cells.

We plan following tasks.

1. We will produce recombinant proteins to perform part of the experiments.
2. We will perform *in vitro* experiments in order to check, how gelsolin and its complexes with LamR and ILK influence adhesion and invasion of melanocytes and melanoma cells.
3. We will check which alpha integrin/s forms complex with gelsolin through ILK.
4. We will perform *in vivo* experiments in order to check, how gelsolin and its complexes with LamR influence adhesion to laminin and invasion of chicken embryonic cells.