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Supportive effect of WJ-MSC on vascular network of hippocampal slices injured by oxygen-glucose deprivation *in vitro*

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Objectives: Ischemic stroke results in rapid dysfunction of tissue homeostasis leading to disruption of the proper interactions within structural elements of the neurovascular unit (NVU). Recent publications suggest an important role of endothelial progenitor cells in the reconstruction of damaged microvessels, thus contributing to a faster recovery of the NVU in damaged brain. The aim of this study was to evaluate the ability of mesenchymal stem cells derived from human Wharton jelly (WJ-MSC) to differentiate into endothelial progenitor cells (WJ-EPC) and then support vascular network in rat hippocampal organotypic culture (OHC) model of ischemic injury.

Materials & Methods: Mesenchymal stem cells isolated from umbilical cord slices were cultured in classical growth medium (MSCGM) or in endothelial differentiating medium (EGM-2). Cells were characterized by immunocytochemistry, flow cytometry and molecular methods based on expression of mesenchymal and endothelial specific markers (CD90, CD73, CD105, vWF, CD31, VEGF, VEGFR2). Potential angiogenic activity of WJ-EPC was evaluated *in vitro* by capillary-like structure formation test and DiI-Ac-LDL-uptake assay. After 5 days of incubation OHCs undergo oxygen-glucose deprivation (OGD). Subsequently, WJ-MSC or WJ-EPC was co-cultured with intact or post-ischemic slices. Supporting effect of WJ-MSC and WJ-EPC supplementation on vascular network was verified immunohistochemically with rat EC-specific antibody (anti-RECA-1), which allowed calculation of the percentage area of blood vessels in CA1 and CA3 hippocampal regions.

Results & Conclusions: Our results showed that WJ-MSC after 7 days of incubation in EGM-2 medium acquired typical for EPC cobblestone-like morphology, were able to form capillary-like structures on Matrigel and took up DiI-Ac-LDL. Both cell types were positive for MSC and EC markers CD73, CD90, CD105, VEGFR2, VEGF, but only EPC-differentiated cells expressed vWF and CD31. Moreover, WJ-MSC and WJ-EPC co-cultured with injured OHCs decreased atrophy of the blood vessels and protected CA1 cells against post-ischemic death. These results indicate protective effects of the cells of mesenchymal origin in OGD hippocampal slices, which make them a promising candidate for the treatment of brain ischemia.

Biography

Patrycja Siedlecka completed her Master of Science degree in biotechnology at University of Life Sciences in Lublin, Poland. She is a PhD Student at Stem Cell Bioengineering Laboratory at Mossakowski Medical Research Centre Polish Academy of Sciences in Warsaw. She is working on the neuroprotective and anti-inflammatory mechanisms of stem/progenitor cells derived from umbilical cord blood and umbilical cord on nerve tissue. Her current work focuses on the supportive effect of mesenchymal stem cells on vascular network of hippocampal slice culture injured by oxygen-glucose deprivation. She is a member of the Polish Neuroscience Society (PTBUN).

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