Flies in Space!
The Physiology of Space Travel

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Why we use flies to study Human Heart Disease

- Shares 75% of Human Genes
- Muscle structural proteins
- Ion Channels

- SMALL Size

- Short lifespan
  - Fly 1wk ~ Human 10yr

- LOADS of genetic tools
Our Effort began with a Box

Prize was the cost to transport this box to the ISS for 30 days
COST - $60,000
Vented Fly Boxes from Nanoracks and Cargo Transfer Bag
Flies in Space Protocol

This program is delayed in Space
Flies in Space Protocol

1 day 1g

30 days μg

Embryos / Larva → Pupa/Adults

F0 Parents → F1 Adults

15 Vials of flies

VFB

~ 1-3 weeks old
Flies in Space Protocol

~35 day Mission

Multigenerational / Multi-Age Cohort
F0 + F1 +F2?

~ 400 Adult flies
Flies in Space Protocol

~35 day Mission

Multigenerational / Multi-Age Cohort (0-3 wks)
F0? + F1 + F2?

24 hr Egg Lay

2.5 - 3 week old F1 Cohort
F2 larva and a few adults, often identifiable as “virgins”

Remove Parents before flight
Space X 11 Experiment

3- Adult F₀ cohort
6- Egg Lay

CTB → 9 VFBS
Space X 11 Experiment

Adult Cohort

Egg Lay
- Effects on Heart Function
- Effects on Cardiac Structure

Actin – muscle protein

Ground Control

Space Flown
  Reduced Size

Walls et al, Cell Report 2020
- Effects on Cardiac Structure

Actin – muscle protein

Ground Control

Space Flown
- Effects on Cardiac Structure

RNA Seq showed significant DOWN regulation of muscle proteins and Collagens

Walls et al, Cell Report 2020
- Effects on Protein Homeostasis

Proteasome / Garbage Disposer

Increased Gene Expression

Reduced Gene Expression

Walls et al, Cell Report 2020
Prolonged Weightlessness Increases Proteasome Number and Protein Plaques

Ground Control

PolyQ^{46}\text{-GFP} \quad \text{Anti-GFP}

Space Flown

\text{Anti-Proteasome}

\text{Merge}

DAPI

Walls et al, Cell Report 2020
Multi-organ Effects of Weightlessness

- Decreased Cardiac Size & Contractility
- **Reductions** in Cardiac Fibrosis
- Decreased Gene Expression of Muscle Proteins
- Defects in Protein Recycling in nerves and muscle
- Clues to prevent muscle loss in space
Does altered gravity elicit an All or None response?

- NASA is going back to the Moon – Artemis Program
- Base planned for the Moon’s south pole
- Missions to Mars in the 2030’s
- Need to assess
  - Micro g
  - Lunar g (0.17 g)
  - Mars g (0.38 g)
Allows for separation of generations

- Light cycle control
- Filming for behavior assessment
- Fixation of generational cohorts
- Return of live flies
Multi-use Variable-g Platform MVP

Platform 1
Platform 2
Food Cylinder
C. Elegans Hardware Overview

- Microscope & Camera
- Peristaltic Pumps for Feed / Waste & Oxygenation
- Culture Bag in imaging frame

Nathanial Szewczyk Lab – Ohio University
Multi-use Variable-g Platform MVP

Platform 1

Platform 2

Food Cylinder
Muti-gravity effects on muscle & nervous tissue in worms and flies

Lunar g (0.17 g)
Mars g (0.38 g)
Earth (1 g)

Micro g
Comparison of gravity effects

Fly Brain

Dopaminergic Neuron Number
-Tyrosine Hydroxylase

Apoptosis - Cleaved Caspase 3

Fly Muscle

Muscle Actin
Mitochondria

Fly Heart

Muscle Actin
ATP Synthase

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Comparison of gravity effects

Worm Brain

Worm Body Wall Muscle

Apoptosis Marker - \textbf{Lgg1/Atg8 GFP}

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Comparison of gravity effects on ISS

Question: What keeps organisms from losing muscle mass in space and with disuse?

Simultaneously Test:
- 4 gravities (~0, 0.17, 0.38, 1)
- 2 organisms (flies & worms)
- 2 distinct tissues (nervous tissue & muscle)

What are the Similar (conserved) Outcomes:
- Changes in apoptosis?
- Changes in mitochondrial form and function?
- Changes in gene expression?
- Tissue-specific?
- Dose dependent?
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