Resilience and Reserve in Aging
Animal Models of Recovery from Surgery

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Can we develop preclinical models to test resilience?

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

LeBrasseur, J of Gerontology, 2017
Phenotypes of Younger (6 mo), Middle-Aged (12 mo), and Older (20 mo) 4-way Cross Study Participants

CB6F1 ♀ x C3D2F1 ♂

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unpublished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....)


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unpublished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.

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**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Brown, Mazula, J. Miller, R. Miller, Maleki…unpublished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
## Surgery Challenge

<table>
<thead>
<tr>
<th>Heated anesthesia platform</th>
<th>Surgical procedure Body temp</th>
<th>Sternal recumbence Time to ambulate</th>
<th>Younger Day 0 Day 1 Day 8</th>
<th>Older Day 0 Day 1 Day 8</th>
</tr>
</thead>
</table>

Brown, Mazula, J. Miller, Roos, Maleki, B. Zhang… unpublished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

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unpublished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

  - Encouraging preliminary data
  - A Texas-sized bucket of data
Mid-life Resilience as a Determinant of Later-Life Health
Murine Models of Physical Resilience

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• Can interventions improve later-life resilience? Stay tuned…. 
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
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