RCCNAUSTIN2019

Resilience and Reserve in Aging

Animal Models of Recovery from Surgery

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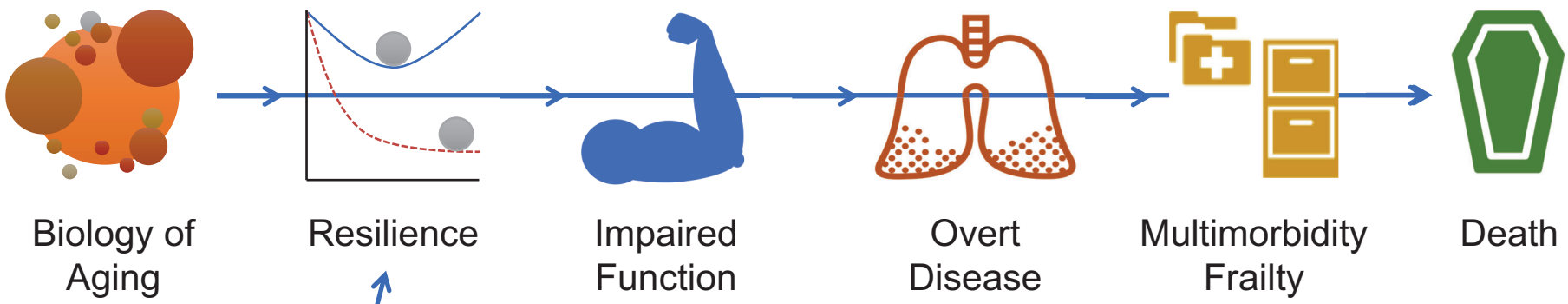
Targeting the Biology of Aging

Paradigms for Translation



Can we develop preclinical models to test resilience?

NIA initiative in partnership with Austad, Huffman, Ladiges, Richardson, and Salmon

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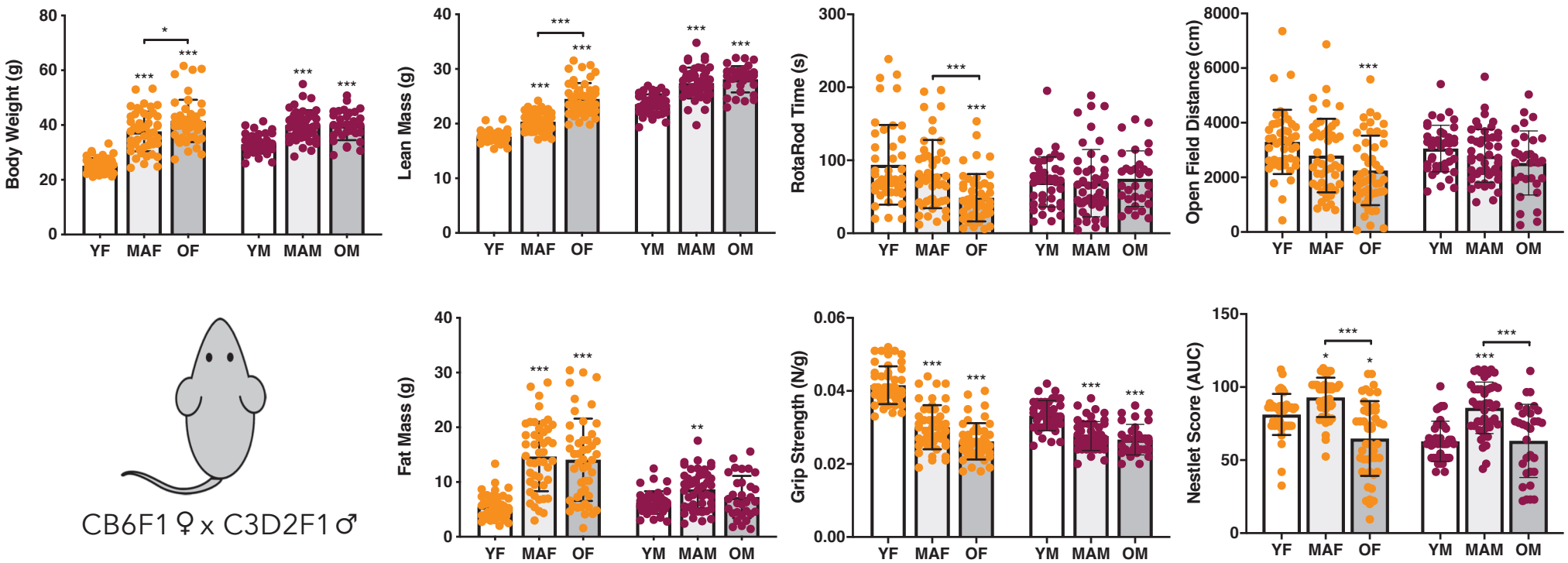
LeBrasseur, *J of Gerontology*, 2017

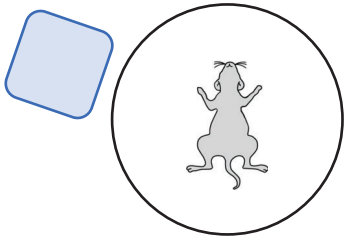
Phenotypes of Younger (6 mo), Middle-Aged (12 mo), and Older (20 mo) 4-way Cross Study Participants

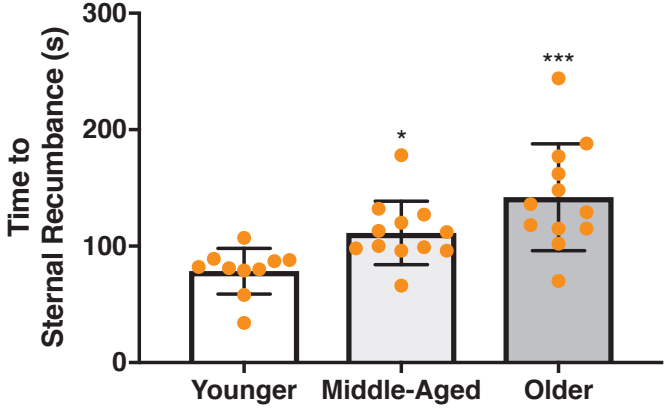


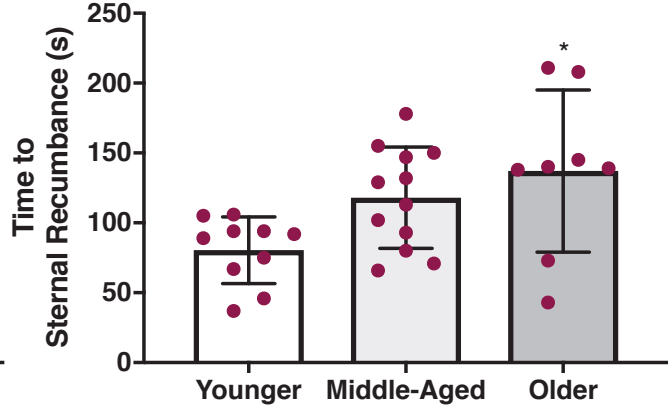
Brown, Mazula, Miller, Maleki…*unpublished*

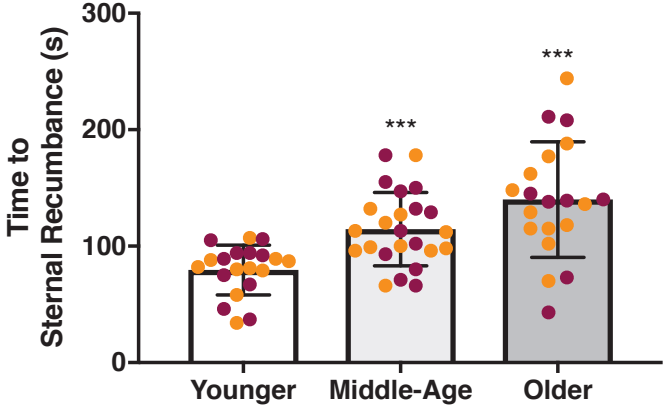
Anesthesia Challenge

Anesthesia Challenge: 5 minutes exposure to 4% isoflurane. Time to sternal recumbence in younger, middle-aged, and older female (●) and male (●) mice. (Also, circle escape, body weight….)









Simple. Age-sensitive. Higher variability in older mice.

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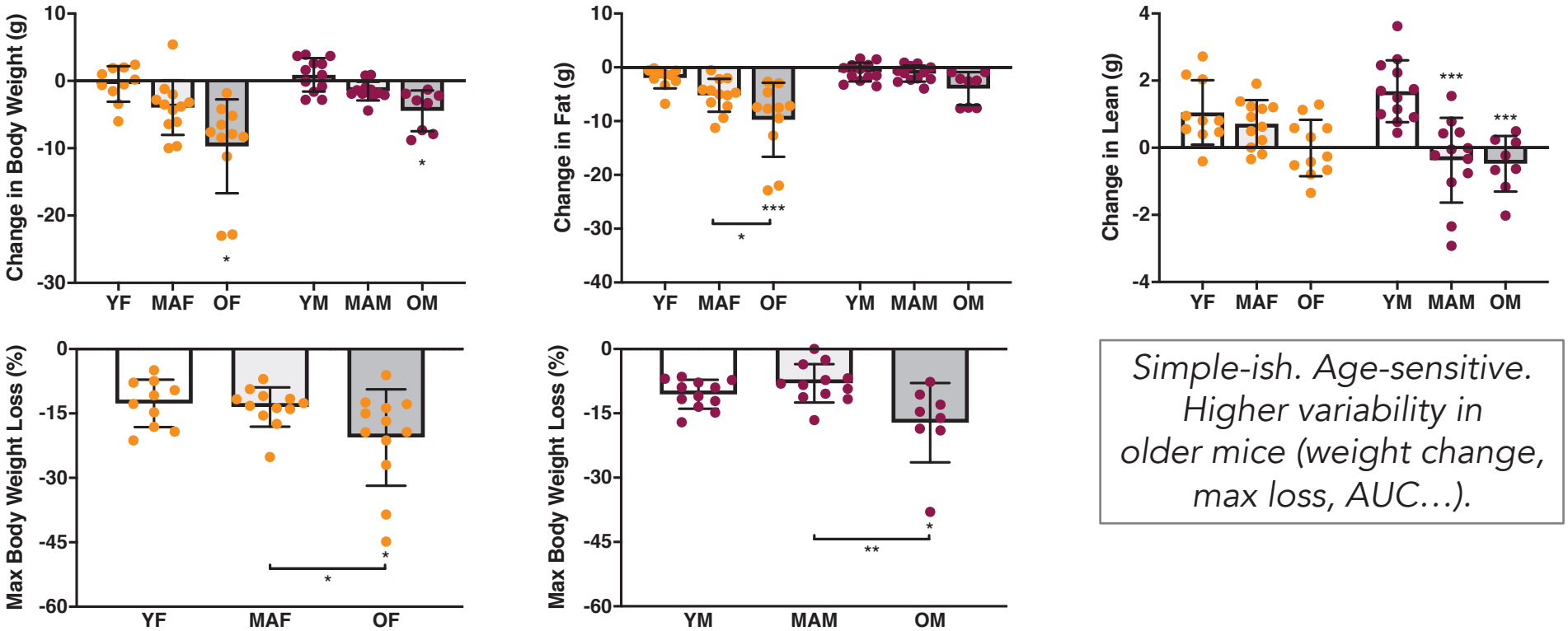
Brown, Mazula, R. Miller, J. Miller, Maleki…*unpublished*

Cisplatin Challenge

Cisplatin Challenge: One 5-day cycle of cisplatin (2 mg/kg/day). Changes in body weight and composition between baseline and 30-days after challenge in younger, middle-aged, and older mice.

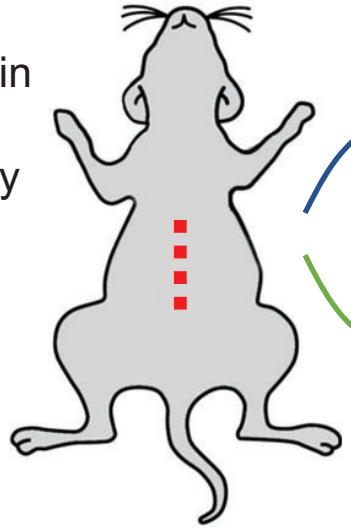


Simple-ish. Age-sensitive. Higher variability in older mice (weight change, max loss, AUC…).

Brown, Mazula, J. Miller, R. Miller, Maleki…*unpublished*

Surgery Challenge

Physical Challenge
- 2% isoflurane, 20 min
- 2 cm incision
- 2 min exposed cavity
- 2 layers of sutures



Acute Outcome Measures
- Body temperature
- Time to sternal recumbence
- Time to ambulate

Longer-term Outcome Measures
- Wound healing
- Body weight
- Body composition
- Physical activity

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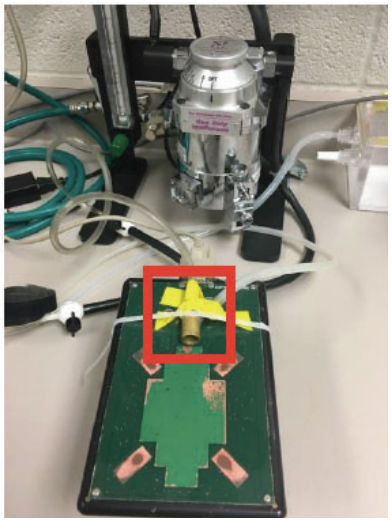
Surgery Challenge

Heated anesthesia platform



Surgical procedure
Body temp

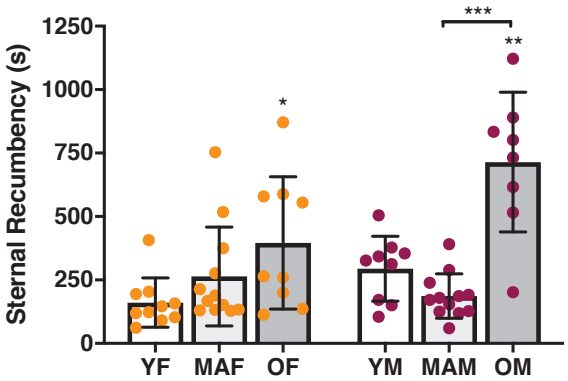
Sternal recumbence
Time to ambulate

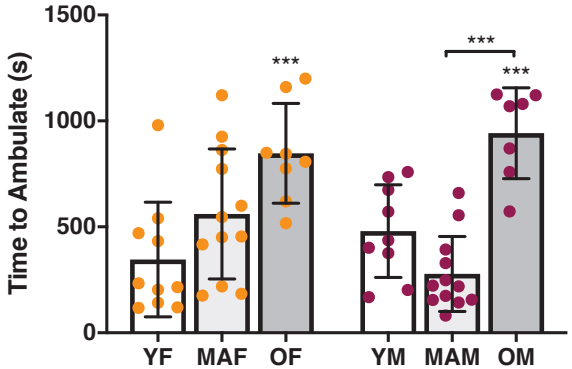
Younger
Day 0 Day 1 Day 8

Older
Day 0 Day 1 Day 8

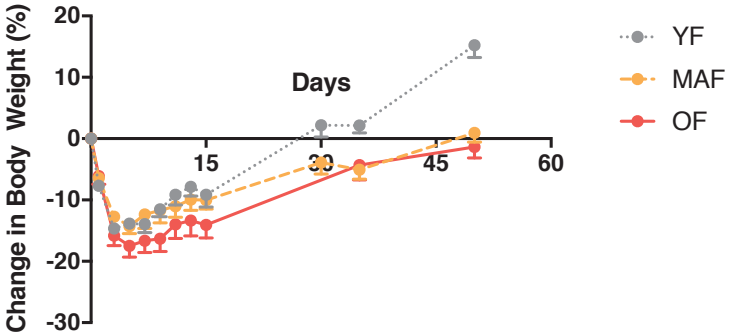
Brown, Mazula, J. Miller, Roos, Maleki, B. Zhang…*unpublished*

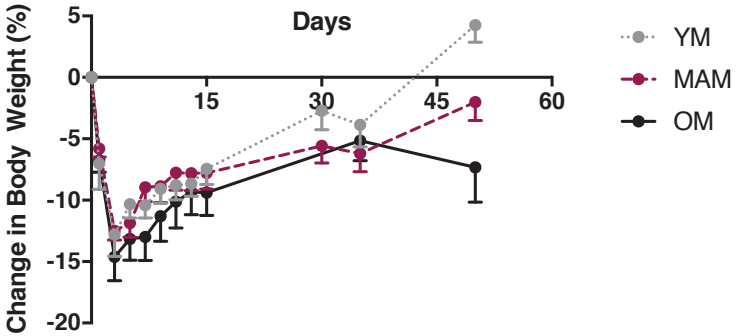
Surgery Challenge in Younger, Middle-aged, and Older mice





More complex challenge. Some outcomes age-sensitive with higher variability in older mice.





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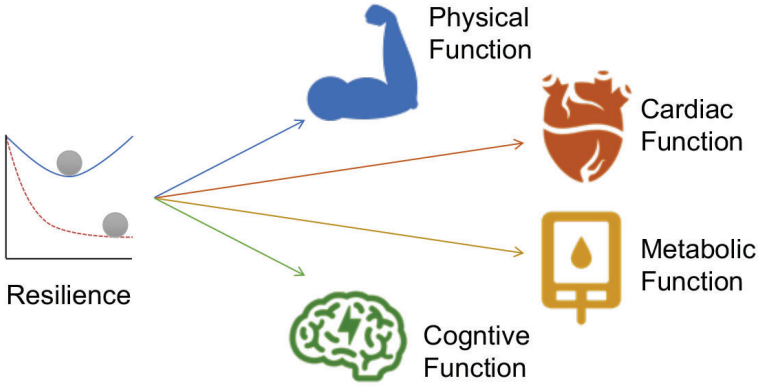
Murine Models of Physical Resilience

- Potential for anesthesia, chemotherapy, and surgical challenges based on:
  - **Age-related changes** in select measures of resilience
  - Higher **variability in older mice**, indicative of more and less resilient
  - Translatability
  - Disease agnostic-ity; **integrate multiple physiological systems**
  - Relative simplicity, scalability
- Mid-life (12 mo) resilience **predictive** of later-life (18 & 24 mo) **healthspan**? **Lifespan?** In collaboration with Rich Miller.
  - Encouraging preliminary data
  - A Texas-sized bucket of data



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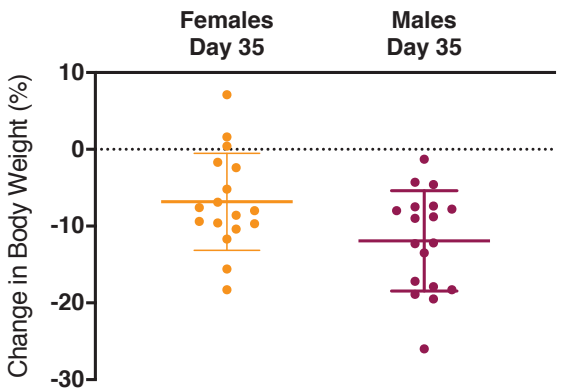
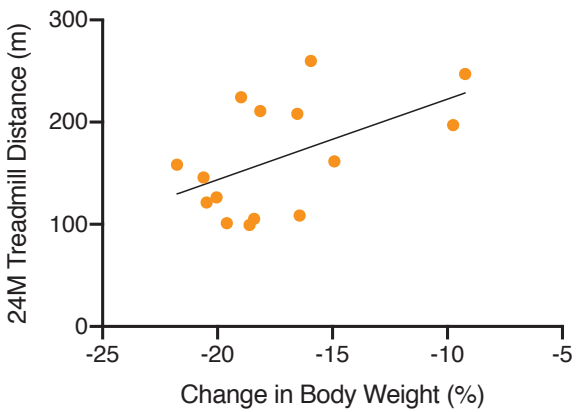
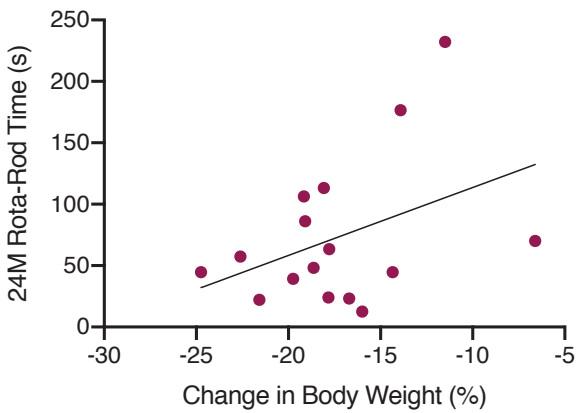
Mid-life Resilience as a Determinant of Later-Life Health







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  - Encouraging preliminary data
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- Can interventions **improve** later-life resilience? **Stay tuned….**

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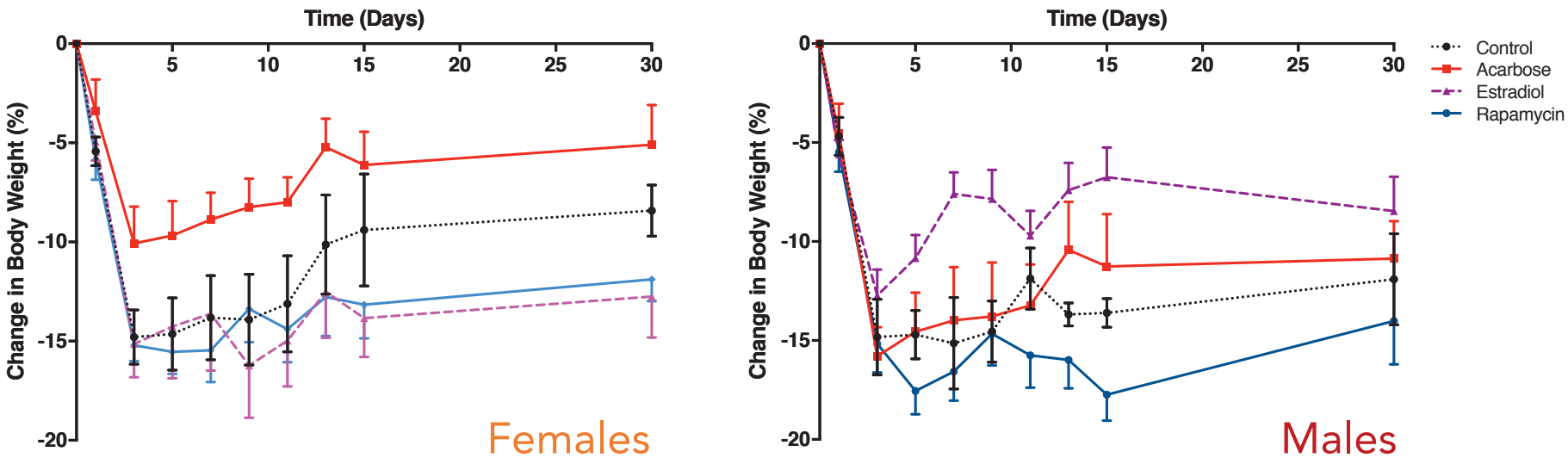
Interventions to Optimize Resilience in Older Mice

8 weeks prior to surgical challenge, 8 weeks post

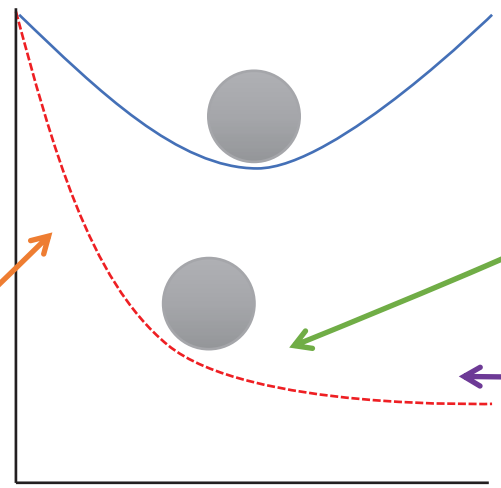


Targeting the Biology of Aging and Resilience

Paradigms for Translation

Biological age as a **predictor**
(Posters: 830-67 & 68)

Interventions as
boosters "prehab"
(Poster: 835-84;
exercise and TRF)



Interventions as
rebounders

Interventions as
rehabilitators

Acknowledgements

Team Members
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