Peptide-Conjugated Coatings Enhances Mitochondria Transplantation to Damaged Endothelium

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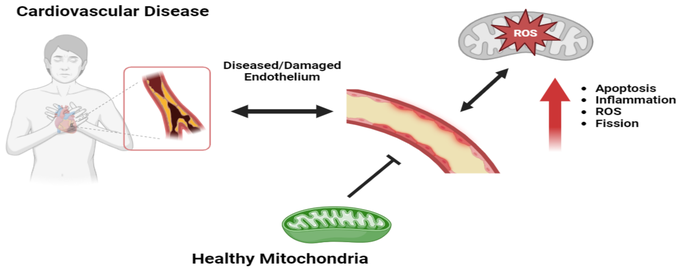
Introduction

Background: Mitochondria transplantation has emerged as a promising regenerative therapy for cardiovascular disease[1], but suffer from a lack of specificity, limited uptake, uncontrolled biodistribution, and subpar efficiency[2]. To overcome this, we are developing engineered mitochondria particles using phospholipid-peptide polymer conjugates to target mitochondria to the damaged endothelium



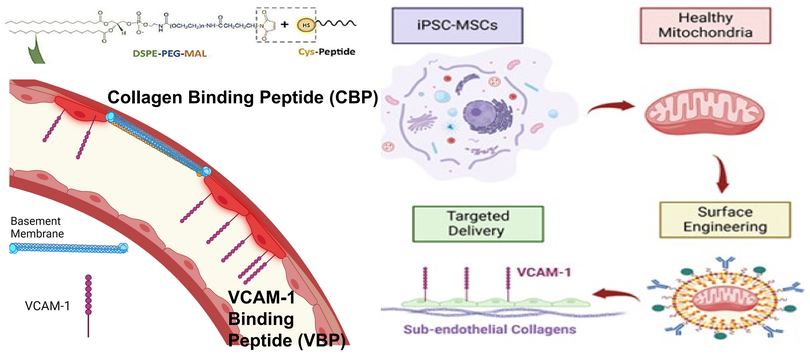
Goal: Develop an endothelium-specific coating for targeted mitochondria transplantation

Hypothesis: Coating isolated mitochondria with collagen binding peptide (CBP) or VCAM-1 binding peptide (VBP) enhances uptake by endothelial cells

JC-1 staining of DHAECs after 24 hrs of Mt treatment

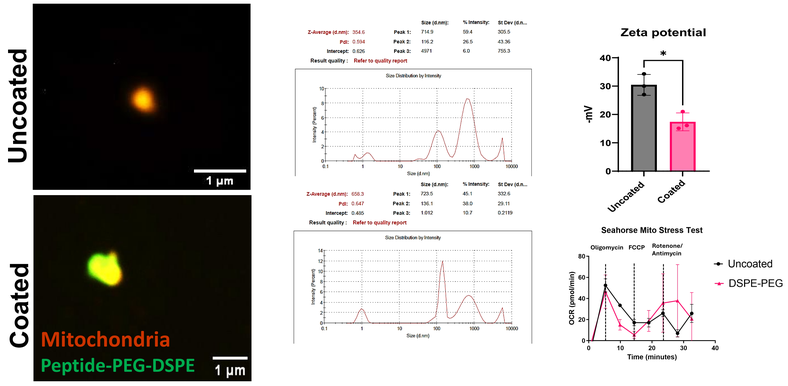
Methods

- Mitotracker Red-labelled mitochondria (Mt) were isolated from induced pluripotent stem cell-derived mesenchymal stem cell (IPSC-MSCs) obtained from a young, healthy donor
- Mt were coated with biotinylated peptide-PEG-DSPE conjugates at a 1:1 ratio of polymer to mitochondria mass. Either collagen binding peptide (CBP) or VCAM-1 Binding Peptide (VBP) was used.
- Diabetic human aortic endothelial cells (DHAECs) were treated with mitochondria for 24 hours to measure uptake and downstream effects on

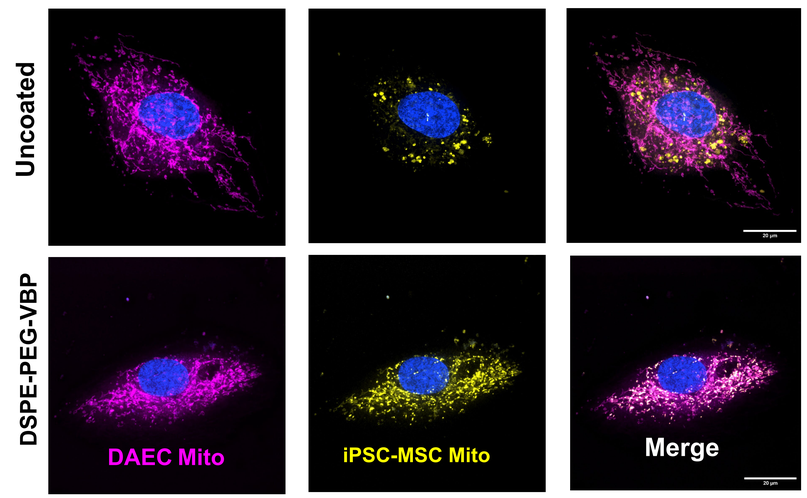


Results

Characterization of DSPE-PEG Engineered Mitochondria

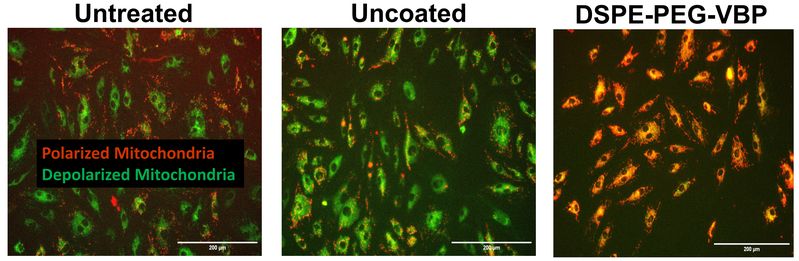


DSPE-PEG Functionalization Enhances Uptake



Uptake of Isolated Mt into DHAECs after 24 hours

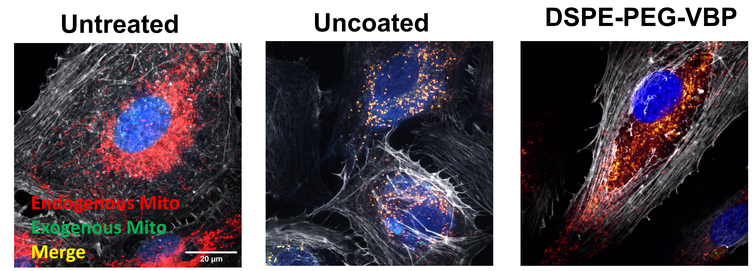
DSPE-PEG Mitochondria Restore Polarization in DHAECs

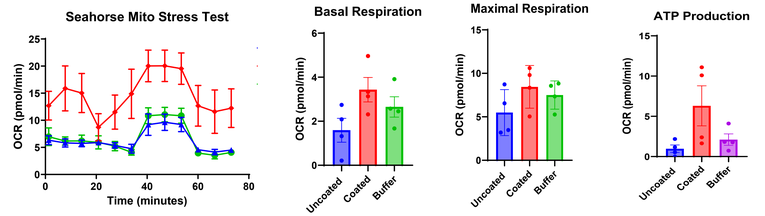


JC-1 Staining of DHAEC 24 hours after treatment with mitochondria

Results

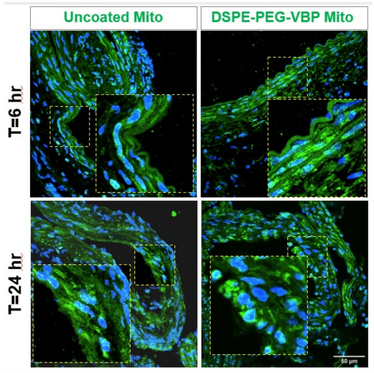
DSPE-PEG-VBP Mitochondria Increase Mitochondria Mass and Sustains Improved Respiration



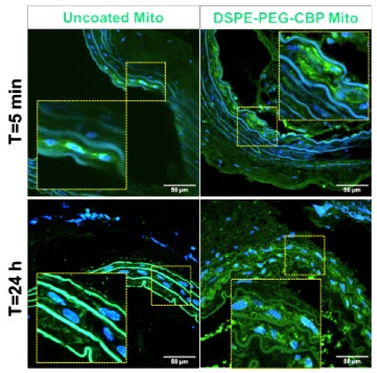


Future Directions (In Vivo Studies)

Systemic Delivery for AAA (BAPN Elastase Model)



Perioperative Local Delivery (Balloon Injury Model)



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References

1. Masuzawa, A., et al., *Transplantation of autologously derived mitochondria protects the heart from ischemia-reperfusion injury.* American Journal of Physiology-Heart and Circulatory Physiology, 2013. **304**(7): p. H966-H982.
2. Huang, T., T. Zhang, and J. Gao, *Targeted mitochondrial delivery: A therapeutic new era for disease treatment.* Journal of Controlled Release, 2022. **343**: p. 89-106.