Cardiovascular-Rescue Effect of Stem Cells via Nanotube-Mediated Mitochondrial Transfer

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Introduction: Stem cells have been shown to have therapeutic effects on heart failure caused by heart diseases such as ischemic and hypertension. Several in vivo studies on rodent and swine have shown that injected human amniotic stem cells (HuAmSCs) can engraft and differentiate in the hearts. However, the low differentiation rate of injected stem cells has been preventing stem cell-based therapy from becoming a clinical treatment despite stem cell's positive effect on treating heart diseases. Recently, mitochondria have been observed to be transferred through tunneling nanotubes (TnTs) from stem cells into cardiomyocytes, suggesting an explanation for the transient effects of stem-cell injections on heart-function improvement. An understanding of mitochondrial transfer between stem cells and cardiomyocytes might enable rescuing strategy for damaged cardiomyocytes.

Methods and Materials: Primary Day-3 neonatal rat cardiomyocytes (CMs) were incubated (95% N_2 and 5% CO_2) for 5h in a hypoxia chamber. The cells were then seeded in a cell culture channel that was in parallel with another channel seeded with cocultured HuAmSCs. This permitted TnT formation between HuAmSCs and CMs in the microchannels connecting the two cell culture channels.

Two-photon (2p) microscope with an excitation wavelength at 740 nm was used to image the autofluorescence of NADH in mitochondria while they were transferred through TnTs.

To determine the functional change before/after the stem cell 'rescue', second harmonic generation (SHG) images were acquired to measure the time history of sarcomeric contraction. The contractility was calculated as the ratio of the minimum sarcomeric length during contraction and the relaxed sarcomeric length in each contraction.

Result and Discussion: The statistical results showed significant improvement of contractility in HuAmSCs-CM coculture group after 24 h, showing the cardiac rescue effect of the stem cell related to TnT-mediated mitochondrial transfer.

Potential Future Research: We plan to explore whether mitochondrial transfer occurs in the stem cell transplantation experiments in which heart-function improvement has been observed.