KSN 2018
Seoul, Korea · May 17 - 20

Abstract Type : Oral
Presentation No. : OR 02 AK-03

Construction of mesenchymal stem cells secreting angiogenic or anti-inflammatory factors by ZFN and CRISPR/Cas9 genome-editing technology for the treatment of acute kidney injury

Hye-Jeong Park, Jeong-In Cho, Hyo-Ju Jang, Eui-Jung Park, Hyo-Jung Choi, Kwon Moo Park, Tae-Hwan Kwon
Department of Biochemistry & Molecular Biology, Kyungpook National University School of Medicine, Korea, Republic of

Objectives: Stem cell therapy has been proposed as a potential therapeutic strategy for acute kidney injury (AKI). By exploiting genome editing and cell sheet technology, we aimed to generate mesenchymal stem cells (MSCs) secreting angiogenic factors [vascular endothelial growth factor (VEGF) and angiopoietin-1 (ANG1)] or anti-inflammatory factors [erythropoietin (EPO) and alpha-melanocyte stimulating hormone (a-MSH)] for therapeutic application in AKI.

Methods: To integrate each gene expression cassette into the safe harbor locus, AAVS1, of the human umbilical cord-derived MSCs (hUC-MSCs) chromosome, AAVS1-targeting Zinc Finger Nuclease (ZFN) or AAVS1-targeting CRISPR/Cas9 system was exploited.

Results: Junction PCR analysis demonstrated the ZFN- or CRISPR/Cas9-aided gene integration in hUC-MSCs. Flow cytometry and osteogenic and adipogenic differentiation assay revealed that stemness was maintained despite genome engineering. Protein measurement in conditioned media by ELISA and immunoblotting confirmed the production and secretion of each integrated gene product (VEGF, ANG1, EPO, or a-MSH). *In vitro* assay demonstrated the angiogenic functions (increased HUVEC migration and increased mRNA expression of MMP-9 and Tie-2 in co-cultured HUVEC) of genome-engineered hUC-MSCs secreting VEGF or ANG1. For the stem cell therapy in AKI, a scaffold-free cell sheet system was established using a temperature-responsive polymer (poly(N-isopropylacrylamide).

Conclusions: Taken together, cell sheet system of hUC-MSCs secreting angiogenic or anti-inflammatory factors is successfully established. This is to be examined in animal models of AKI to demonstrate the therapeutic effects of stem cell-based regenerative strategy against AKI.