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Tissue-specific MSCs demonstrate differential mitochondria transfer abilities that may affect their regenerative potential

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Abstract

Mesenchymal Stem Cells (MSCs) have shown remarkable regenerative potential to treat many diseases through various mechanisms. Mitochondria transfer through stem cell has emerged as an efficient strategy to repair and regenerate damaged cells in asthma, damaged alveolar cells in lung and renal tubular cells. Though mitochondria transfer through stem cells has also been observed in case of cardiac and neuronal cells, but the ability of regeneration has not been well investigated. In this study, we have compared regenerative potential of MSCs from different tissue origins and shown their ability to repair cardiac and neuronal cells under oxidative stress. MSCs were obtained from different tissue sources such as bone marrow (BM), adipose (AD), dental pulp (DP) and Wharton's jelly (WJ). Antimycin A has been used to induce oxidative stress by elevating levels of reactive oxygen species (ROS). Cardiac and neuronal cells under oxidative stress were stained with cell trace violet and then co-cultured with tissue-specific MSCs whose mitochondria were labeled green with Mitotracker green. Quantification of double positive cells using flow cytometer was used to assess the differential mitochondrial transfer abilities. We observed that differential mitochondria transfer occurred from tissue specific MSCs to neuronal and cardiac cells, $P< 0.05$. It was also observed that percentage of mitochondrial transfer percentages from MSCs to neuronal and cardiac cells differed significantly, suggesting that the recipient cell origin also matters. The level of reduction in ROS was also assessed by labeling with MitoSox Red and assessed by flow cytometer. We found that Adipose and Bone Marrow MSCs display higher tendencies to transfer mitochondria and lower ability to reduce ROS levels in stressed cells, than dental pulp and Wharton's Jelly MSCs. In addition, it was noted that percentage of mitochondrial transfer percentages from MSCs to U87-MG and rat cardiomyocytes differed significantly. Higher ATP levels and mitochondria copy number were observed in dental pulp and Wharton's jelly MSCs suggest that these are highly bio energetically active MSCs, P values <0.001. This suggests that MSCs can repair damaged mitochondria in neuronal and cardiac cells under stress and that WJ-MSCs and DP-MSCSs are better source for mitochondria transfer than AD-MSCs and BM-MSCs. Thus, the origin of MSCs and recipient cell matters in regeneration. More importantly this study establishes that MSCs can rescue damaged neuronal and cardiac cells through mitochondria transfer and can be used to treat many degenerative neuronal and cardiac diseases.

Biography

Swati Paliwal is working in All India Institute of Medical Sciences, India as a research associate.

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