Stem Cell & Regenerative Medicine 2018- Promigratory and Proangiogenic Effects of Adiporon on Bone Marrow-derived Mesenchymal Stem Cells: In vitro Study

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esenchymal stem cells (MSCs) are currently the most convenient primary source of stem cells applicable in cell therapy and regenerative medicine. Due to low number of viable MSCs after cell transplantation novel approaches are required to improve viability, robust migration and proper homing of the cells. Recent evidence demonstrated that AdipoRon, a small-molecule AdipoR agonist has cytoprotective effect on post-ischemic cardiomyocytes. Herein we investigated the effect of AdipoRon on major factors involved in survival, migration and angiogenesis of rat bone marrow-derived MSCs cells. The expression level of cyclooxygenase-2 (COX-2), hypoxia-inducible factor-1 (HIF-1), C-X-C chemokine receptor type 4 (CXCR4), C-C chemokine receptor type 2 (CCR2), vascular endothelial growth factor (VEGF), matrix metalloproteinase-2 (MMP-2) and MMP-9 were assessed by Real-Time PCR, compared to untreated MSCs. Prostaglandin E2 (PGE2) production was investigated using ELISA assay. Measurement of Caspase-3 activity was carried out by an enzymatic assay. The migration potential of MSCs was observed by scratch test. AdipoRon significantly promoted the MSCs viability. The Real-Time PCR results indicated that the expression of COX-2, HIF-1, CXCR4, CCR2, VEGF, MMP-2 and MMP-9 were higher in AdipoRon- treated MSCs compared to control groups. The PGE2 level was enhanced by AdipoRon preconditioning; in contrast the caspase-3 activity was attenuated in these cells compared to the control group. Scratch test showed that AdipoRon could promote the migration ability of MSCs. Preconditioning of MSCs with AdipoRon prior to transplantation could enhance cell survival, angiogenesis and migration via activating the COX-2/ PGE2/HIF-1 pathway and other contributing factors.

Objectives: To investigate the effect of AdipoRon on

major factors involved in survival, migration and neovascularization of rat bone marrow-derived mesenchymal stem cells.

Keywords: AdipoRon; Adiponectin; Cyclooxygenase-2; HIF-1; Mesenchymal stem cell; Prostaglandin E2.

Results: AdipoRon promoted the MSCs viability. Real-time PCR indicated that the expression of cyclooxygenase-2 (COX-2), hypoxia-inducible factor-1 (HIF-1) C-X-C chemokine receptor type 4 (CXCR4), C-C chemokine receptor type 2 (CCR2), vascular endothelial growth factor matrix metalloproteinase-2 (MMP-2) and MMP-9 were upregulated in AdipoRon-treated MSCs compared to control groups. Prostaglandin E2 (PGE2) level, as well as migration ability of MSCs (scratch assay) was enhanced by AdipoRon preconditioning.

Conclusion: Preconditioning of MSCs with AdipoRon prior to transplantation could enhance cell survival, angiogenesis and migration via activating the COX-2/ PGE2/HIF-1 pathway and other contributing factors.

The global Stem Cell market is expected to grow at an incredible CAGR of 25.5% from 2015 to 2022 and reach a market value of US\$297 billion by 2022. The emergence of Induced Pluripotent Stem (iPS) cells as an alternative to ESCs (embryonic stem cells), growth of developing markets, and evolution of new stem cell therapies represent promising growth opportunities for leading players in this sector.Due to the increased funding from Government and Private sector and rising global awareness about stem cell therapies and research are the main factors which are driving this market. A surge in therapeutic research activities funded by governments across the world has immensely propelled the global stem cells market. However, the high cost of stem cell treatment and stringent government regulations against the harvesting of stem cells are expected to restrain the growth of the global stem cells market.Whereas the Europe Stem cell market is estimated to grow at a CAGR of 9.45% by the end of the forecast period of 2018-2026. The market is chiefly progressing due to increasing R&D investments in adult stem cell research in the region, ease of administration and the growing incidences of chronic disease due to the changing lifestyles of the population. The countries analyzed in the Europe Stem cell market are UK, France, Germany, Spain, Italy and rest of Europe. Most of these countries have a stable economic environment, enabling their population to spend more on their health. In this report, the Europe stem cell market has been segmented based on technology, product and applications. At present, the regenerative medicine application accounts for a high revenue share. Because of their use in regenerative therapies, stem cells are increasingly finding applications in the fields of neurological and hematological disorders, and in areas such as organ transplants, Crohn's disease, systemic lupus, and infertility. The worldwide Stem cell & regenerative medicines market is functional with several parameters like product type, application, sources, geography and users. In focused to the product type stem cells market is divided into human embryonic stem cells, adult stem cells, IPsec's, etc. Whereas, regenerative medicines applied the potential of these stem cells to regenerate, repair & replace tissues or the organ which are affected due to injury, natural aging process, and some diseases.