

DEVELOPMENT OF TECHNOLOGY AND STUDY OF OPTIMIZED SECRETED PRODUCTS OF STEM CELLS FOR COLLATEROGENESIS

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Introduction. Cell therapy using stem cells is a promising strategy for the treatment of ischemic diseases, nevertheless low viability of implanted cells, is one of the main problems limiting stem cell therapy. In addition, there is a risk of proliferation of the transformed cells in mesenchymal stem cells carrying properties of cancer stem cells. Using conditioned media from stem cells instead of stem cell themselves avoids the risks that may arise with the direct use of stem cells. Conditioned media from various stem cells contains a different number of cytokines and growth factors, necessary for the natural process of new vessel formation.

Methodology. The objective of current proposal is to fabricate biodegradable polymer based micro- and nanoparticles containing growth factors secreted by human amniotic membrane derived mesenchymal stem cells for induction of angiogenesis. When injected, produced nanostructures will degrade and gradually release growth factors into ischemic environment of tissue. We hypothesize that this time-dependent and prolonged release of growth factors will facilitate and improve development of collaterals, thus restoring blood flow into ischemic tissue. We believe that this method, rather than direct administration of stem cells, would bypass critical clinical issues, such as potential tumorigenesis and the graft versus host incompatibility that occurs in allogeneic transplantations.

Results and discussion. The effectiveness of angiogenesis induction by growth factors secreted by various types of stem cells was shown in in vitro experiments using endothelial cells of human umbilical vein and in vivo experiments using mice. Experiments were performed to encapsulate the growth factors into biodegradable polymer using two methods: electrospray and double emulsion. The size of the prepared capsules was from 500 nm to 20 microns. The biodegradable polymer, PLGA, was used for this study. Electrospray was performed on Electrosprayer brand Yflow. The encapsulation efficiency was checked by UV spectrometer. The size distribution was calculated using Zetasizer. Morphology of the capsules was determined by atomic force microscope.

Conclusions. In vitro and in vivo experiments using animal model show that conditioned media of multipotent stem cells contains cocktail of growth factors which are able at certain degree induce formation of blood vessels. This property of stem cell conditioned media further could be facilitated to develop cell-free technology for inducing angiogenesis suitable for clinical application.

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