

The peripheral nervous system is responsible for transferring information between the central nervous system and individual organs and one of its parts are spinal nerves coming out of the spinal cord. The process of peripheral nervous system development begins quite early during embryonic development. During the first stages, the so-called neural crest cells detach from neural tube. Then they migrate within designated pathways to spread in the developing organism. Then they stop to migrate and form structures called **dorsal root ganglia (DRG)**. They are clusters of nerve cell bodies (somas) that contain all needed cell organelles. Since then, nerve cells do not migrate further, but they only produce protrusions called **neurites**. Some of them are oriented towards the spinal cord, while the others extend towards the target organ. The extending neurites are accompanied by non-neuronal helper cells called **Schwann cell precursors**. They support neurites and at the same time they use them as a substrate for movement. The role of mature Schwann cells is neuron enveloping with myelin, which facilitates the transmission of signals and plays a role in neuronal regeneration. Schwann cell precursors are also a source of other types cells, e.g. endocrine cells, autonomic neurons or melanocytes, which are pigment cells.

For the proper development of the organism, cells of different types must be able to migrate to specific places in the body to build specialized tissues and organs. For this purpose, the cells need the contact with the substratum, what is called adhesion. Substrates for the cells are proteins of extracellular environment (so-called extracellular matrix). One of them is **laminin**, which at this stage of development of the peripheral nervous system has a permissive effect on the cell migration and neurites elongation. The response of cells to signals from the extracellular environment is possible due to specific receptors for these proteins located on the surface of a cell. Receptors are transmitters of outside-inside information, thus stimulating various cellular processes, e.g. migration, adhesion or cell division (proliferation). Specific receptors for laminins are integrins and non-integrin receptors. **LamR is one of the receptors for laminin that transmits signals independently of integrins.** LamR is a protein found both in the cell nucleus, where it participates in the control of proliferation, as well as in the cell membrane, where it plays a role in cell adhesion and migration.

Our previous research on LamR show that LamR is present in nerve cell bodies and in Schwann cell precursors. Although it is not present in neurites and is not secreted outside the cell, blocking its function disrupts the proper development of neurites and reduces the number of precursors of Schwann cells migrating in the presence of neurites. At this stage, however, we do not know the mechanisms responsible for these changes. The project assumes the continuation of research on LamR in the context of the development of the peripheral nervous system, and thus determining the mechanisms responsible for diminished neurite outgrowth after blocking the function of LamR.

The peripheral system development is similar in human and chicken, therefore, a research model of the project will be chicken embryos, which DRG necessary for further analysis will be isolated from.

The aims of research are estimation whether there are changes in the process of DRG cells adhesion after blocking LamR and verification whether the diminished neurite outgrowth after blocking LamR is associated with soma or neurites. Moreover, we will determine whether the reduced DRG neurites outgrowth after blocking the LamR function may be the result of disruptions in the direct interaction between LamR and laminin, or indirect, i.e. the impact on the interaction between laminin and integrins, the impact on the interaction between neurites and Schwann cell precursors, or on other pathways related to neurite outgrowth. In addition, we will focus on estimation of the direct effect of LamR on Schwann cell precursors, and to be more specific - on migration, adhesion and proliferation.

Understanding the mechanisms by which LamR affects the development of the peripheral nervous system at the level of DRG development is crucial in the context of development of new therapies based on this receptor properties. This knowledge could help to design blocking or activating neurites elongation therapies depending on the type of developmental pathologies or peripheral nervous system diseases. **Currently, attempts are being made to utilize the biological properties of LamR in the treatment of neurodegenerative diseases (e.g. Alzheimer's disease), nervous tissue tumors e.g. glioblastoma and viral, bacterial and prion infections.** This shows high therapeutic potential of the LamR receptor, what is a huge motivation to deepen the knowledge about it.