POTENTIAL MECHANISM OF CONNEXIN 43 AND SGSM3 THROUGH HIF-1A-MEDIATED MODULATION INBONE MARROW-DERIVED MESENCHYMAL STEM CELLS

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Abstract - Connexin 43 (Cx43) contributes gap junction-mediated communication as a gap junction protein but has shown channel independent functions. Many reports have suggested that Cx43 regulates other cellular mechanisms, including cell cycles, differentiation,and proliferation. Recent evidence suggests that connexins, and in particular Cx43, may have additional effects that may be important in cell death and survival by mechanisms independent of cell to cell communication. In the previous study, we found that Cx43-interaction protein, small G protein signaling modulator 3 (SGSM3) plays a critical role in stress cells.Moreover, their interaction plays a key role in Cx43 internalizationfor connexin turnover in cardiomyocytes of infarcted hearts. Here, we investigated for SGSM3, a potential partner of Cx43, in an attempt to identify for enhancing survival markers in bone marrow-derived mesenchymal stem cells (MSCs). Cx43 co-immunoprecipitated analysis identifying two proteins, and gap junction proteins were predicted that SGSM3 was highly correlated with Cx43 in GeneMANIA network analysis. Results of Hif1aand Sgsm3 siRNA knockdown experiments suggest that SGSM3 possibly plays a role in the cellular response to stress or ischemia with Cx43 dependently on Hif1α. In conclusion, these data demonstrate a role for SGSM3 in Cx43 endocytic trafficking and further substantiate its role in Cx43 turnover. This knowledge of SGSM3-mediated regulation of Cx43 may help to identify a novel therapeutic target to counteract the loss of Cx43 or impairment of Cx43-GJIC that disrupt normal cell functions and are associated with many human diseases.

Key words - Connexin 43, Small G protein signaling modulator 3,Mesenchymal stem cells, Hypoxia