

## **The influence of ibuprofen on immunomodulatory and regenerative potential of human bone marrow-derived mesenchymal stromal cells**

Damage of tissues activates natural repair mechanisms in which many types of cells in our body are involved. Among them, mesenchymal stromal cells (MSCs) play an important role. MSCs are stem cells, therefore they can mature and transform into cells of various tissues, for example cartilage, bone or fat. Their main function is to create a special environment for the blood cells precursors in the bone marrow. These cells also have the ability to shape the immune response both through direct contact with immune cells and as a result of secretion of various factors. The ongoing inflammation is manifested by redness, swelling and pain of the affected site, which can be associated with a major discomfort to the patient. Standard therapy is based on non-steroidal anti-inflammatory drugs (NSAIDs), of which ibuprofen is the most commonly used. These drugs are known for their anti-inflammatory and analgesic properties, therefore, recommendations for peri-operative pain treatment indicate NSAIDs as appropriate pharmacotherapy both before and after the procedure. However, it has been proven that NSAIDs impair the natural tissue regeneration process, which can be crucial in the treatment of various types of injuries. This is probably due to an interruption of signaling pathways both at the whole organism level and locally - at the target site (e.g. in muscles or tendons). The exact mechanisms are yet not fully understood, hence our assumption that NSAIDs may have a negative effect on the physiological regenerative mechanisms, i.e. by affecting MSC cells. We assume that ibuprofen significantly modifies the ability of MSC to shape immunological processes by changing the level of gene expression and / or changing the profile of proteins secreted by these cells into the environment. The main objective of the project is to assess the effect of ibuprofen on MSC cells in terms of their role in regenerative processes.

The experiments will be conducted using human MSCs derived from the bone marrow. The effect of ibuprofen on MSCs will be analyzed by comparing MSCs cultured in the presence of ibuprofen (test samples) for controls (MSC cultured under standard conditions). To this end, a series of tests will be carried out, which will allow to identify genes and proteins which expression changes under the influence of the drug. There will also be an experiment performed, in which MSC cells will be grown together with macrophages (cells of the immune system responsible for "eating" microorganisms that have penetrated into our body, as well as those involved in regeneration processes). Thanks to this, it will be possible to determine whether and how ibuprofen affects the interaction between both cell populations.

MSC cells derived from the bone marrow have been very popular among scientists for years. Despite the ever-growing number of publications with the participation of the MSC, this subject still leaves much confusion. The study of the effect of ibuprofen on the properties of MSC cells will allow to better explain the natural mechanisms of shaping the immune response and to define in detail the role of MSC in these processes. Providing information on the impact of ibuprofen on the stem cells of our body and on the functioning of the immune system is also useful due to the growing, uncontrolled consumption of NSAIDs around the world. Finding the answers to the questions raised in the project will undoubtedly contribute to the broadening of knowledge in basic sciences, such as cell biology or immunology. In the future, the presented results may also have a clinical relevance, both regarding the guidelines for the use of ibuprofen, as well as cell therapy with the use of MSC.