Mitochondrial transplantation as a therapeutic strategy to attenuate diabetic endothelial dysfunction

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Introduction

- Diabetic endothelial dysfunction is driven by mitochondrial dysfunction and leads to macro- and microvascular complications, such as atherosclerosis and impaired wound healing.
- Mitochondrial transplantation is a promising strategy to enhance mitochondrial functionality in diabetic endothelium cells and restore damaged tissues.

Hypothesis: Mitochondrial transplantation to diabetic endothelial cells restores endothelial function via alleviating mitochondrial dysfunction induced in diabetes.

Methods

1. Mitochondria Cyto-Tracer transduction optimization and selection of iPSC-MSC
   - 1 ug of mitochondrial protein per 5,000 DHAEC

2. Coculturing iPSC-MSCs with DHAECs
   - Immunostaining was performed using CD-31 antibody
   - Flow cytometry was performed using conjugated CD-31-APC antibody

3. Establishment of mitochondrial dysfunction in DHAECs
   - DHAECs were conditioned in the EGM-2 supplemented according to the table for 5 days.
   - Control (no changes)

Optimal MOI was identified as MOI=30 yielding in 93±2.96% transduction efficiency.

Results

- Flow cytometry demonstrated mitochondrial transplantation efficiency up to 30.03% that increased with increasing ratio of MSCs to DHAECs.

Conclusions

- iPSC-MSC Mito-GFP transduction conditions were optimized at MOI=30.
- Mitochondrial transfer from iPSC-MSC to DHAEC and autologous mitochondria transplantation were validated and transfer conditions were optimized.
- Diabetic environment stimulation led to endothelial and mitochondrial dysfunction in DHAEC.
- Mitochondria fate in recipient cells, post-translation functional improvements, and exact mechanism underlying those will be studied in future work.

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References