STRESZCZENIE ANGLOJĘZYCZNE

The implementation of mesenchymal stem cell-based (MSCs) therapy seems to be a promising strategy in suboptimally controlled chronic inflammatory diseases of the respiratory system, inducing asthma. Previous preclinical studies have confirmed, that MSC may limit airway inflammation, however, the mechanism underlying those changes remains elusive. Insufficient knowledge regarding MSC-mediated processes of airway inflammation regulation, as well as their stability and long-term effect, restrict optimization of effective stem cell-based therapy.

Therefore, here I aimed to investigate the influence of adipose tissue-derived MSCs on 1) non-inflamed lung tissue and 2) airway inflammation development in a house dust mite (HDM)-induced experimental asthma model.

MSCs were isolated from adipose tissue collected from patients after bariatric surgery. Their characteristic phenotype, multipotency, and immunosuppressive properties *in vitro* were confirmed prior to mice model implementation. Female, 6-8 weeks old, C57BL6/cmdb mice were used in the experiment. To assess the short- and long-term effects of MSC on non-inflamed lung tissue, two groups treated only with cells were included. To induce airway inflammation, mice were challenged with 10μg HDM extract for 5 days each of two weeks. Moreover, to investigate the short- and long-term effects of MSCs administration on airway inflammation, two mice groups were administrated with cells on the 13^{th} and 6^{th} days of the experiment, respectively. Mice treated with saline were included as a control. All animals were sacrificed on the 15^{th} day of the experiment. Histopathology staining, epithelial barrier integrity, frequency of T cell effectors, transcriptomic profile changes, and cytokines levels in BAL were assessed.

MSCs administration to non-inflamed lung tissue did not cause immune cell infiltration and mucus overproduction. However, I found an increase in the frequency of IFN-producing T

cells, while IL-4, IL-17, and IL-10 positive T cell populations were not changed. Moreover, I found a decrease in epithelial tight junction proteins expression, namely Occludin and Claudin 3, while ZO-1 was not affected. Transcriptomic analysis revealed the changes in the expression of genes related to macrophage activation, phagocytosis, and oxidative stress. Moreover, comparative transcriptome analysis showed that the expression of most genes associated with immune response is decreased in the long-term model in comparison to the short-term.

On the other hand, the administration of MSCs in an experimental asthma model leads to the limitation of airway inflammation and mucus production. Unfortunately, I did not observe substantial changes in the frequency of T cell effectors and T cell-related cytokines. However, I noted differences in transcriptomic profiles in both models. Transcriptomic analysis using Metacore revelated the downregulation in signaling pathways related to CCL2, S1P3, and CXCR4. More specifically, most of the differentially regulated genes in MSC-treated groups were clustered in terms related to chemotaxis, lymphocyte proliferation, and leukocyte migration.

In summary, the results indicate that MSC may be considered a safe strategy for limiting airway inflammation via regulation of chemotaxis, migration, and recruitment of immune cells. Moreover, our data suggest that MSC in steady state conditions undergo apoptosis and are cleared by host phagocytes.