Flies in Space!
The Physiology of Space Travel

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SBP Sanford Burnham Prebys
MEDICAL DISCOVERY INSTITUTE

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

SPACE FLORIDA

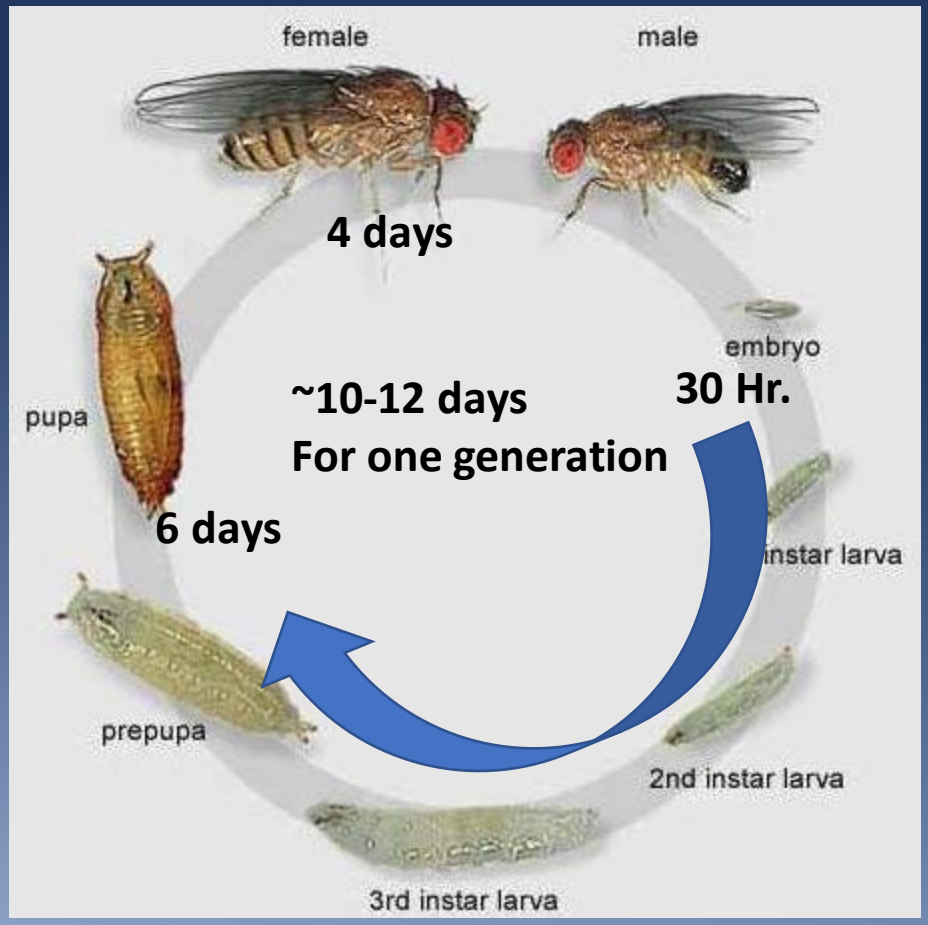
Nanoracks

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

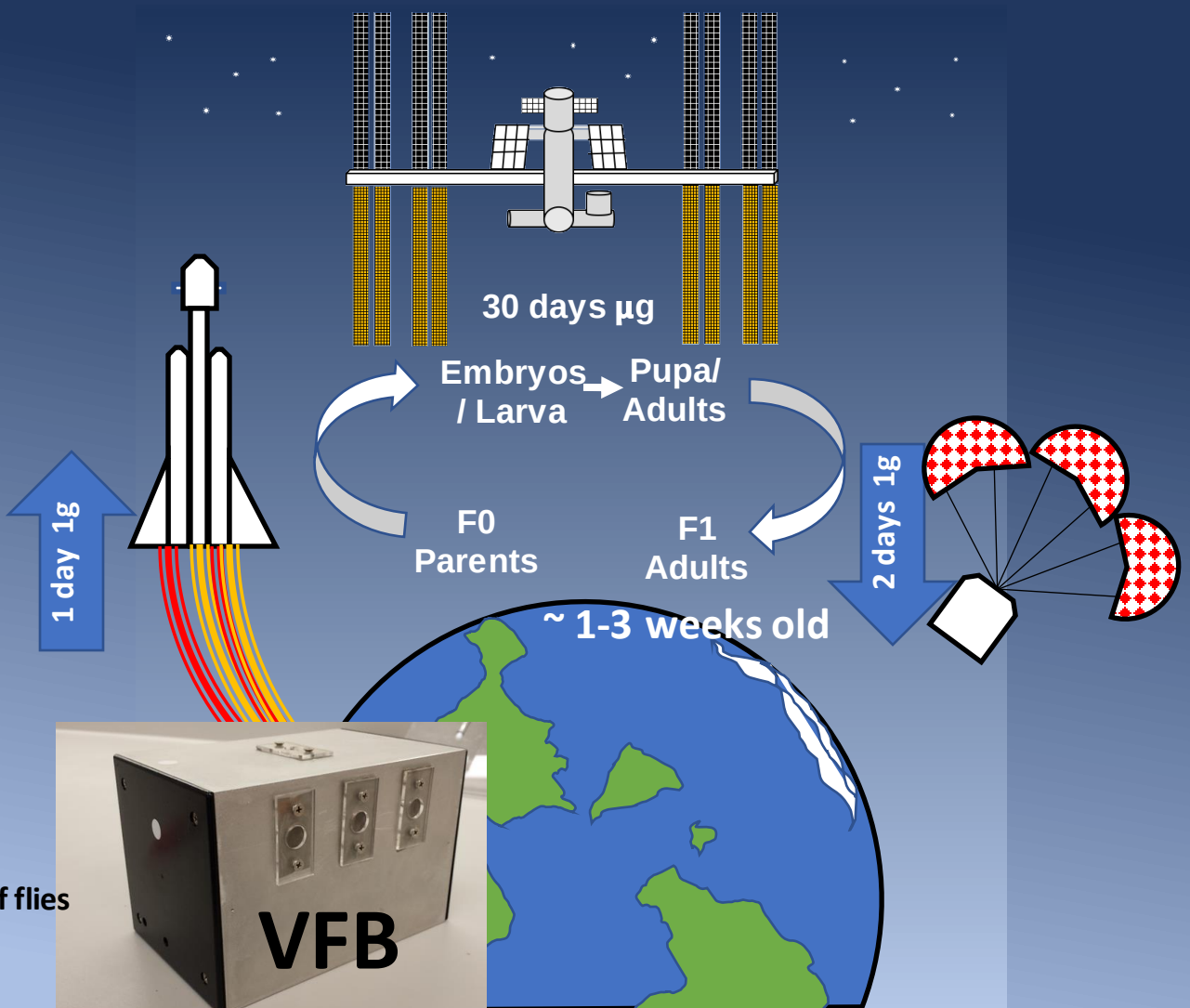
Flies in Space Protocol

F_0 Parents



This program is delayed in Space

Flies in Space Protocol

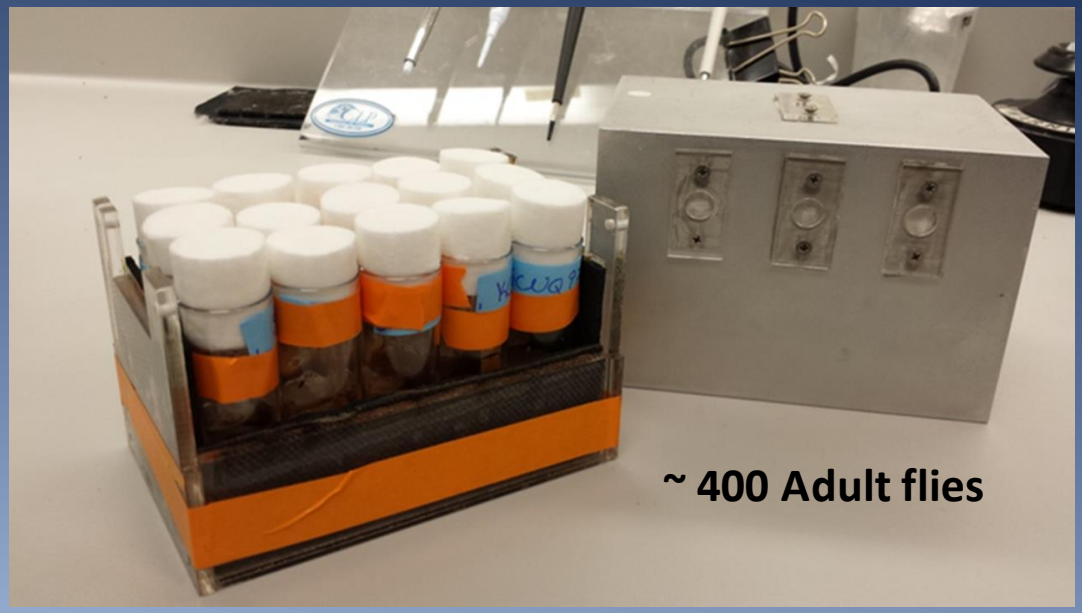


15 Vials of flies

Flies in Space Protocol

~35 day
Mission

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



Flies in Space Protocol

~35 day Mission

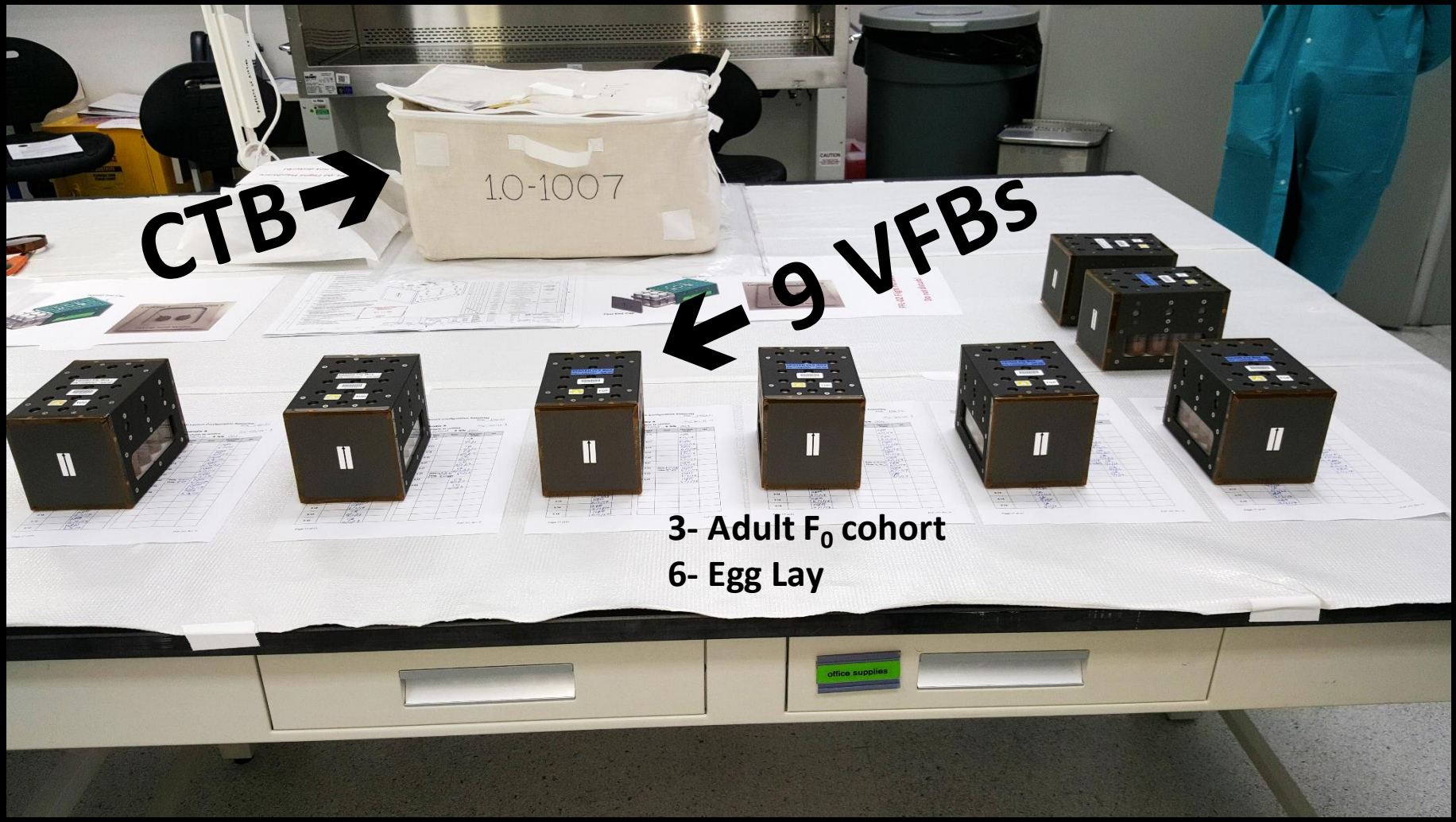
Multigenerational / Multi-Age Cohort (0-3 wks)
F0? **+ F1 +** F2?

24 hr Egg Lay

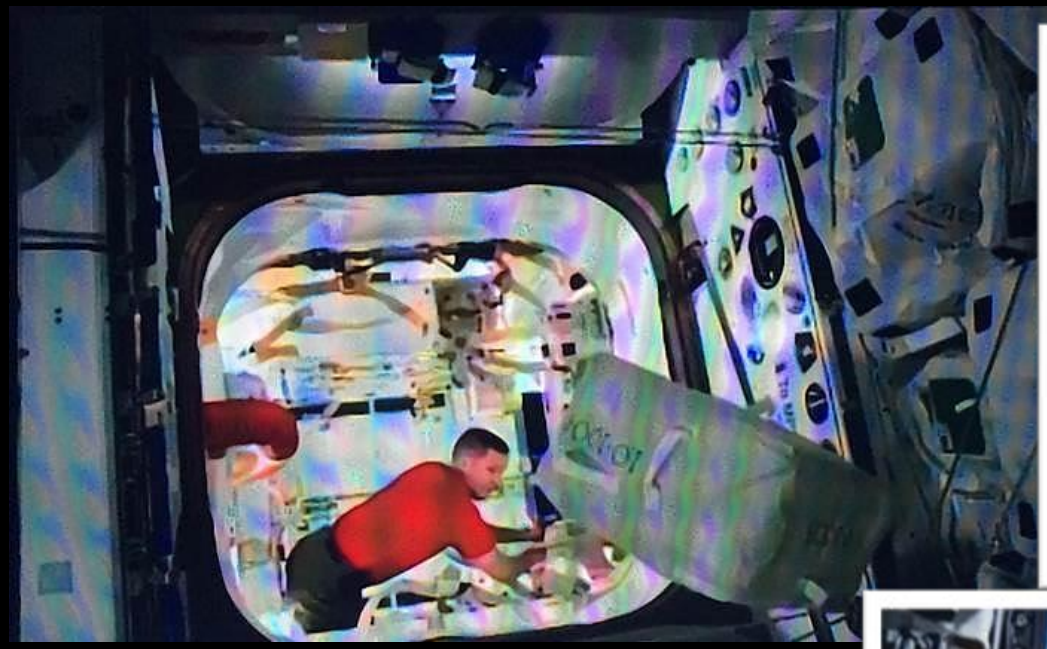
Remove Parents before flight

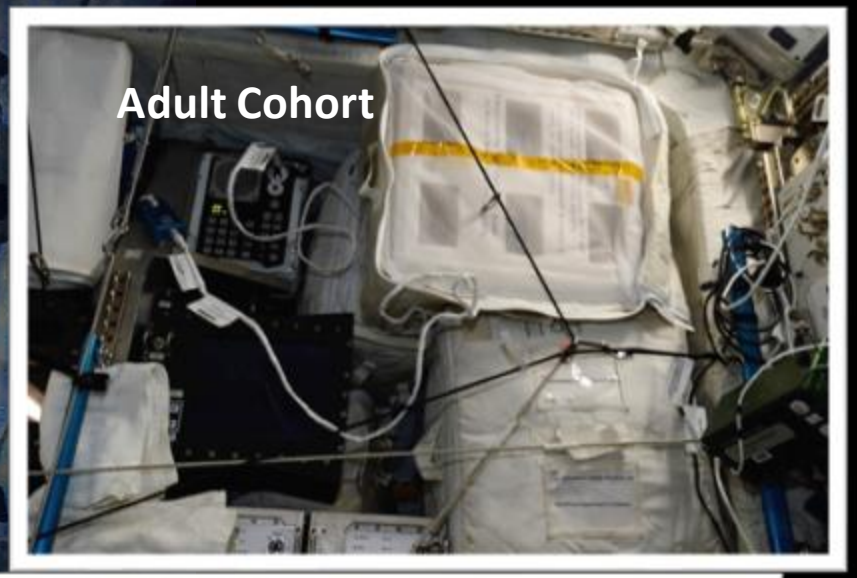
2.5 -3 week old F1 Cohort
F2 larva and a few adults, often identifiable as "virgins"

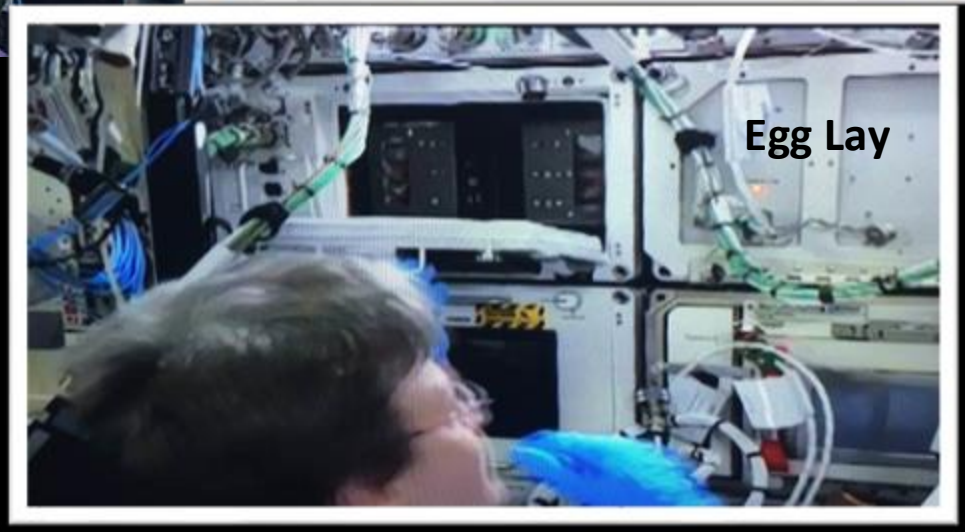
Space X 11 Experiment



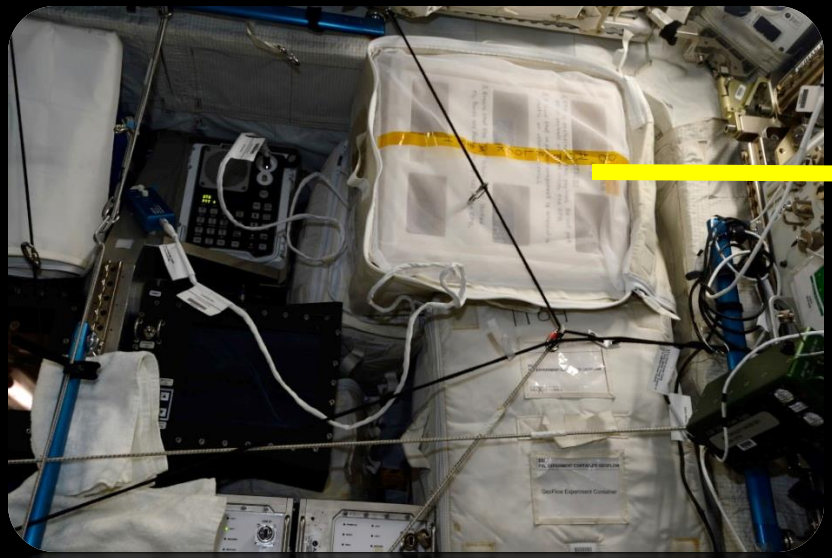
Space X 11 Experiment

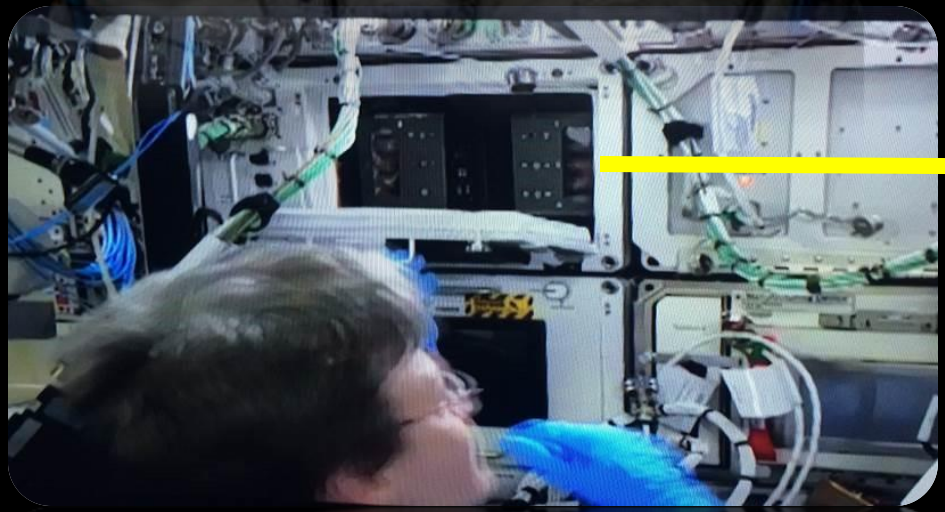


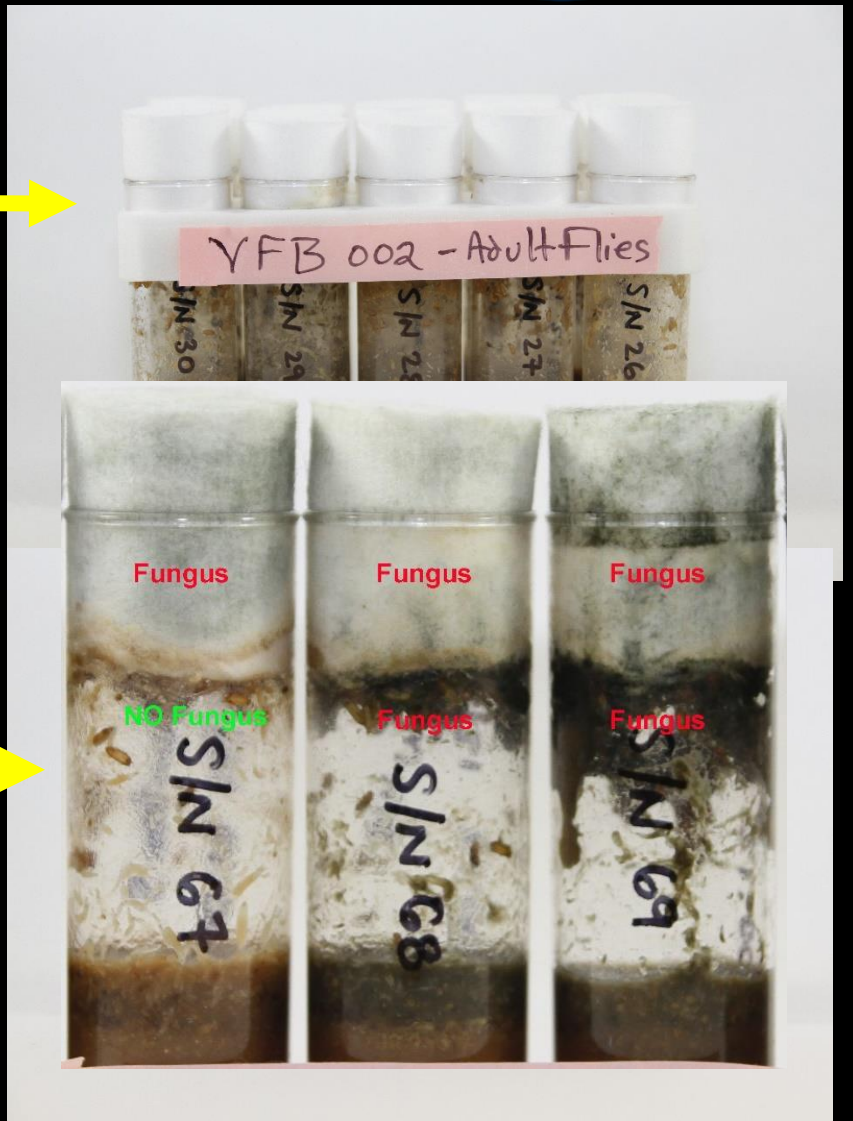




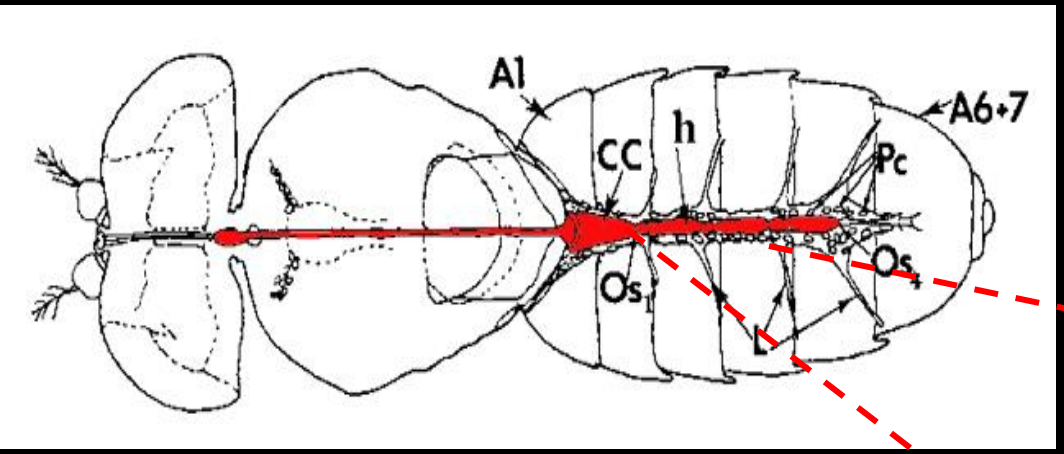
Space X 11 Experiment

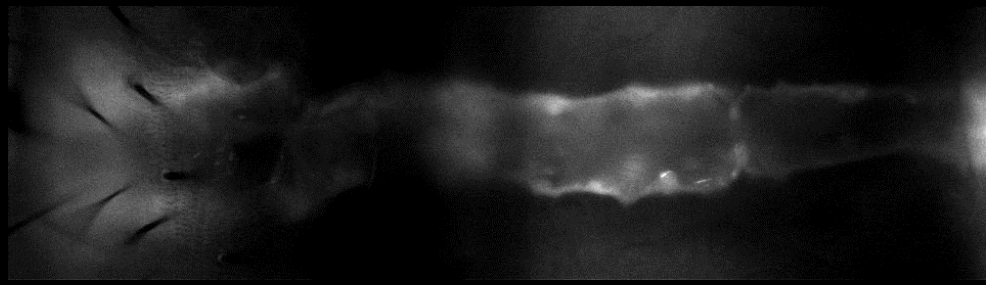






- Effects on Heart Function

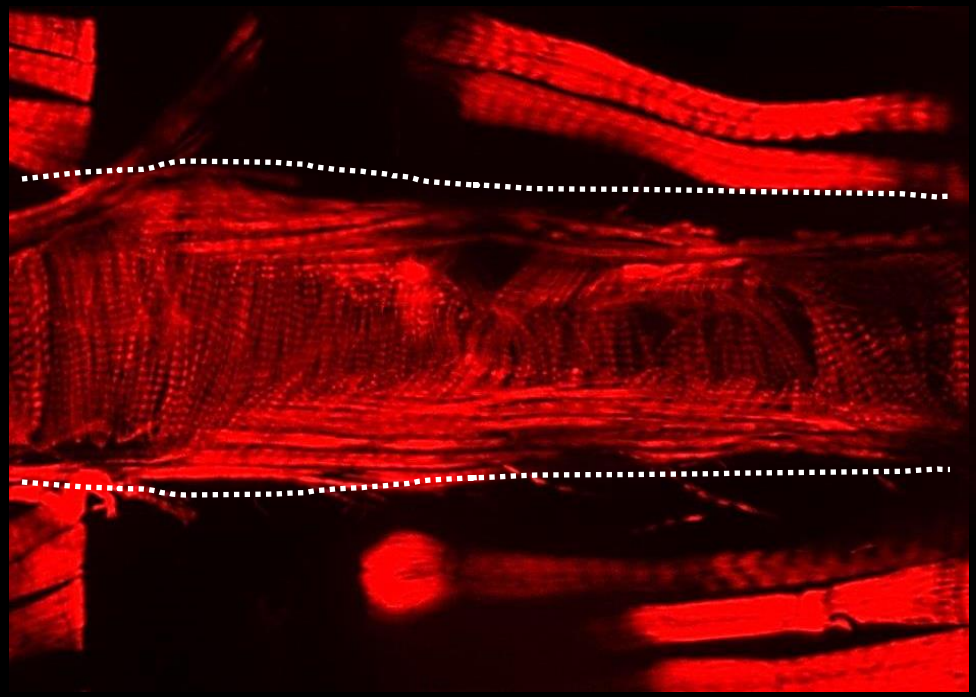




- Effects on Cardiac Structure

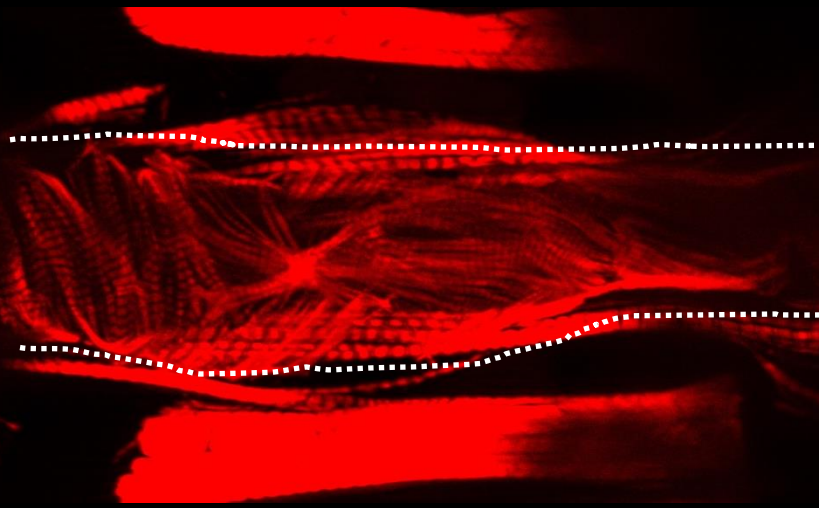
Actin – muscle protein

Ground Control



Space Flown

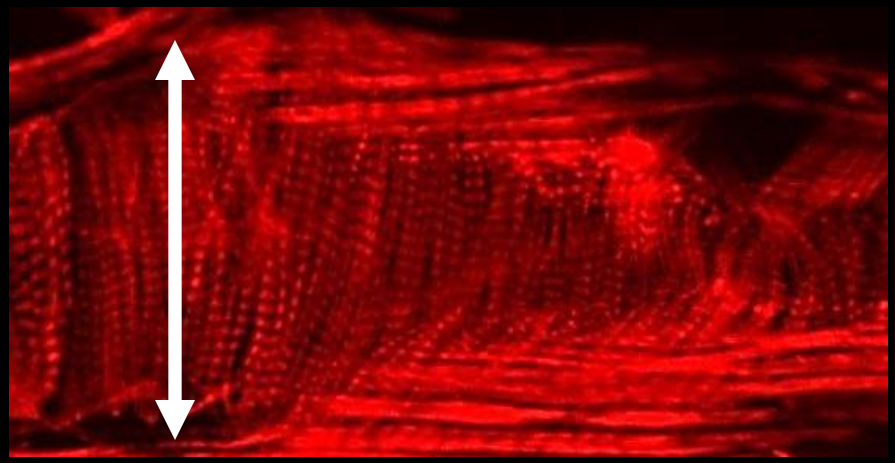
Reduced Size

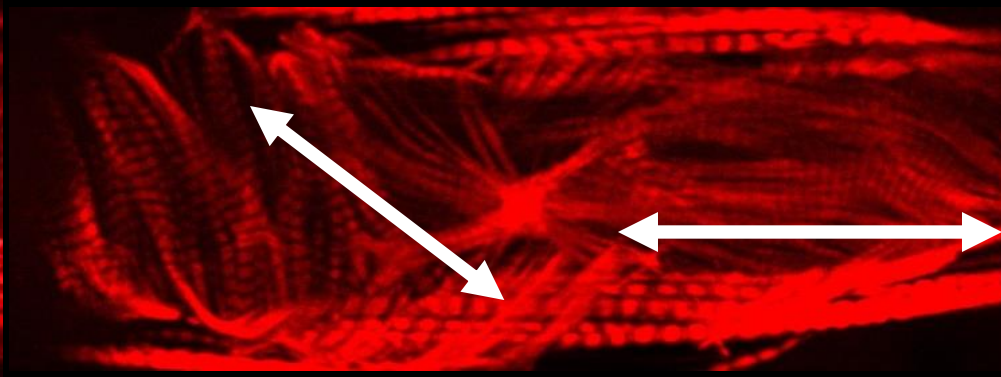


Walls et al, Cell Report 2020

- Effects on Cardiac Structure

Actin – muscle protein





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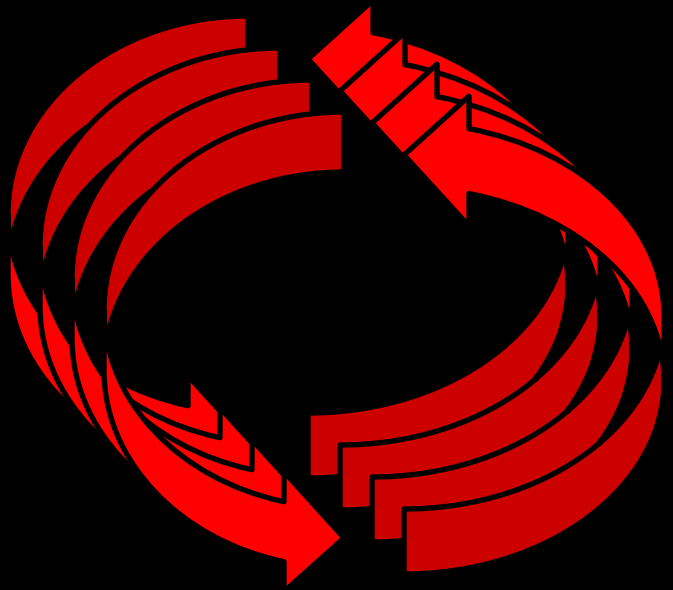

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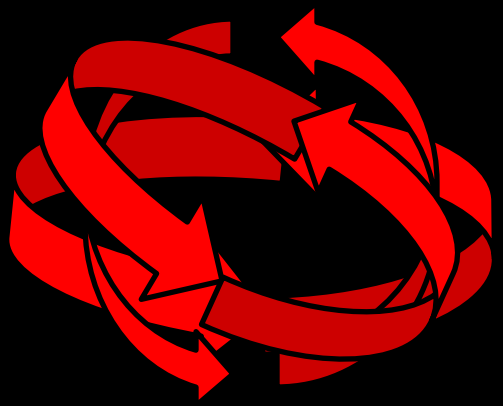

- Effects on Cardiac Structure

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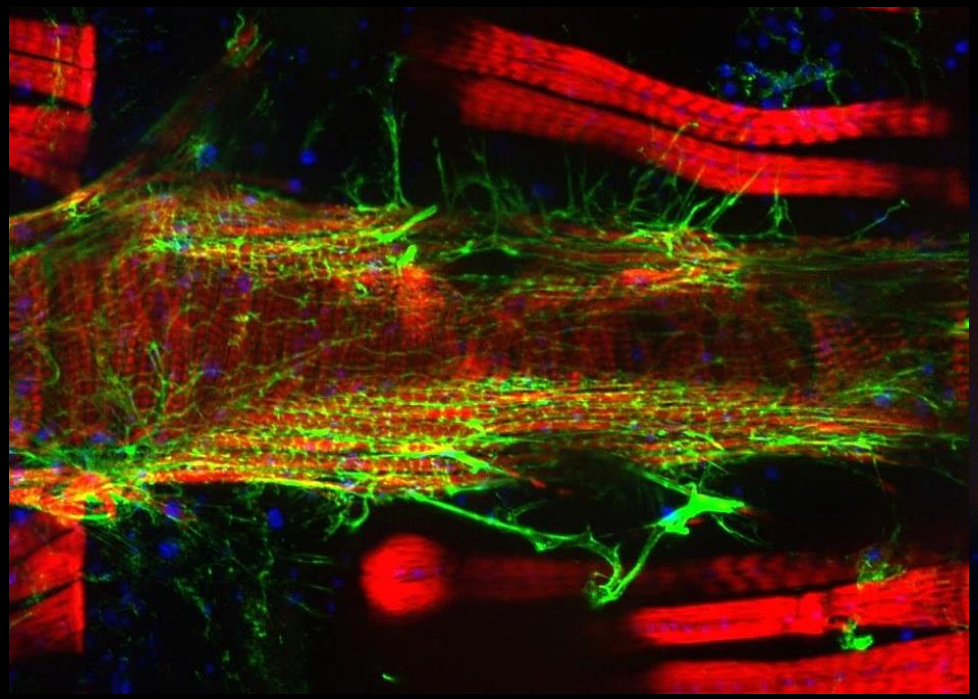

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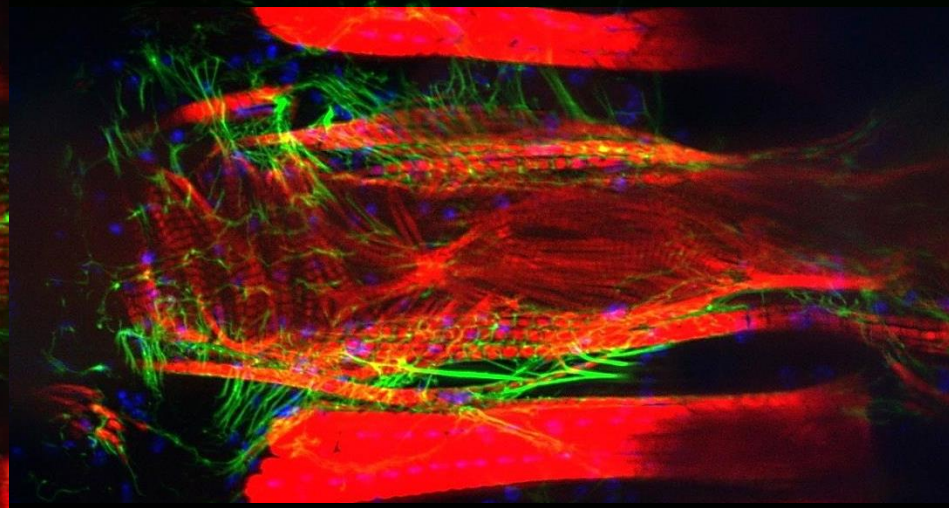


RNA Seq showed significant DOWN regulation of muscle proteins and Collagens

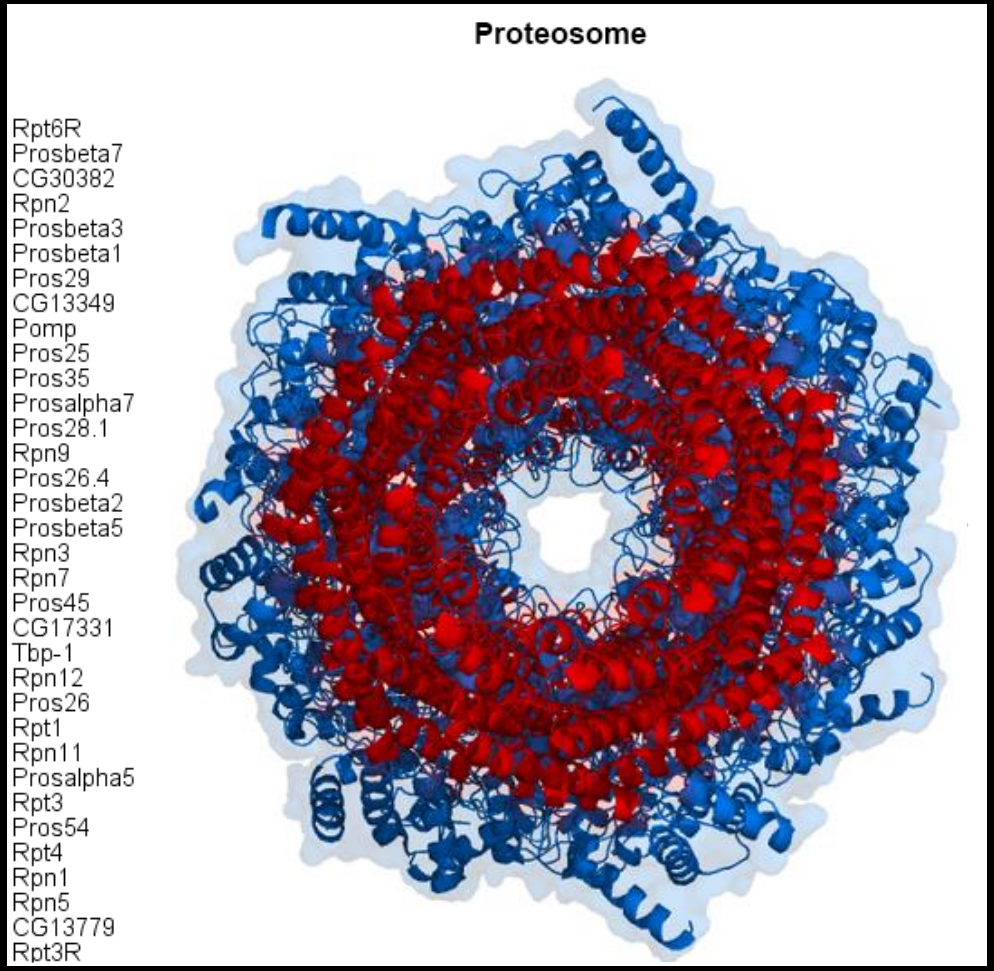
Walls et al, Cell Report 2020

- Effects on Protein Homeostasis

Proteasome / Garbage Disposer

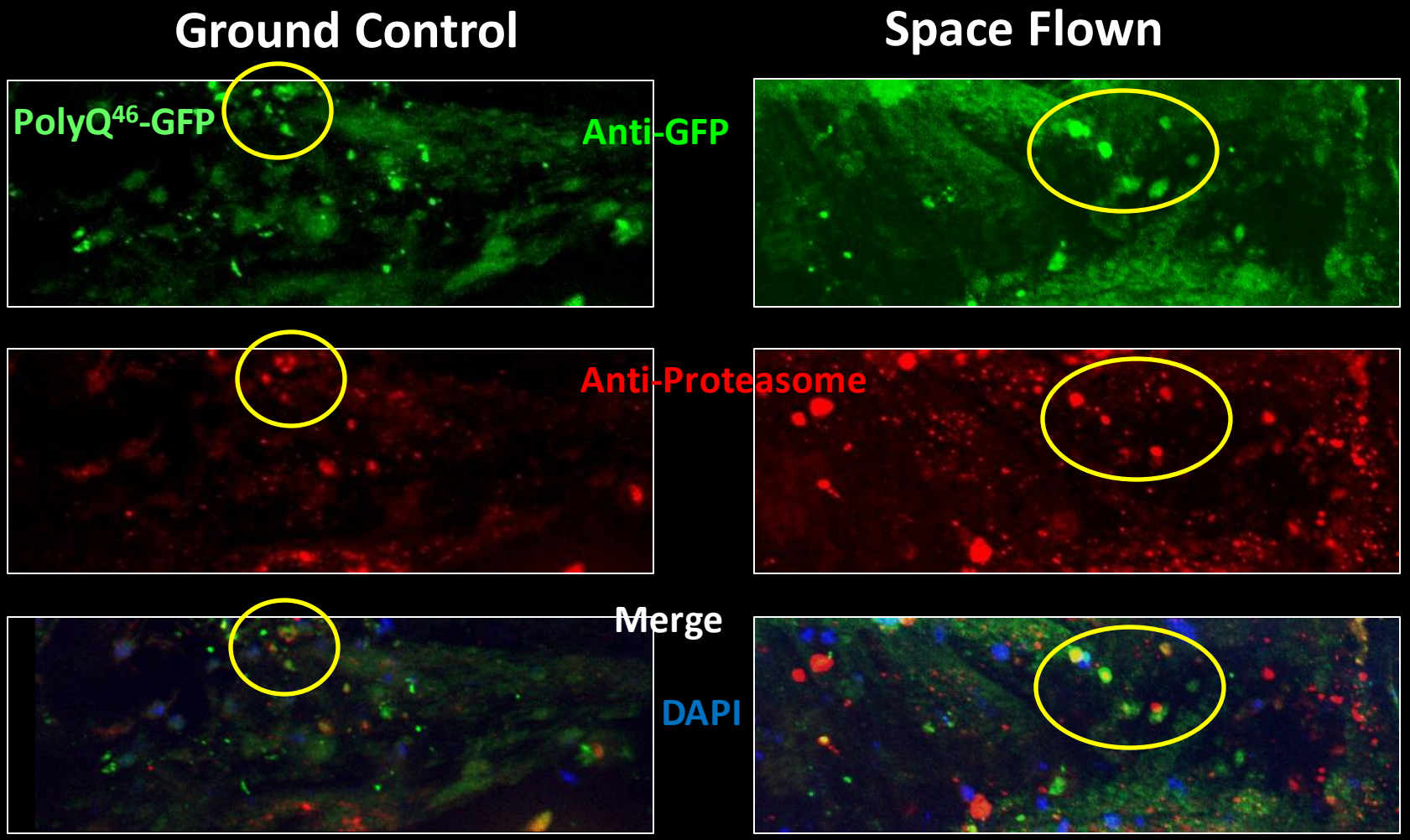
Increased Gene Expression

Reduced Gene Expression

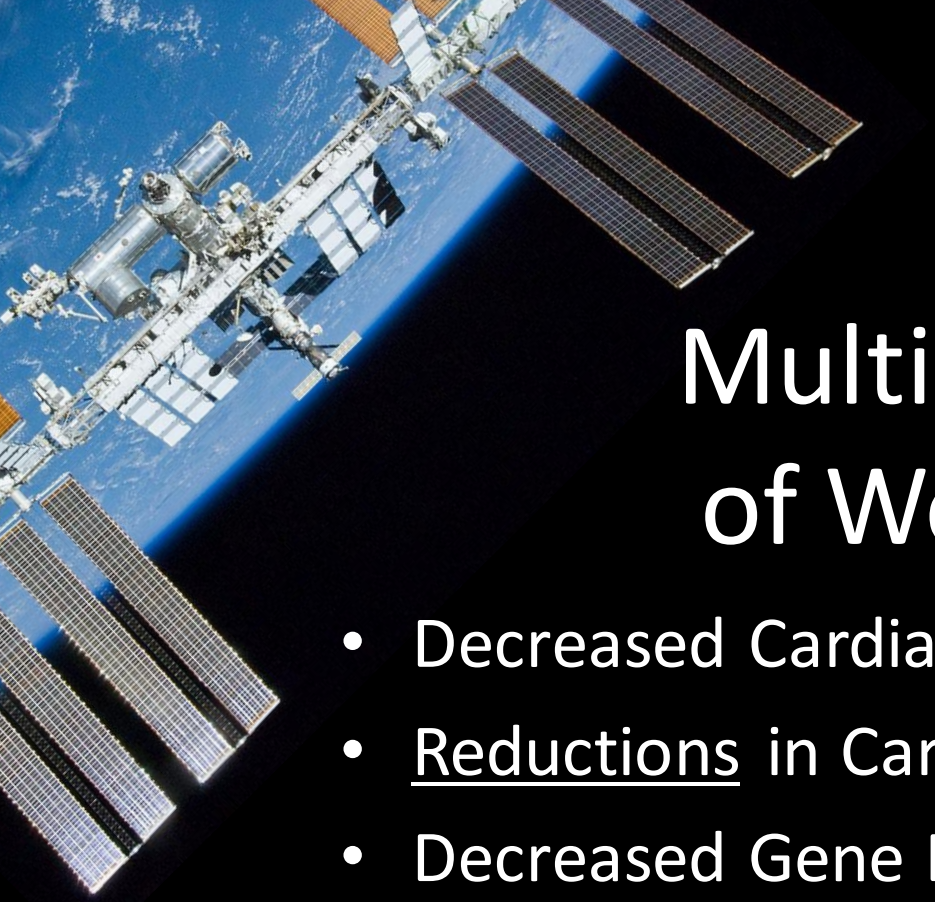


Walls et al, Cell Report 2020

Prolonged Weightlessness Increases Proteasome Number and Protein Plaques



Walls et al, Cell Report 2020

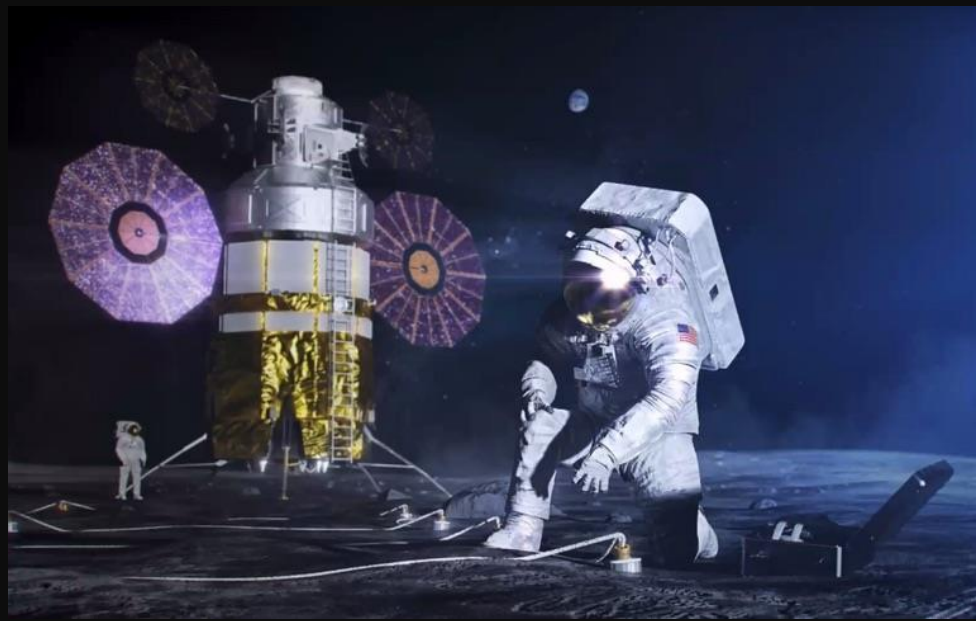


Multi-organ Effects of Weightlessness

- 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

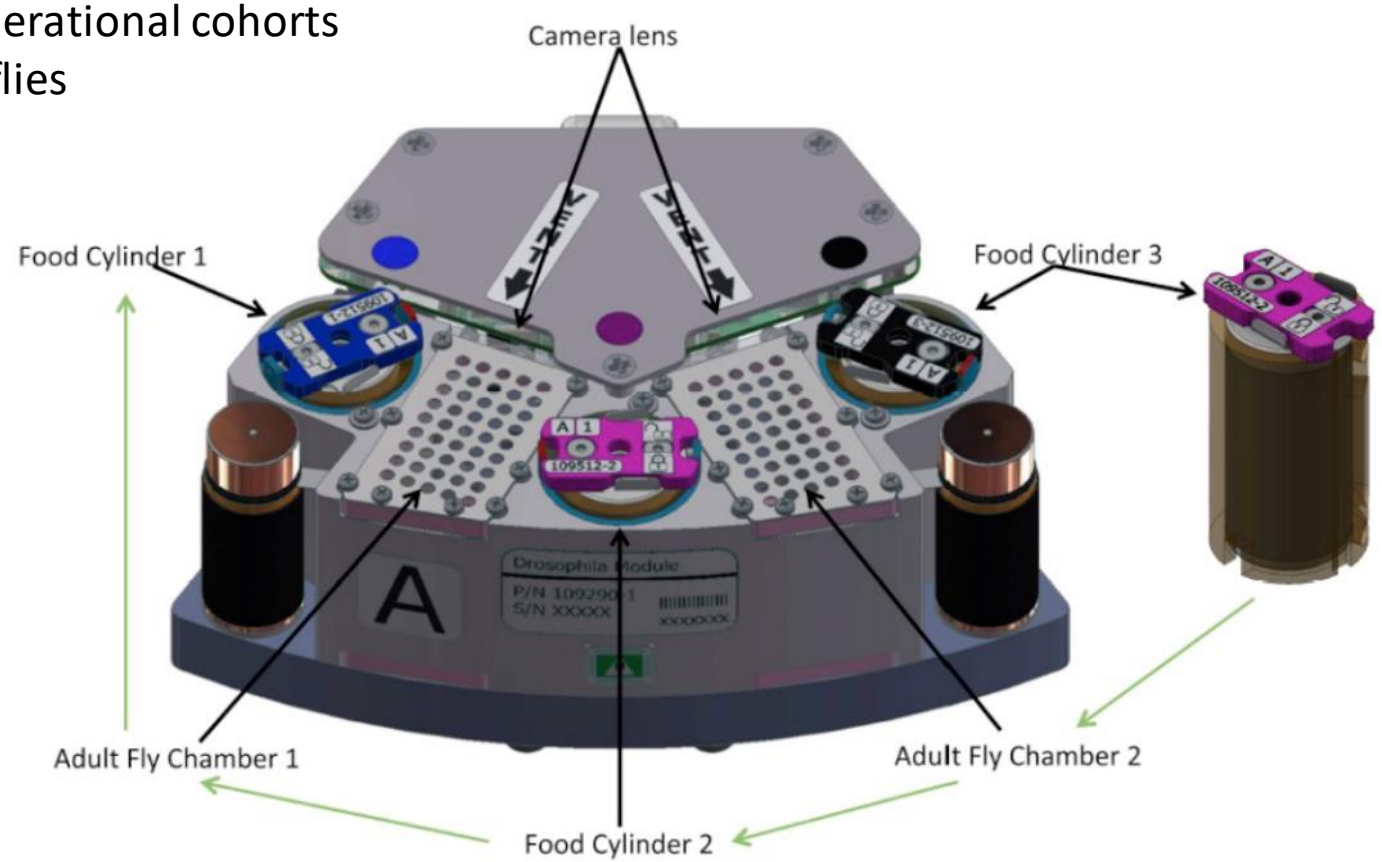
Does altered gravity elicit an All or None response?

- 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)

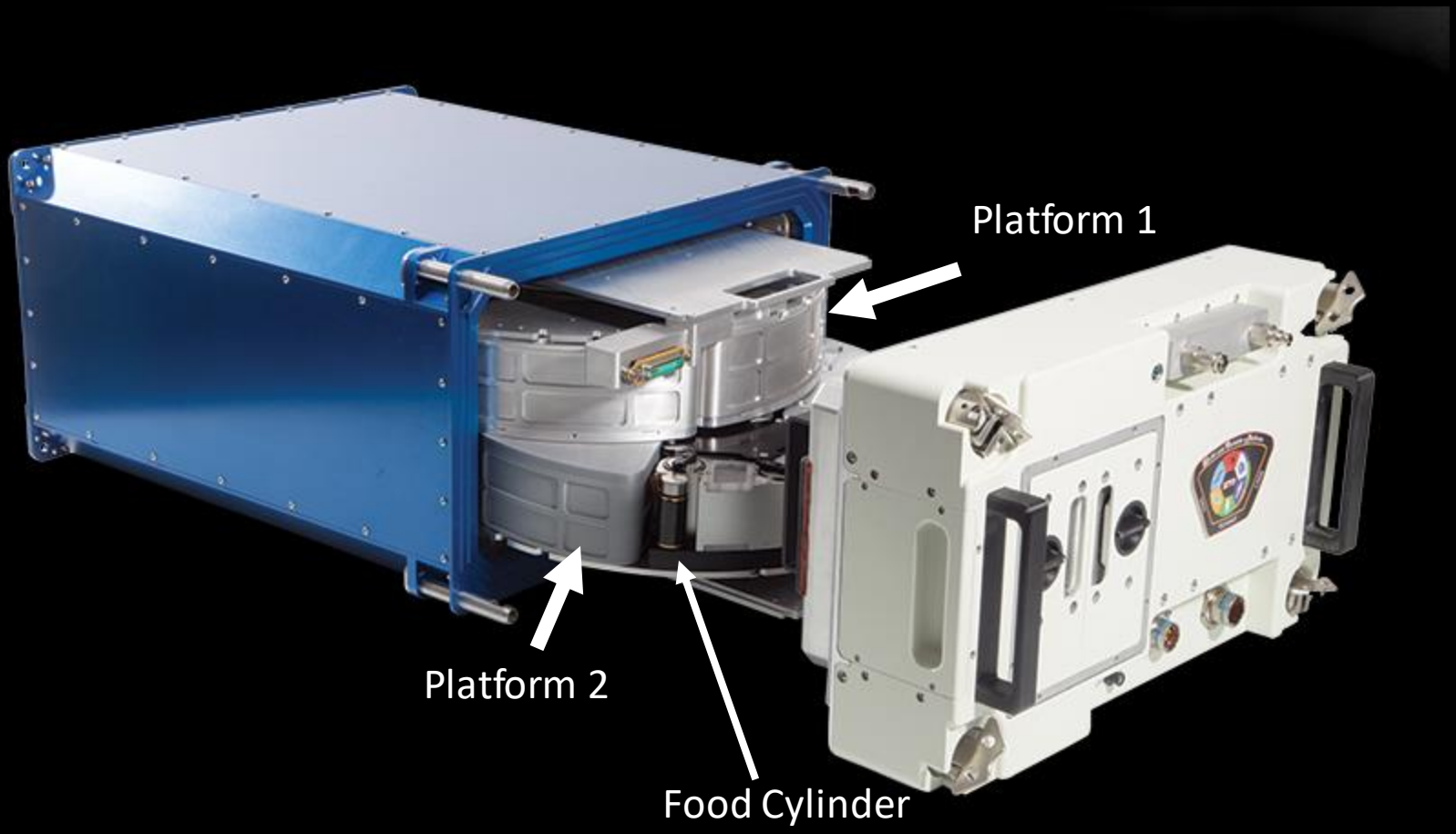


Allows for separation of generations

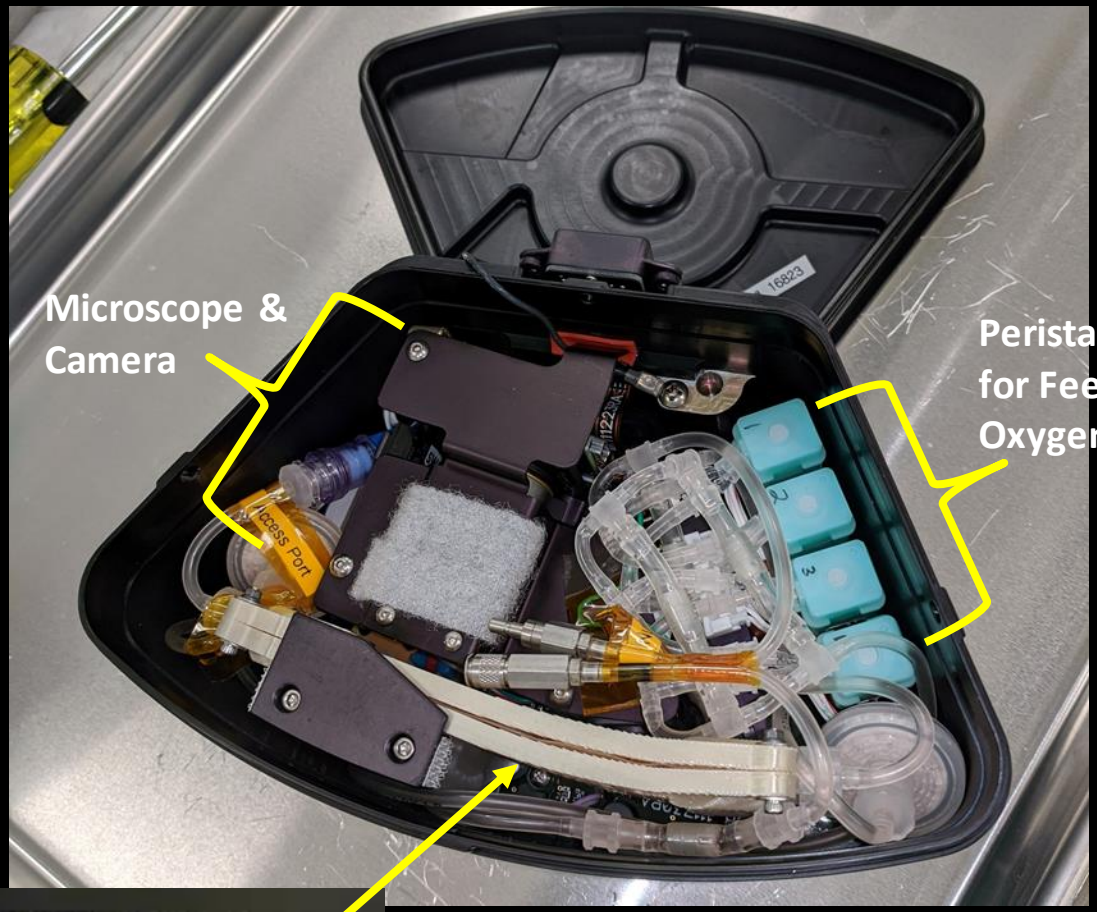
- Light cycle control
- Filming for behavior assessment
- Fixation of generational cohorts
- Return of live flies



Multi-use Variable-g Platform MVP



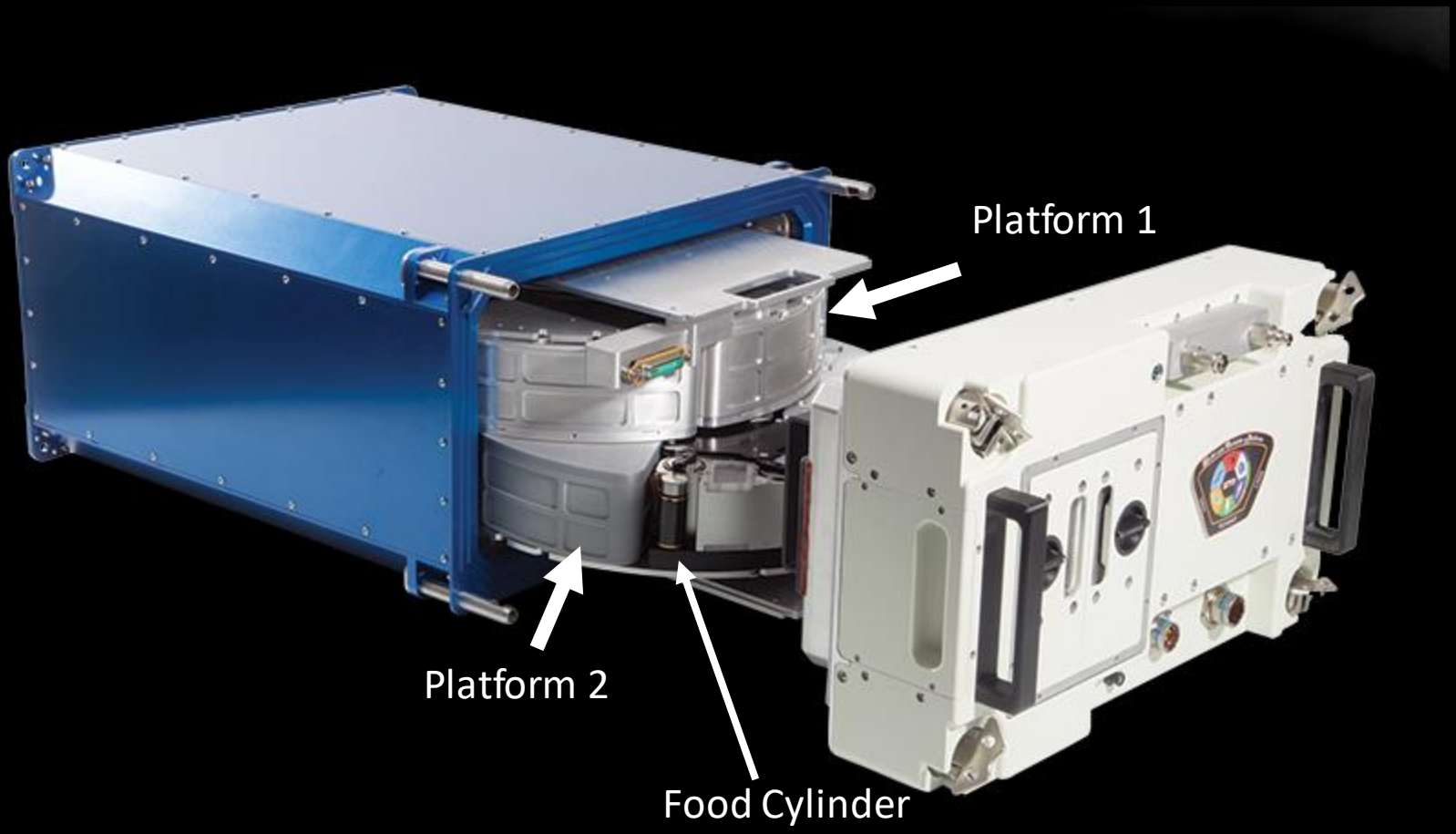
C. Elegans Hardware Overview



Culture Bag in imaging frame

Nathanial Szewczyk Lab – Ohio University

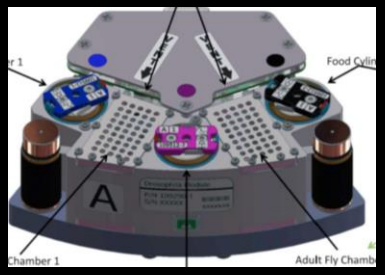
Multi-use Variable-g Platform MVP



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

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

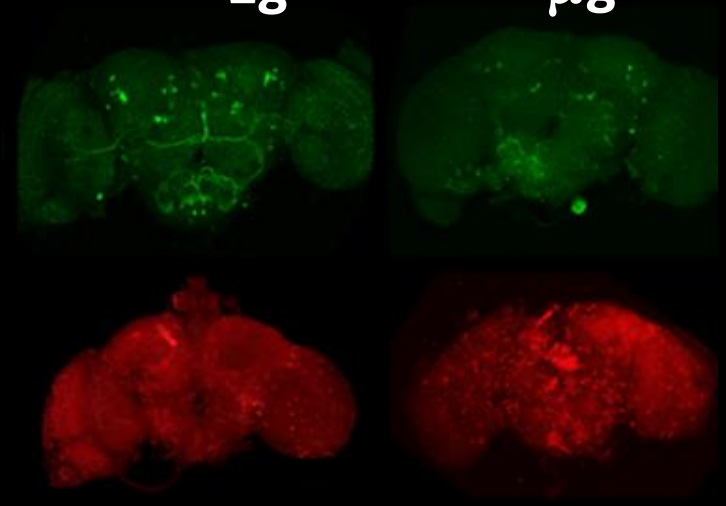
Micro g



Comparison of gravity effects

1g μg

Fly Brain



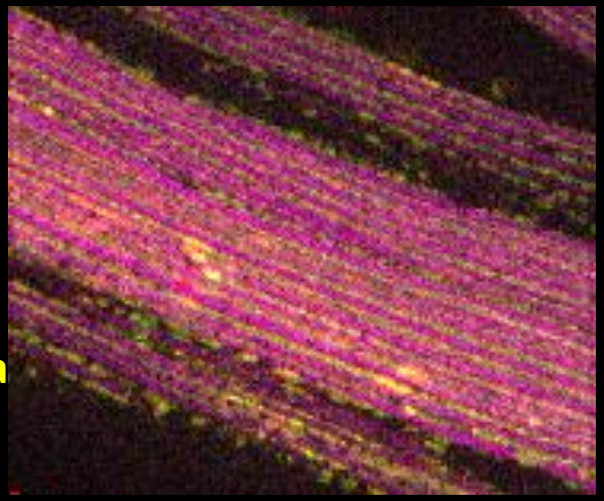
Dopaminergic Neuron Number
-Tyrosine Hydroxylase

Apoptosis - Cleaved Caspase 3

Janani Iyer, Siddhita Mhatre & Sharmila Bhattacharya – NASA, Ames

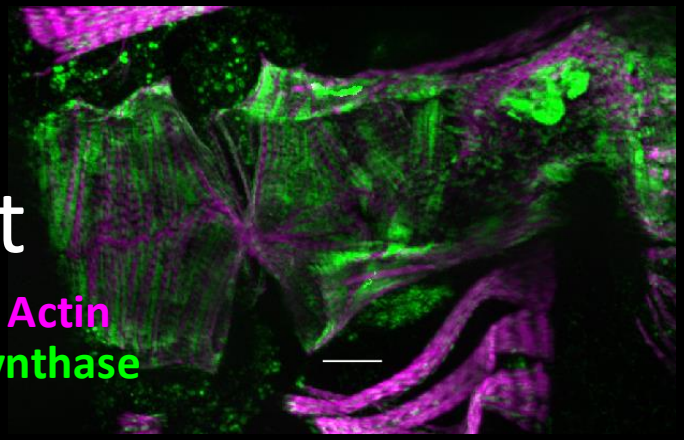
Fly Muscle

Muscle Actin
Mitochondria



Fly Heart

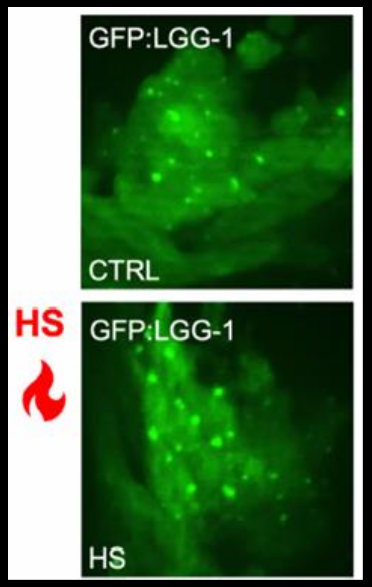
Muscle Actin
ATP Synthase



Katja Birker & Rolf Bodmer – SBP Medical Discovery Institute

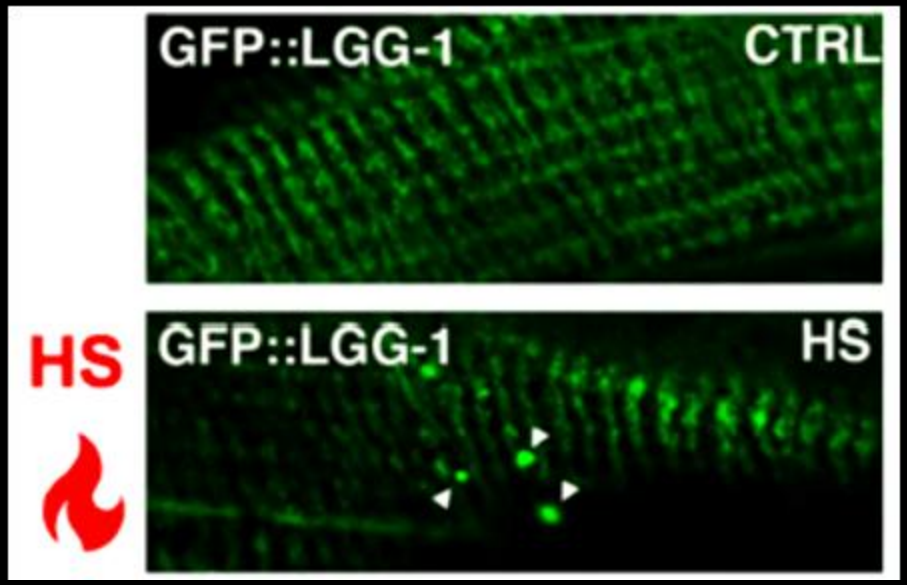
Comparison of gravity effects

Worm Brain



Apoptosis Marker - Lgg1/Atg8 GFP

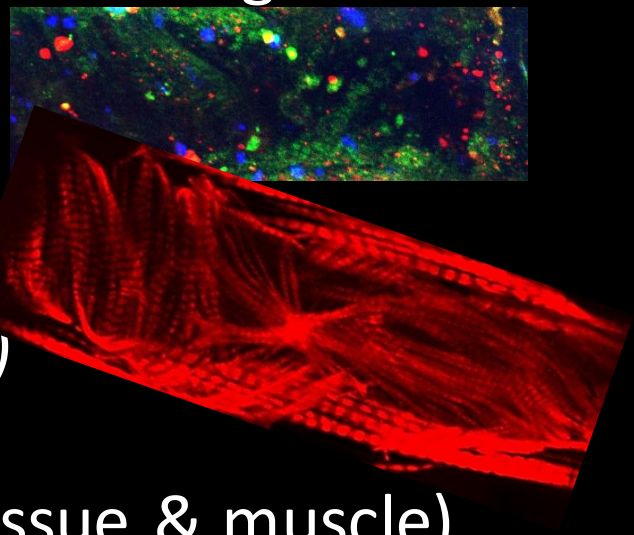
Worm Body Wall Muscle



Caroline Kumsta & Malene Hansen - SBP Medical Discovery Institute

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?

Acknowledgements

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Janani Iyer, PhD

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