Lipopolysaccharides protect Mesenchymal Stem Cell against Cardiac Ischemia-reperfusion Injury by HMGB1/STAT3 signaling

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Abstract

Myocardial ischemia-reperfusion (I/R) is a serious and irreversible injury. Bone marrow-derived mesenchymal stem cells (MSCs) is considered to be a potential therapy for I/R injury due to the paracrine effects. High-mobility group box 1 (HMGB1) is a novel mediator in MSC and regulates the response of inflammation injury. Signal Transduction and Transcription Activator 3 (STAT3) is a critical transcription factor and important for release of paracrine factors. However, the relationship between HMGB1 and STAT3 in paracrine effect of MSC remains unknown. In vitro, Hypoxia/Reoxygenation injury model was established by AnaeroPack System and examined by Annexin V flow cytometry, CCK8 assay and morphology observation. Detection of apoptotic proteins and protein expression of HMGB1 and STAT3 by Western blot. The conditioned medium of MSC with or without LPS pretreatment was cocultured with H9c2 cells for 24h before hypoxia treatment and MSC showed obvious cardiomyocytes protect role, as evidence by decreased apoptosis rate and improved cells viability, and LPS pretreated MSC exhibited better protect role than untreated MSC. However, such effect was abolished in HMGB1 deficiency group, silencing HMGB1 decreased the secretion of VEGF, HGF, IGF, cell viability, and the expression of STAT3. Furthermore, STAT3 silence attenuated the protective effect of LPS in MSC. Collectively, these findings suggested that LPS improved MSC-mediated cardiomcyocytes protection by HMGB1/STAT3 signaling.

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