Mitochondrial Transfer from Menstrual Blood Stromal/Stem Cells Promotes Survival of Cardiomyocytes Following Myocardial Infarction

Dear Editor,

Recently, Mitochondrial Transfer (MT) from stem cells to injured cells has been proposed as a novel therapeutic strategy that could restore the bioenergetics requirement of damaged tissues. This organelle is essential for cellular homeostasis, cell survival, cell growth, cell death induction, calcium storage, cell signaling, and energy supply, especially in energy-demanding cells like cardiomyocytes. Mitochondrial dysfunction is contributed to a majority of pathologic conditions like myocardial infarction (MI) and cardiomyopathies. Mitochondrial impairment results in reduction of Adenosine Triphosphate (ATP) production, induces the generation of intracellular Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS), and activates the caspase cleavage pathway. It has been confirmed that Mesenchymal Stem Cells (MSCs) could transport mitochondria to a range of cells including endothelial cells and cardiomyocytes. It appears that healthy mitochondrial donation by MSCs is a unique phenomenon that leads to replacement of dysfunctional mitochondria in injured cells. It has been designated that the transfer of even a small number of Multipotent Mesenchymal Stem Cells (MMSCs) could transport mitochondria to preserved cardiomyocytes. Although mitochondrial transmission from various sources of stem cells like Bone Marrow Mesenchymal Stem Cell (BM-MSCs), induced Pluripotent Stem Cells (iPSCs), and Dental Pulp Derived Mesenchymal Stem Cell (DP-MSCs) has been stated, there is no report about MT from menstrual blood Stromal/Stem Cells (MenSCs). Recently we have perceived that, transepicardial MenSCs administration may be related to MT phenomena from MSCs not only results in protection of injured targeted cells, but also, it can lead to more MSCs survival due to decreasing their partially depolarized and dysfunctional mitochondria.

Researchers indicated that transmission of mitochondria from BM-MSCs to cardiomyocytes can inhibit apoptosis and reprogrammed differentiated cardiomyocytes to progenitor-like cells. Furthermore, iPSC-MSCs directly protects cardiomyocytes against induced cardiomyopathy through bioenergetic preservation by functional MT. Also MT from MSCs to endothelial cell rescued the injured endothelial cell by reducing apoptosis and promoting proliferation.

Meanwhile, some resident cells in injured site could transfer mitochondria to injured cells; we believe that only endogenous transfer is transient and cannot inhibit progressive injuries following MI. Our studies have shown that; administration of MenSCs post-MI modifies the metabolism and restores the functionality of heart, and also protect myocardium from further subsequent injuries mainly with donation of their healthy mitochondria to cardiomyocytes and endothelial cells. It is likely that the donor mitochondria fuse with mitochondria in the recipient cell, and restore bioenergetic requirements; or the recipient cell removes its injured mitochondria and gets the donated healthy mitochondria. Researchers revealed that human mitochondrial DNA from MSCs could be found in mice 28 days after MSC administration. However, MSC nuclear DNA was not detected 3 days post administration and suggesting that the long-term therapeutic effects of MSCs administration may be related to MT. So, the stem cell-based mitochondria transfer approach from MenSCs can be considered as a newly effective therapeutic strategy to treat cardiomyopathies. However, more in-depth studies are needed to clarify the role of MT in MI treatment.
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Investigation is needed to explore the exact mechanism of the MenSCs-derived mitochondria communication with the recipient cells, restoration of mitochondrial bioenergetics in these cells, cell-signaling pathways involved to this phenomenon, and understand how this organelle donation would lead to regeneration.

**Keywords:** Donation, Mitochondria, Myocardial infarction, Stem cells

**References**


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