

## Streszczenie w języku angielskim

Adipose-derived stem cells (ASC) have a great potential for use in regenerative medicine due to their ability to self-renew, differentiate, and the secretion of many biomolecules with pro-regenerative properties. However, the use of mesenchymal stem cells (MSC) in cell therapy encounters certain limitations, such as low cell survival after transplantation or problems with directing cells toward desired stem cell fate, which reduces the effectiveness of the treatment. Therefore, new approaches to MSC therapy are considered to increase its effectiveness. One of the proposed solutions by the researchers is preconditioning cells with biophysical factors such as low-frequency electromagnetic fields (LF-EMF).

This doctoral dissertation aimed to assess the potential and possibilities of using MSC preconditioning with LF-EMF as a new approach to stem cell-based both in the approach referred to as stem cell-based therapy and stem cell-free therapy. In the presented doctoral thesis, the analysis of the biological response of ASC to LF-EMF with a frequency 50 Hz and magnetic induction 1.5 mT was used, taking into account the importance of understanding the mechanisms of LF-EMF action on ASC as a basis for directing stem cell fate, which determines the effectiveness of stem cell therapy.

The results showed that LF-EMF (50 Hz; 1.5 mT) statistically significantly increases Fibroblast Growth Factor 2 (FGF-2) secretion by ASC after 24 and 48 hours. Moreover, LF-EMF increased secretion of Leukemia Inhibitory Factor (LIF), Placental Growth Factor (PIGF), Stem Cell Factor (SCF), Hepatocyte Growth Factor (HGF), Vascular Endothelial Growth Factor (VEGF), Brain-Derived Neurotrophic Factor (BDNF), Platelet-Derived Growth Factor (PDGF). Additionally, tested LF-EMF increased ASC's proliferative and mitochondrial potential. Furthermore, LF-EMF (50 Hz; 1.5 mT) affected the gene expression related to ASC stemness such as *NANOG* ( $p < 0,05$ ), *OCT4*, *SOX2*, as well as differentiation such as *SOX9* ( $p < 0,05$ ), *RUNX2*, *TUJ-1* ( $p < 0,05$ ). Moreover, ASC was characterized by a statistically significant increase in N6-methyladenosine (m6A) contents in RNA after 24 hours, indicating changes at the epitranscriptomic level induced by LF-EMF preconditioning.

Low-frequency electromagnetic fields may be an effective tool to enhance the pro-regenerative properties of ASC cells. LF-EMF increases the proliferative potential and differentiation capacity of ASCs and modulates their secretome consisting of many biomolecules with immunomodulatory, angiogenic, neurotrophic, and re-epithelializing properties. LF-EMF may influence the stem cells' fate and modulate their regenerative abilities by modifying RNA. However, these changes depend on LF-EMF parameters, exposure time, and the source of MSC isolation, therefore it is important to select these parameters

appropriately to prepare advanced therapy medicinal products to achieve the maximum therapeutic effect while minimizing the side effects of treatment.