

Mitochondrial Transplantation for Myocardial Protection In Ex-situ Perfused Hearts Donated After Cardio- circulatory Death.

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Boston Children's Hospital
Until every child is well™

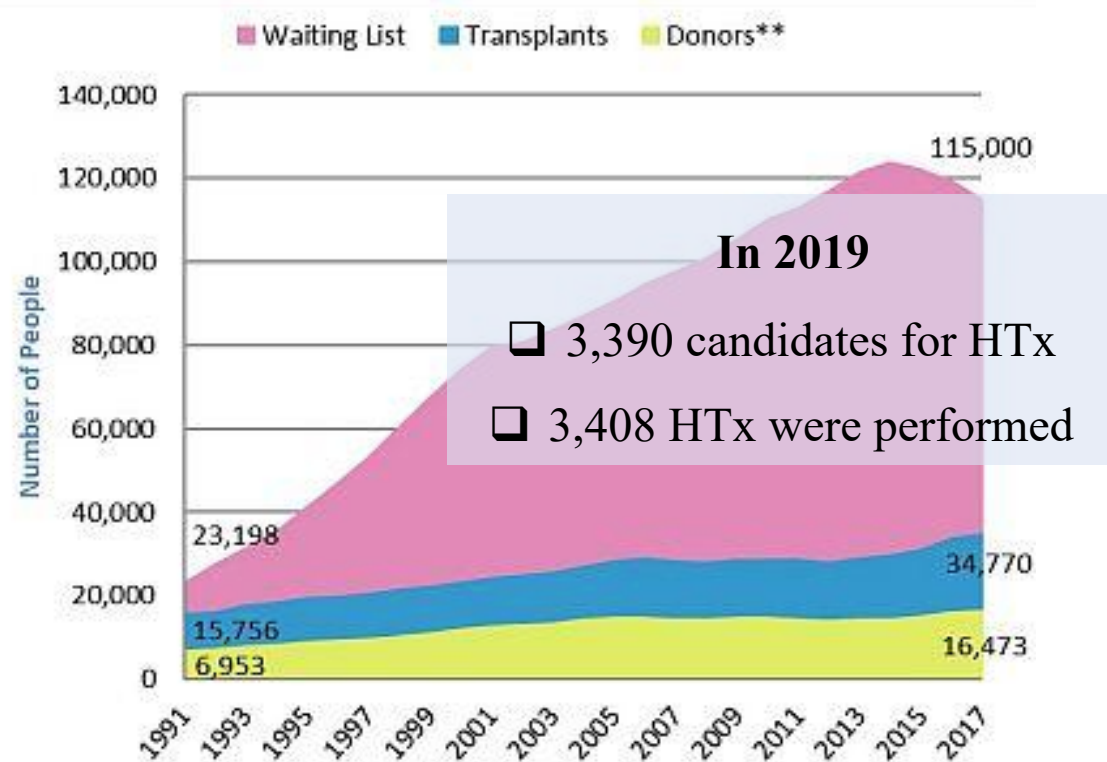


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TEACHING HOSPITAL**

Disclosures

Dr. McCully, Dr. del Nido and Dr. Emani have patents pending for the isolation and usage of mitochondria.

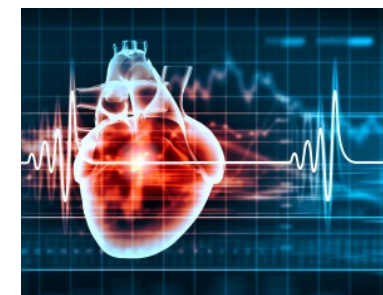
HTx Donation



DONATION AFTER BRAIN DEATH (DBD)



DONATION AFTER CIRCULATORY DEATH (DCD)

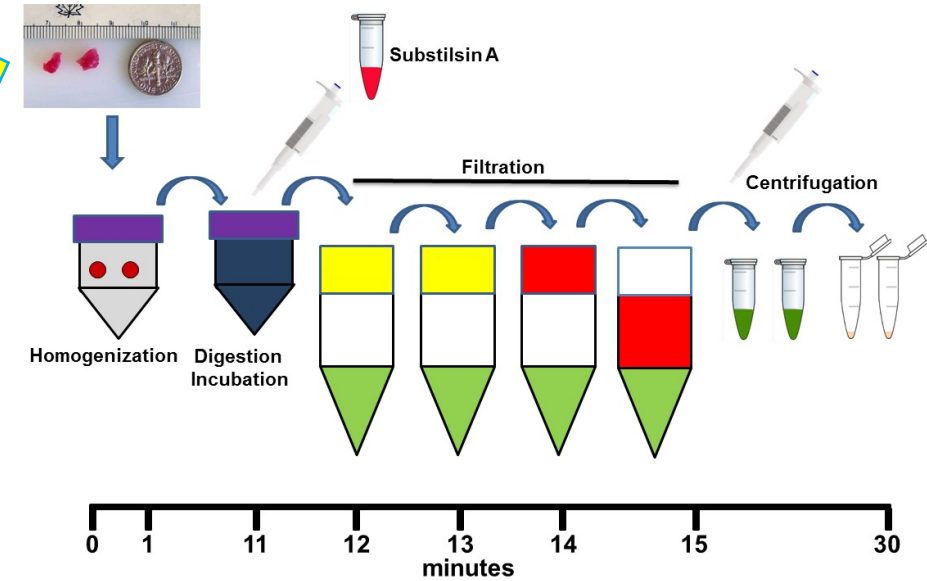
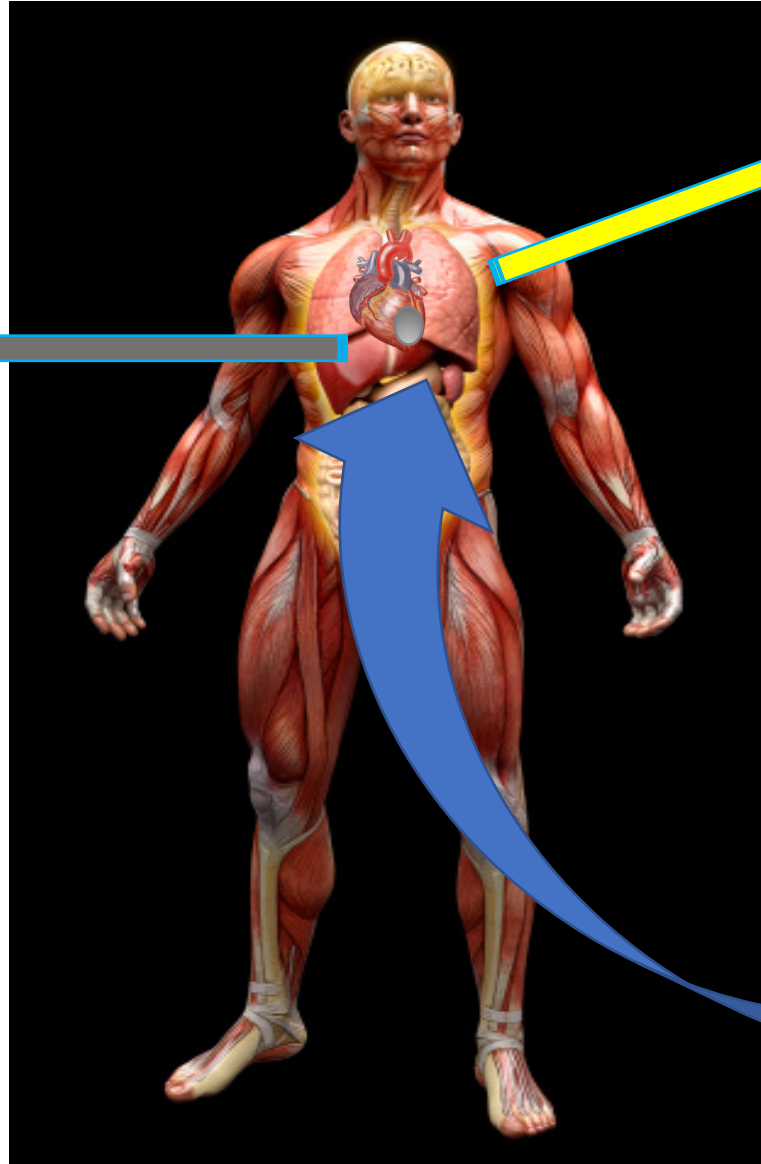


- 30% Increase in HTx activity
- 40% Decrease in waitlist mortality

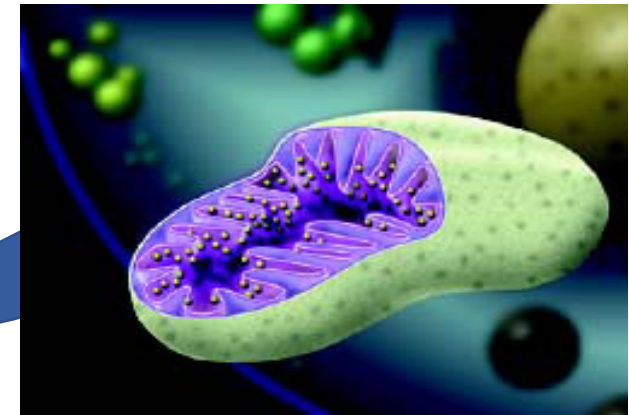
Noterdaeme *et al.* Transpl Int. 2013

Autologous Mitochondrial Transplantation

Damaged Mitochondria

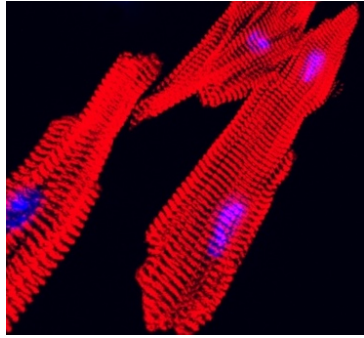


Healthy Mitochondria





Objective



Rationale

Mitochondrial Transplantation

- ✓ Enhances myocardial function
- ✓ Increases myocellular viability
- ✓ Increases total tissue ATP content

Objective

To investigate the effect of mitochondrial transplantation (MT)
in *ex situ* perfused DCD hearts

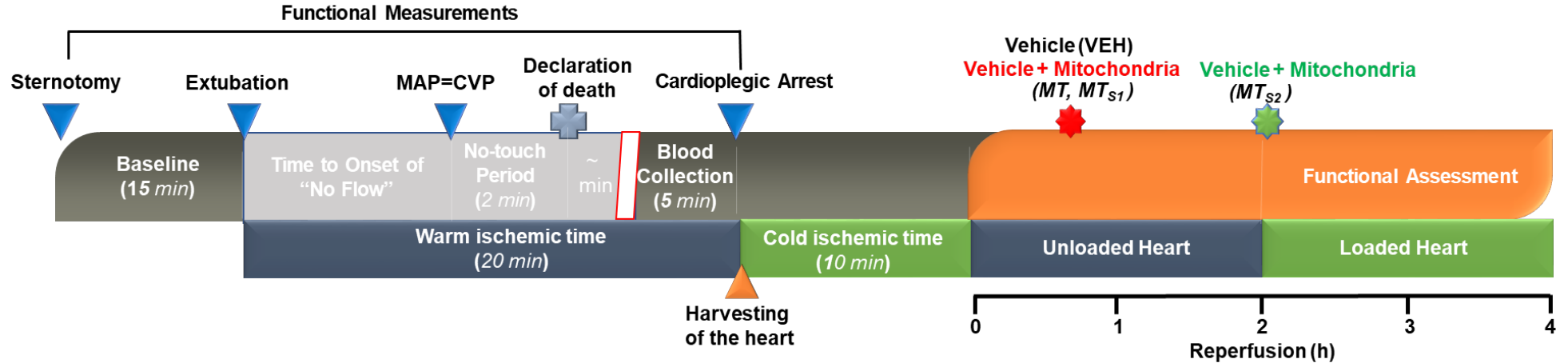
Experimental Protocol

DCD Hearts

VEH; n=8

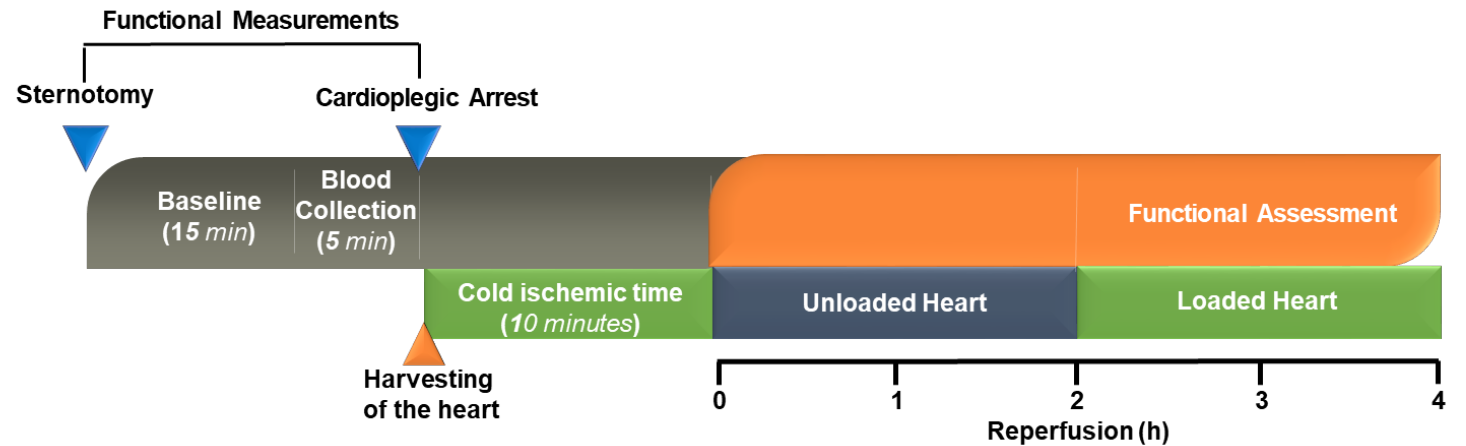
MT; n=8

MTs; n=6



Sham Hearts

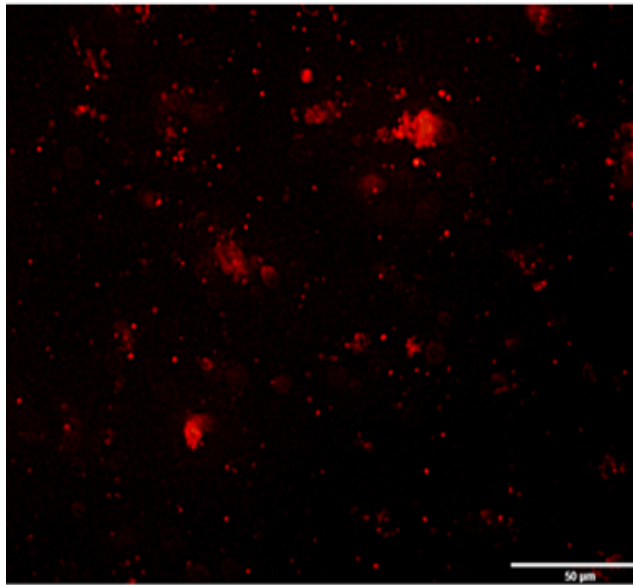
SH; n=6



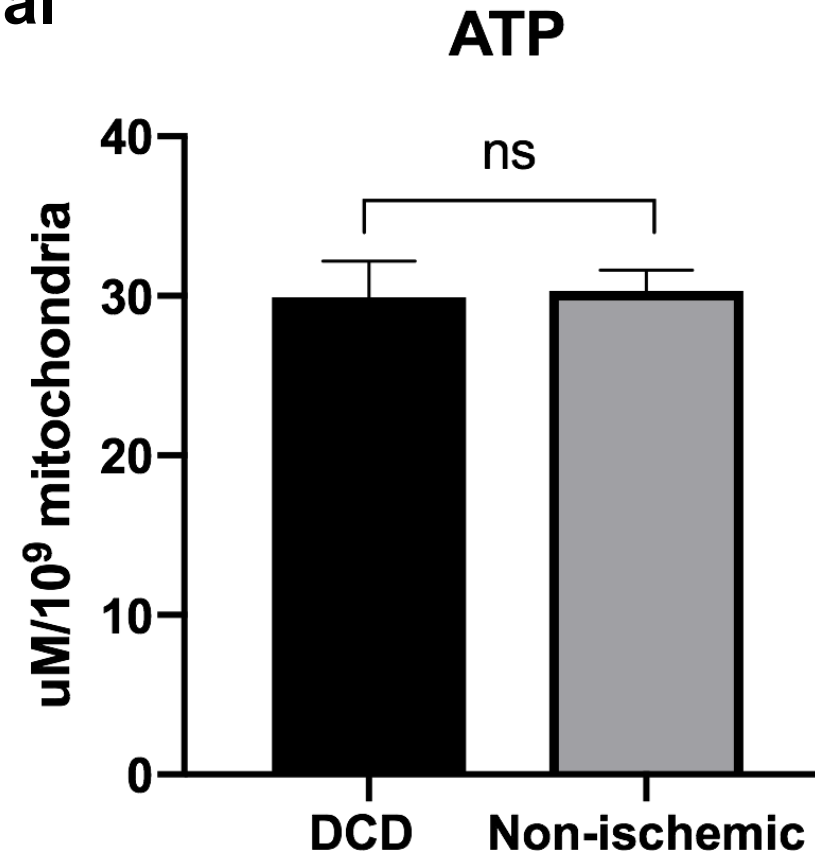
Mitochondria Isolated from DCD Donors

❑ Mitochondria were isolated from skeletal muscle

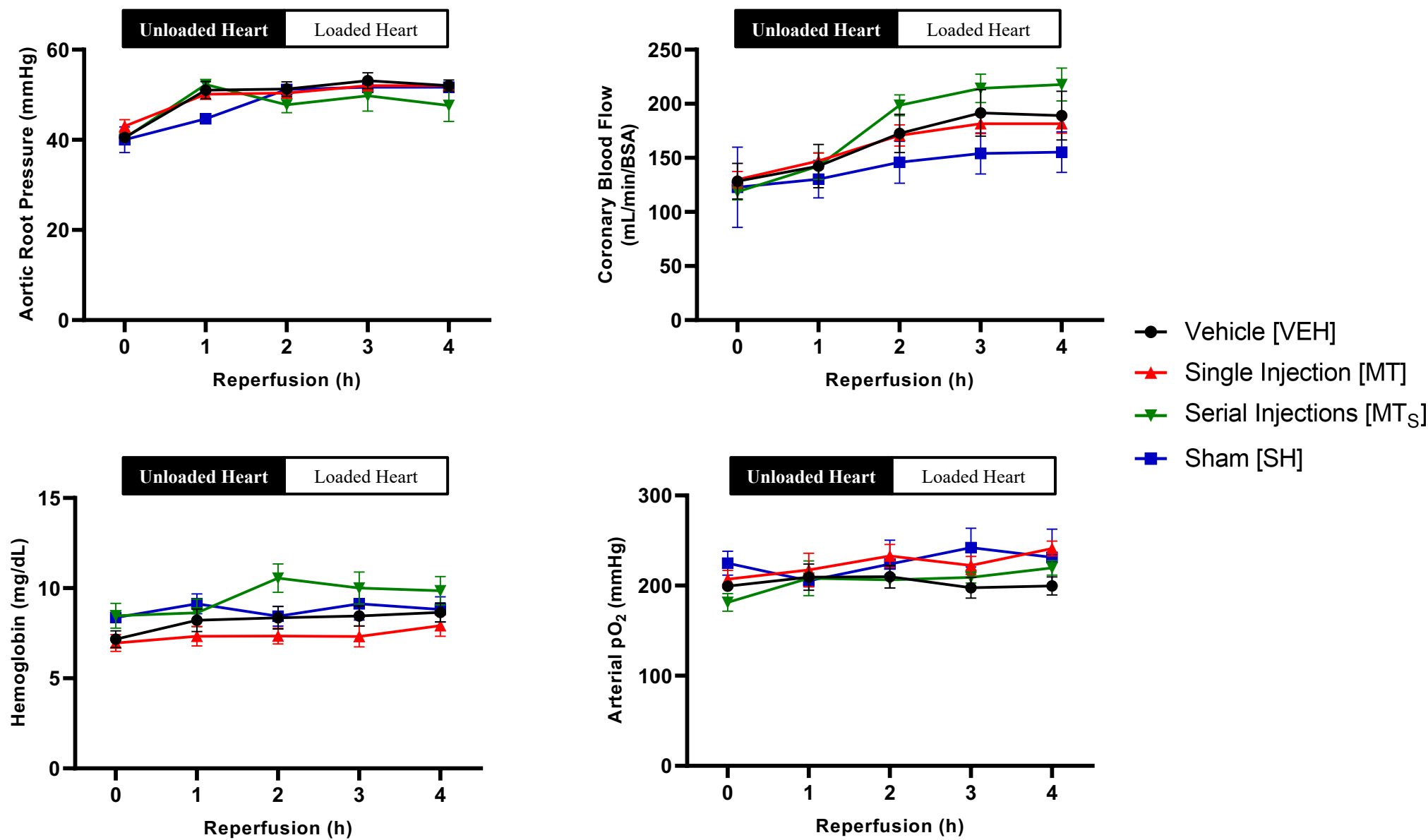
- ✓ **Active membrane potential**
- ✓ **ATP producing**



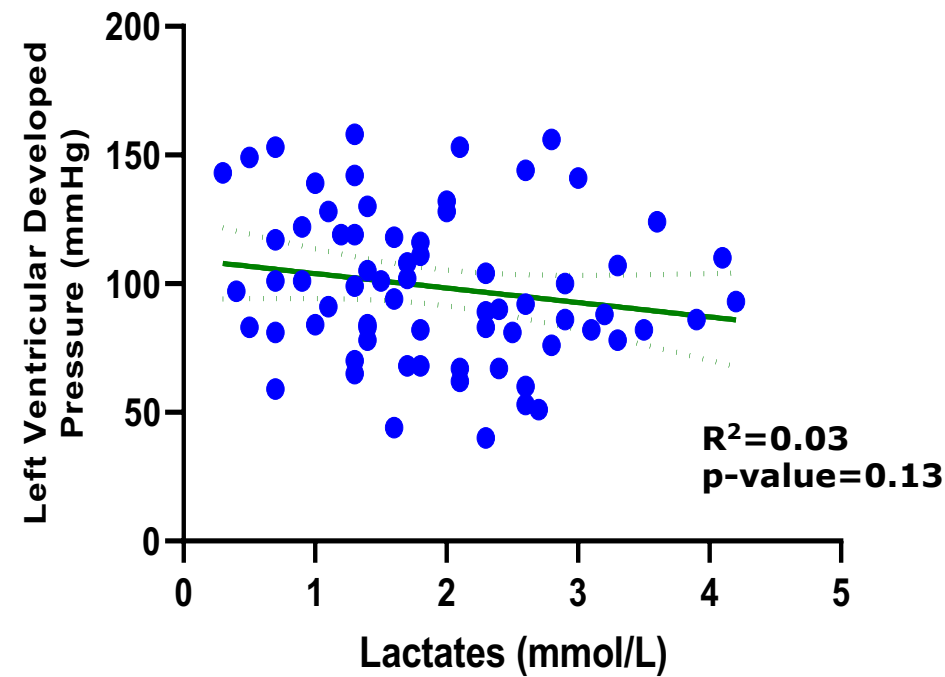
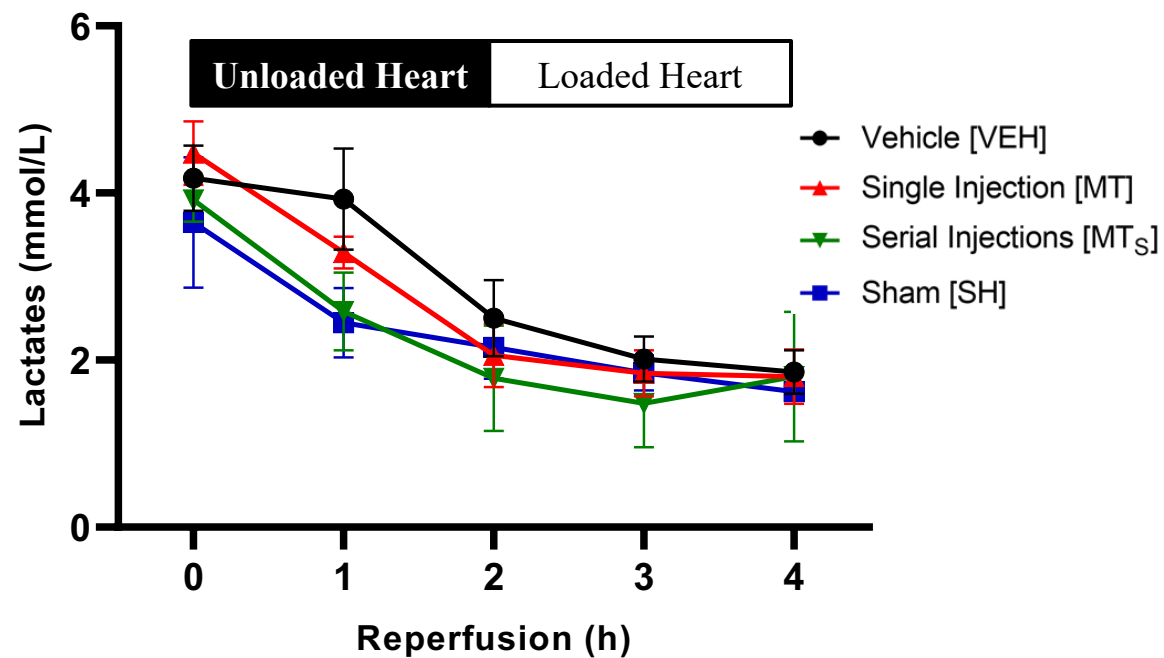
**Mito Tracker
RED CMX ROS**



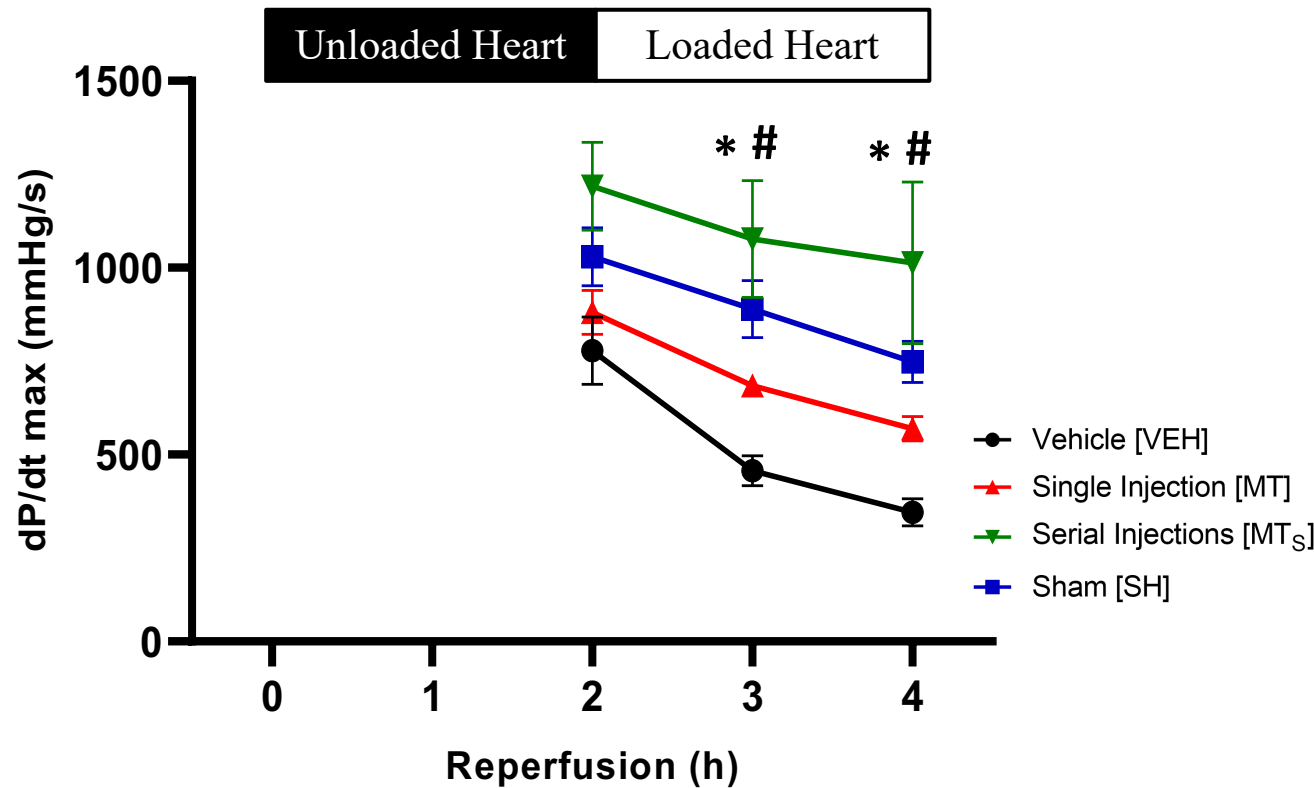
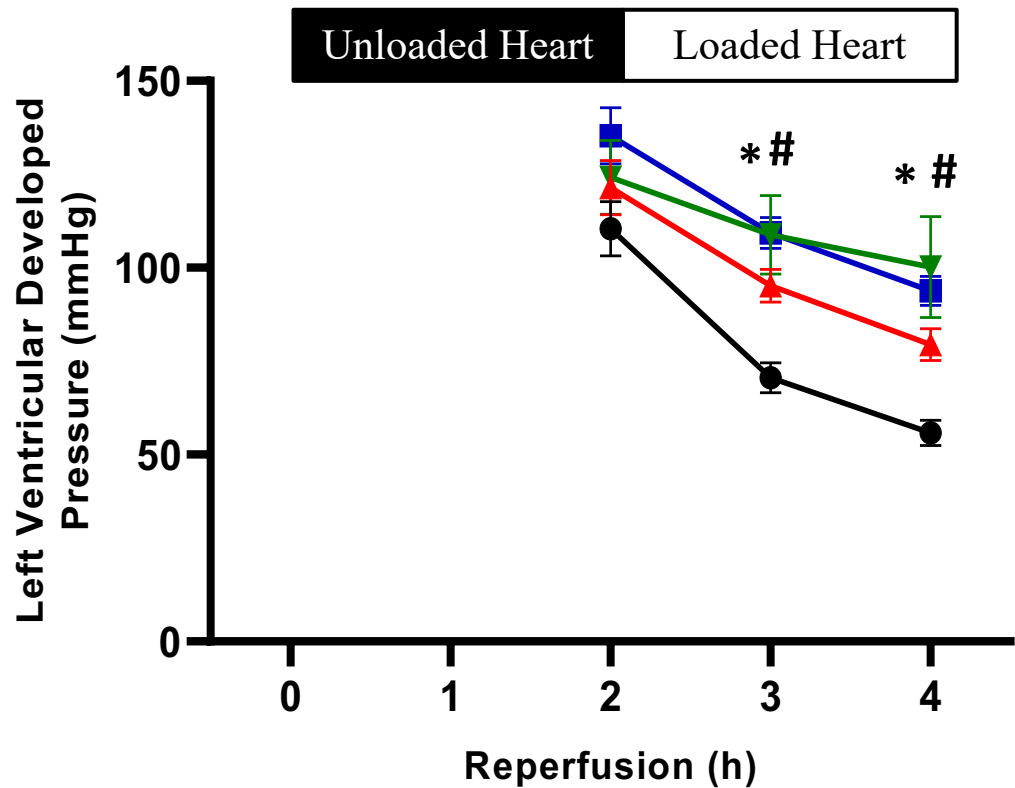
Perfusion Parameters Constant Throughout Reperfusion



No Difference in Lactates

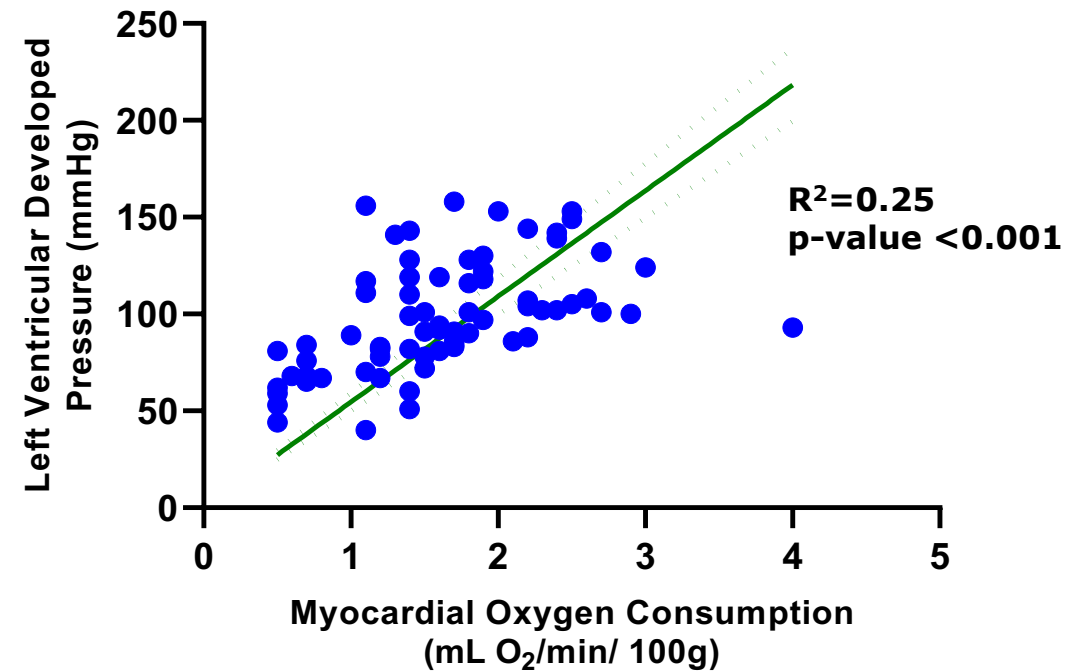
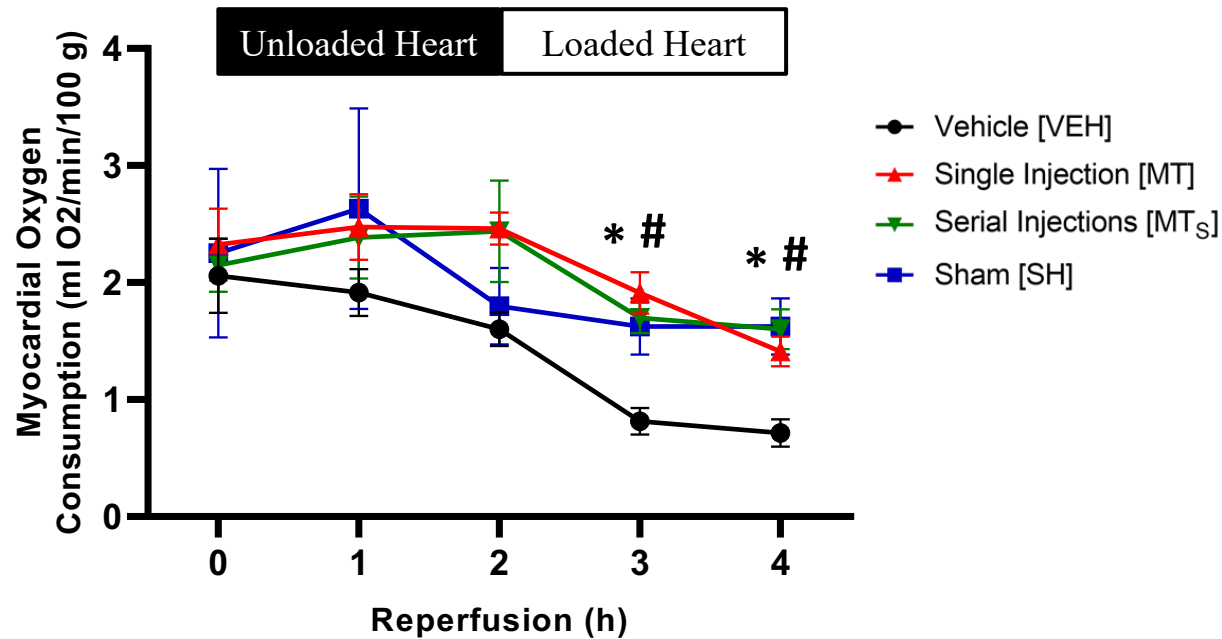


Mitochondrial Transplantation (MT) Increases Myocardial Function



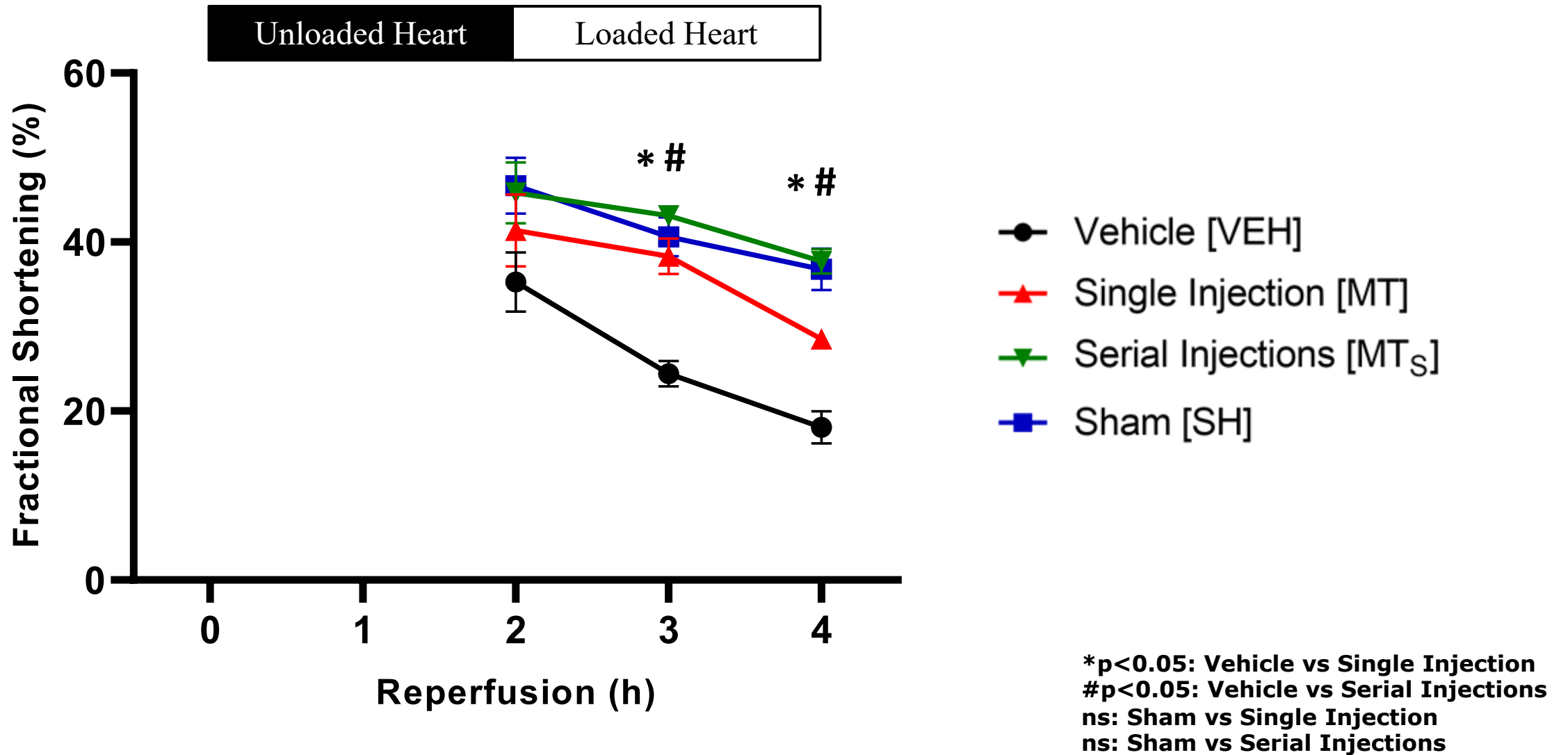
*p<0.05: Vehicle vs Single Injection
#p<0.05: Vehicle vs Serial Injections
ns: Sham vs Single Injection
ns: Sham vs Serial Injections

Mitochondrial Transplantation (MT) Increases Myocardial Oxygen Consumption

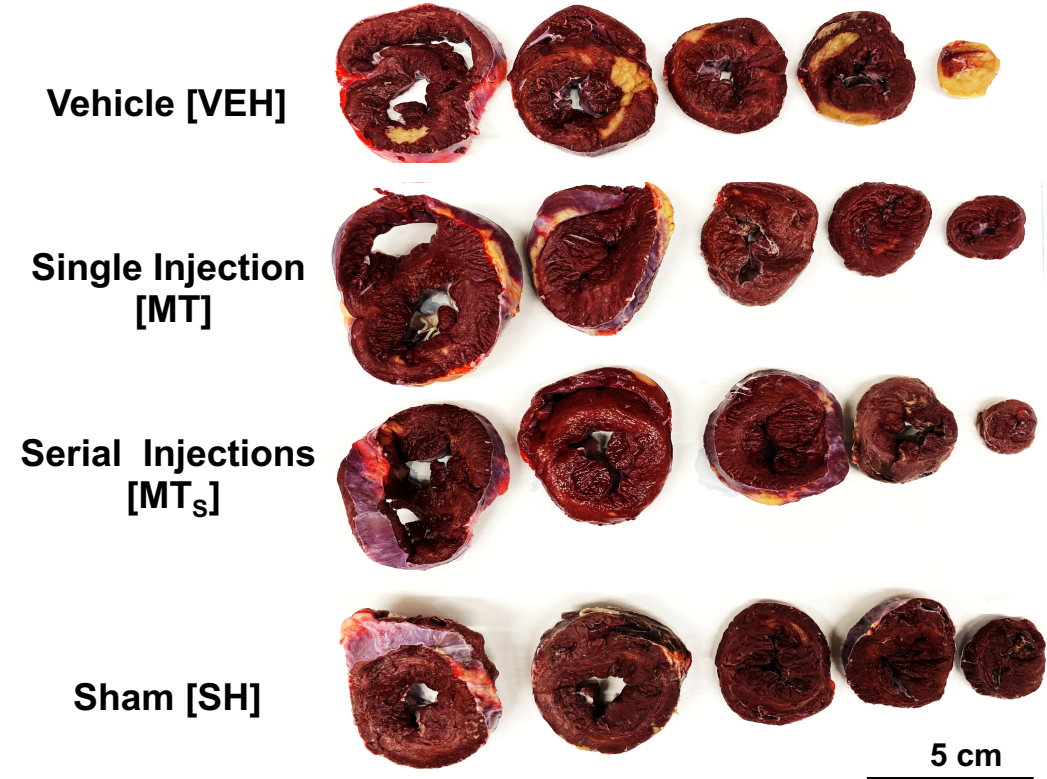
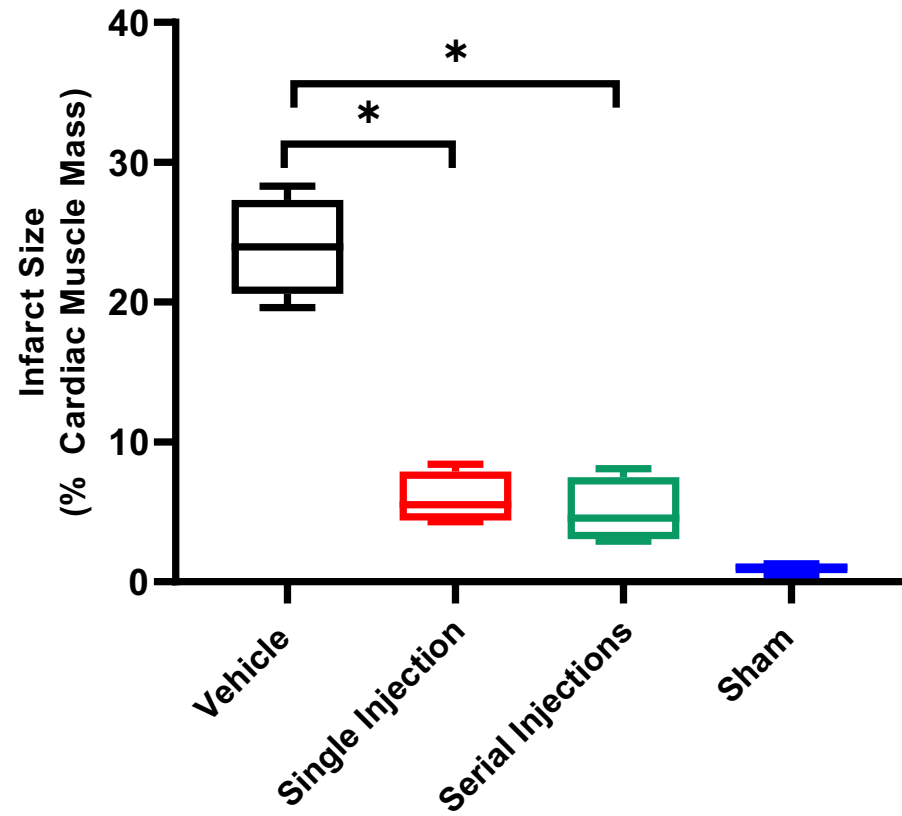


*p<0.05: Vehicle vs Single Injection
#p<0.05: Vehicle vs Serial Injections
ns: Sham vs Single Injection
ns: Sham vs Serial Injections

Mitochondrial Transplantation (MT) Increases Fractional Shortening



Mitochondrial Transplantation (MT) Rescues Myocardial Viability



***p<0.05 vs Vehicle**

Histology

- ❑ Diffuse myocardial tissue injury and edema in **Vehicle hearts**
- ❑ Histological morphology was maintained in **Mitochondria hearts**
- ❑ **No difference was observed between Mitochondria hearts (MT, MT_s) and Sham**

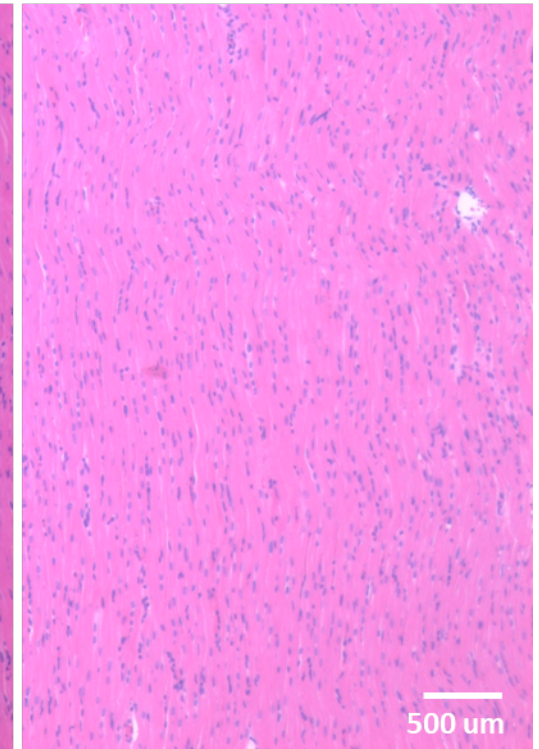
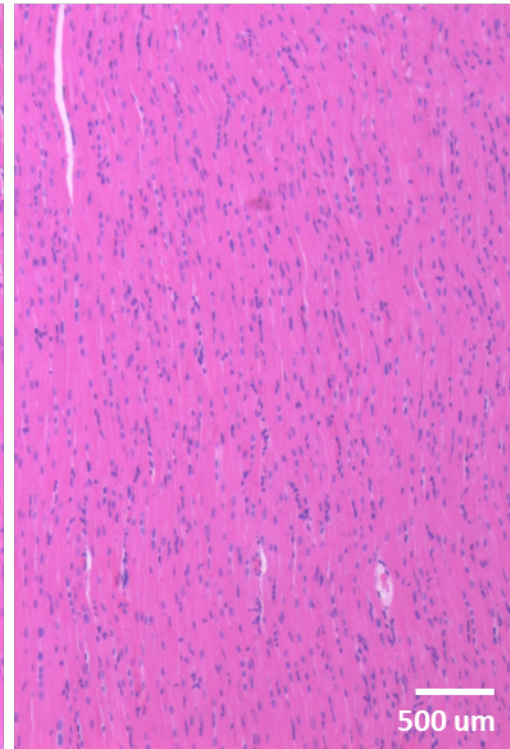
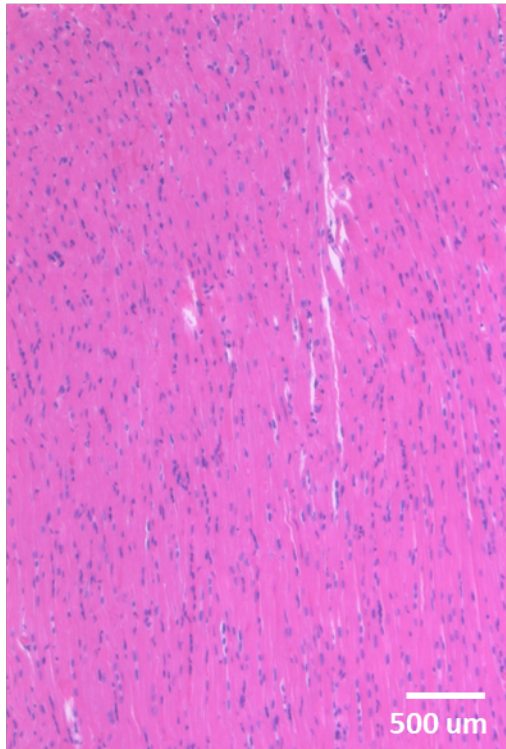
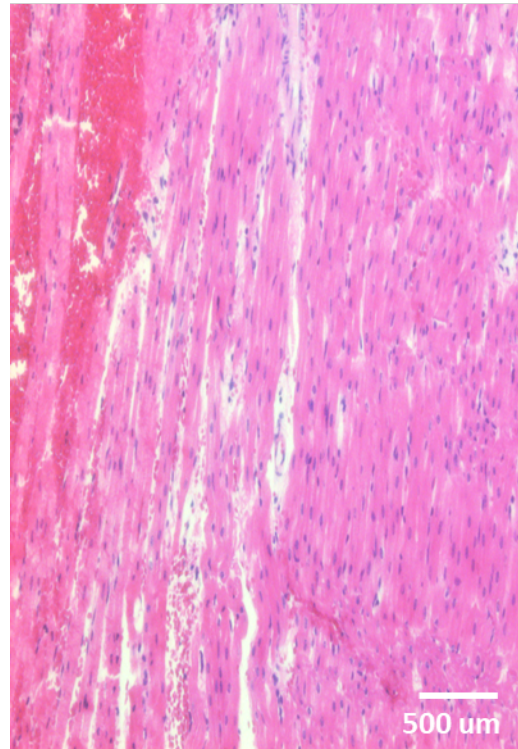
Mitochondria Transplantation

Vehicle [VEH]

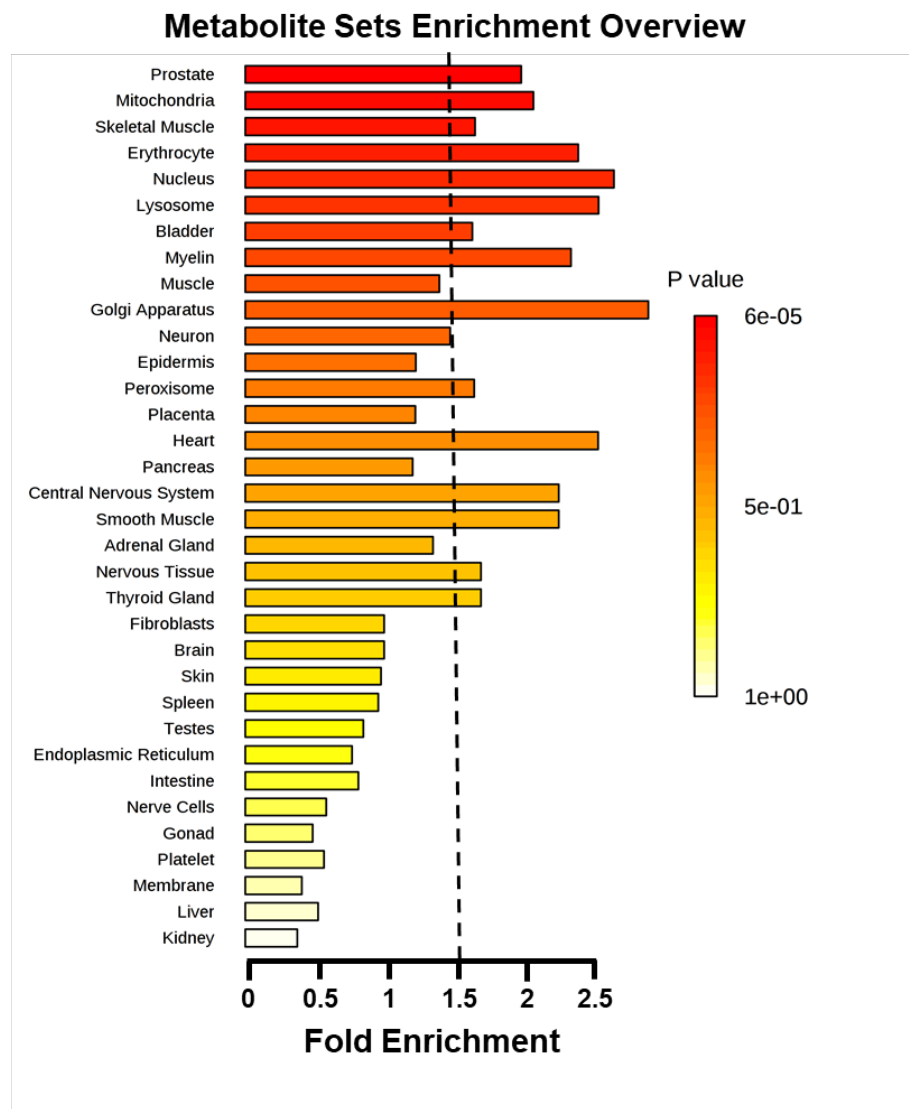
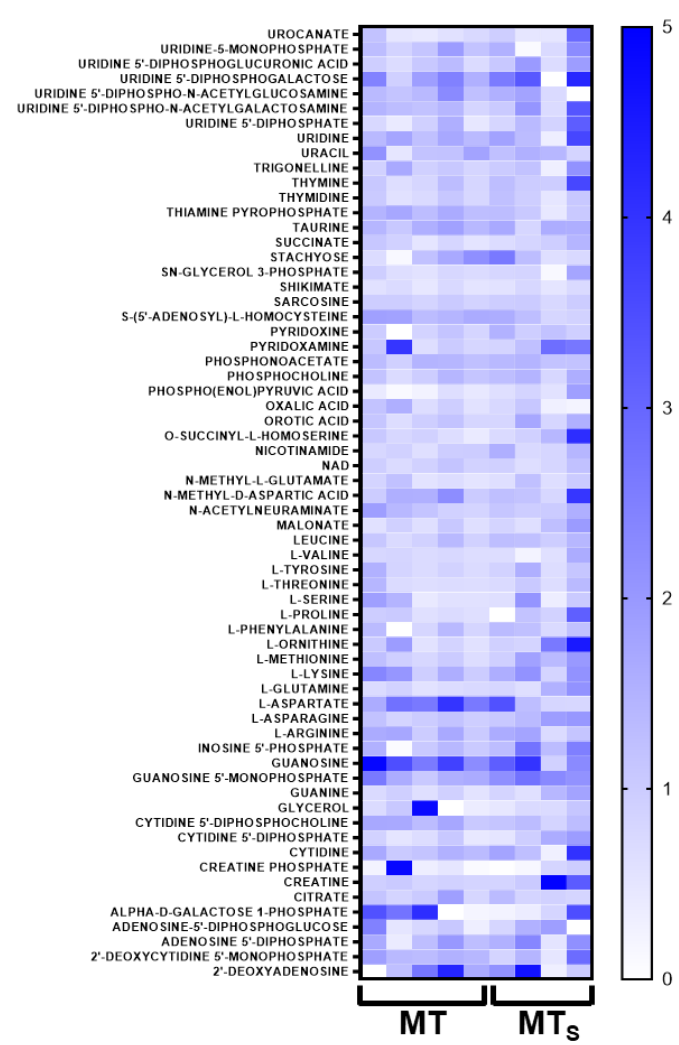
Single Injection [MT]

Serial Injection [MT_s]

Sham



Mitochondrial Transplantation (MT) Upregulates Metabolomic Activity



Pathway analysis showed that mitochondrial electron transport chain was in the top 10 pathways involved in the altered metabolic profile of the hearts that received mitochondria transplantation.

Conclusions

MITOCHONDRIAL TRANSPLANTATION ENHANCES DCD HEARTS

- ✓ No difference between Single and Serial Injections
- ✓ Preserves myocardial **function**
- ✓ Preserves myocardial **viability**
- ✓ Increases myocardial oxygen consumption
- ✓ Significantly increases **metabolomic activity**
- ✓ **Provides a novel methodology to enhance the donor heart pool**

Acknowledgements

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