Abstract

Nanomaterials (NMs) are widely used in medicine for their antimicrobial properties. They are part of antibacterial coatings, creams, pharmaceutical vehicles or additives in drugs and other medical products. However, the impact of NMs on human organism is still not completely established. Nanoparticles (NPs) penetrate the cell membrane and enter to intracellular compartments including the nuclei. Different types of NPs could have various side effects on cell functions. These side effects include the damage of stem cells (SCs) or immune cells lead to slower regeneration and impaired wound healing. Therefore, the simultaneous application of NPs during SC therapy could decrease the therapeutic abilities of SCs. One type of SCs tested in clinical therapies nowadays are mesenchymal stem cells (MSCs). Therefore, we studied the impact of metal NPs (i.e. silver, copper oxide, zinc oxide and titanium dioxide) on characteristics and functional properties of mouse MSCs.

Additionally, the effect of NPs on the expression of phenotypic markers, metabolic activity, differentiation potential, expression of genes for immunoregulatory molecules and on production of cytokines and growth factors was analyzed. We found that all types of tested NPs had a negative impact on the activity of MSCs and thus could alter tissue regeneration.

Furthermore, the impact of NPs on the production of reactive oxygen species (ROS), lipid peroxidation, DNA fragmentation and oxidation, the frequency of micronuclei, apoptosis and cell cycle was investigated. The results showed that tested NPs potentiated a lot of changes in MSC function what could lead to impair tissue healing.

Finally, it was shown that immunomodulatory effects of transplanted MSCs are mediated by macrophage phagocytosis. Therefore, we tested the impact of NPs on the ability of MSCs to stimulate production of cytokines and growth factors by macrophages. We showed that macrophages cultured together with heat-inactivated MSCs treated with NPs produced comparable amounts of cytokines and growth factors as macrophages cultured together with heat-inactivated MSCs without NP treatment. These results suggest that NPs could inhibit therapeutic properties of MSCs by the direct negative impact on their secretory activity. However, NPs did not affect the ability of MSCs to stimulate production of cytokines and growth factors by macrophages.

In summary, results presented in this thesis show that individual types of NPs influence the functional and characteristic properties of MSC. Therefore, NPs should be used with caution during SC therapy.