Molecular Underpinnings of Resilience During Aging

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  - None

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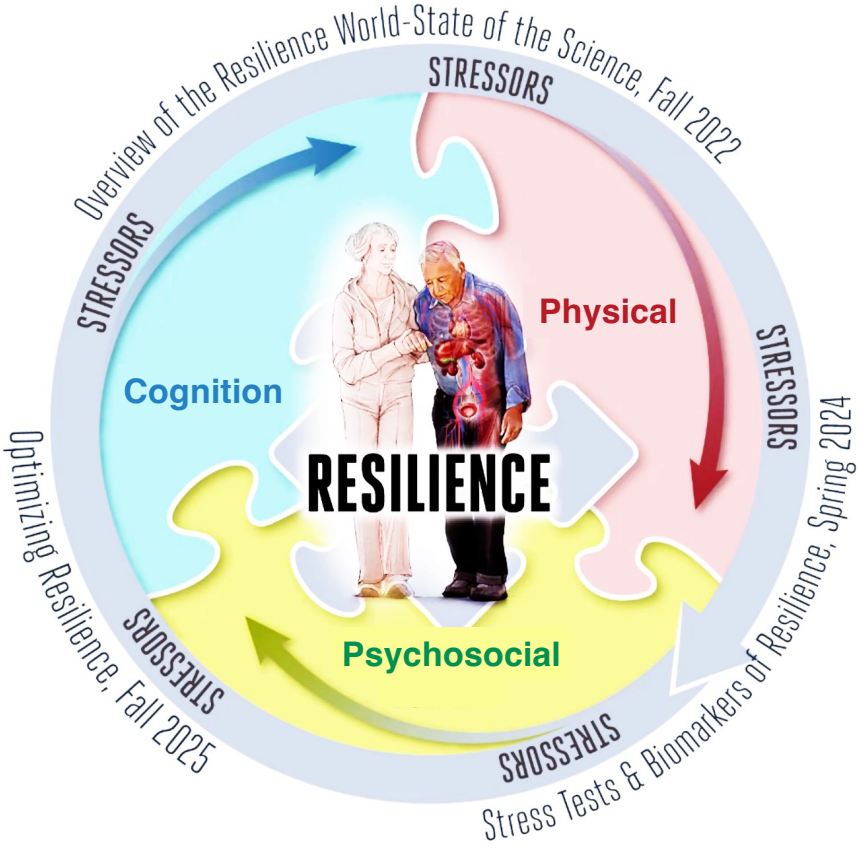
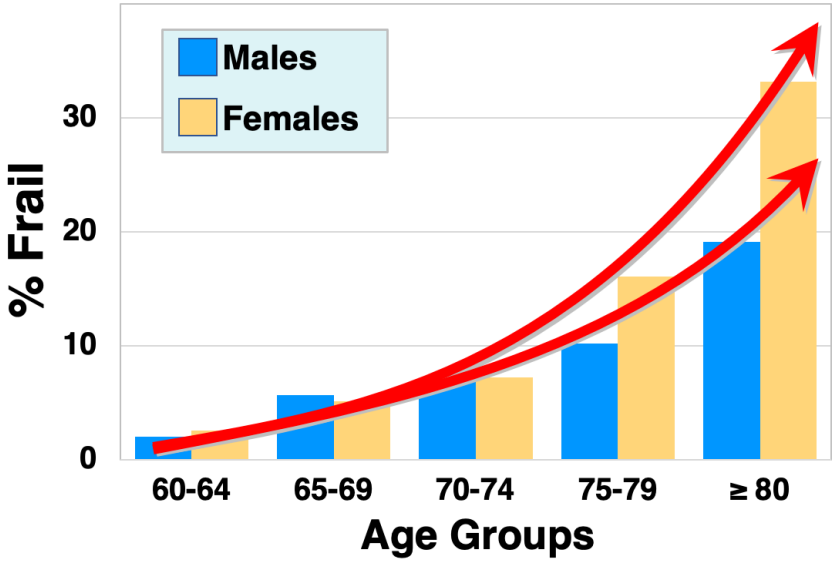


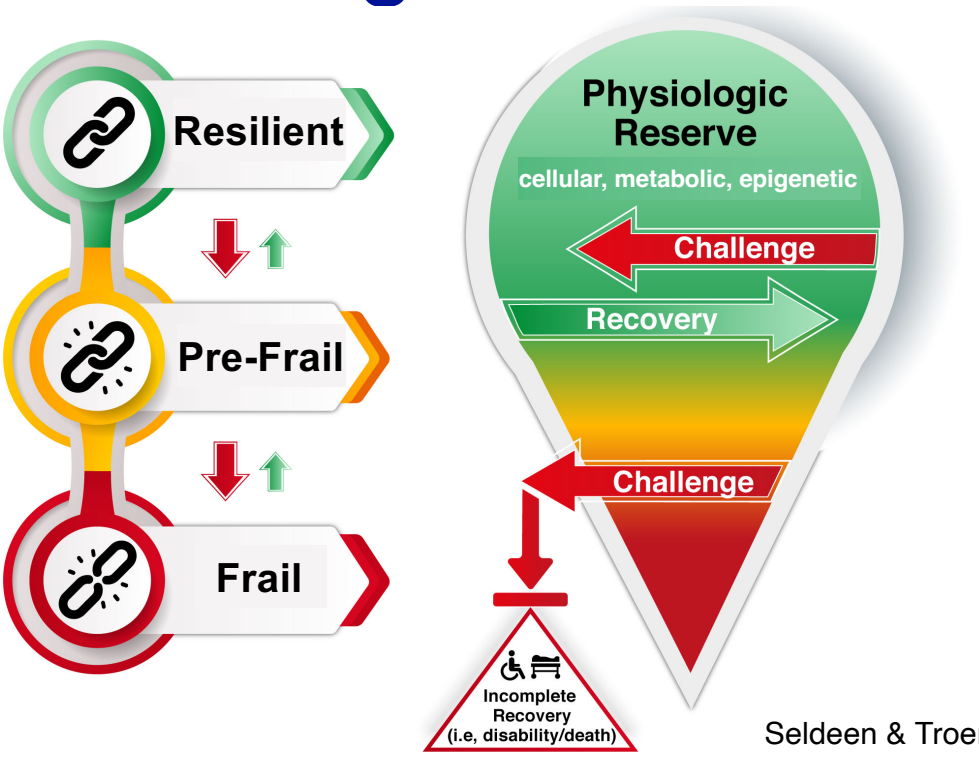
Frailty Prevalence During Aging



What is the trajectory of resilience during aging?

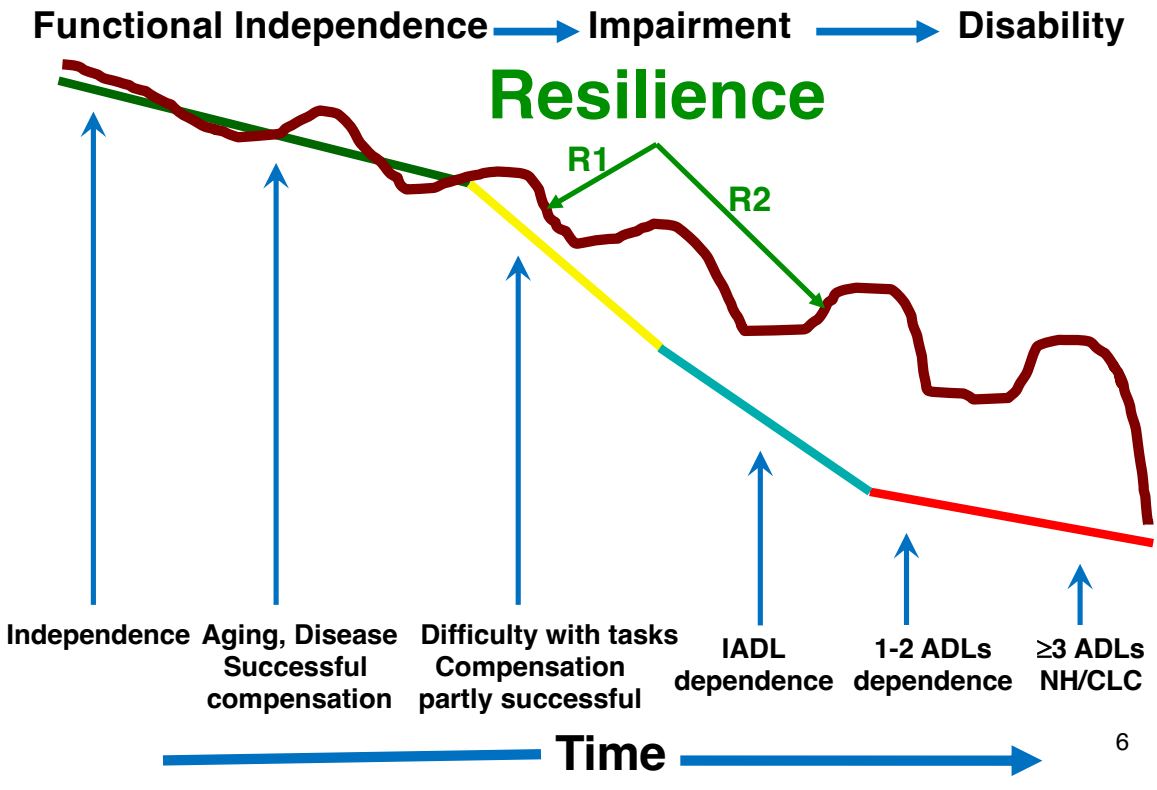
Ahmad et al. PLOS One 2018

Loss of Resilience ⇒ Frailty Progression

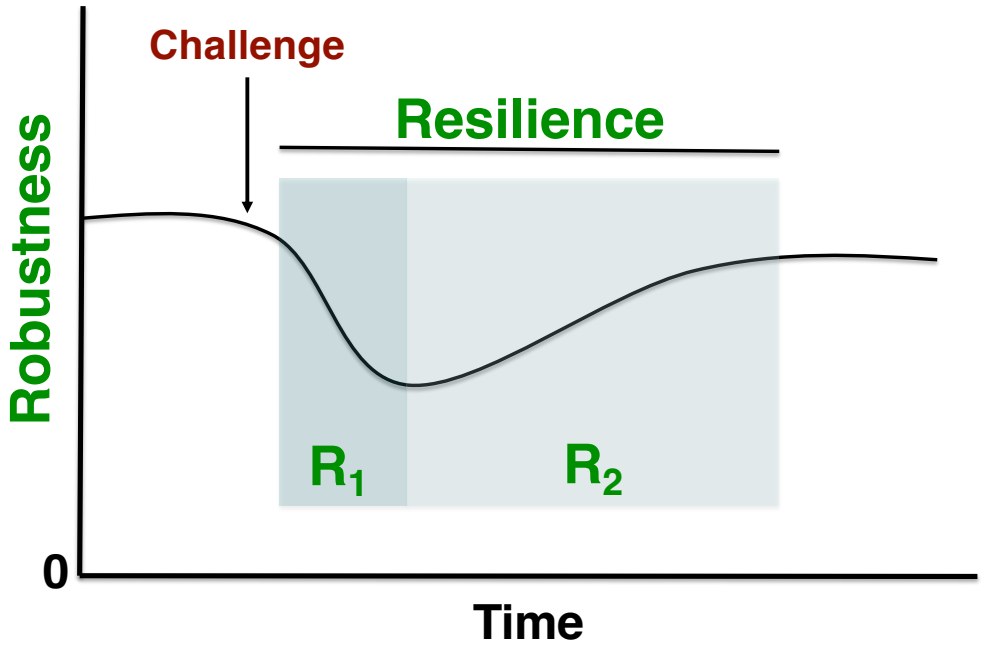


Seldeen & Troen 2022

Resilience Trajectory



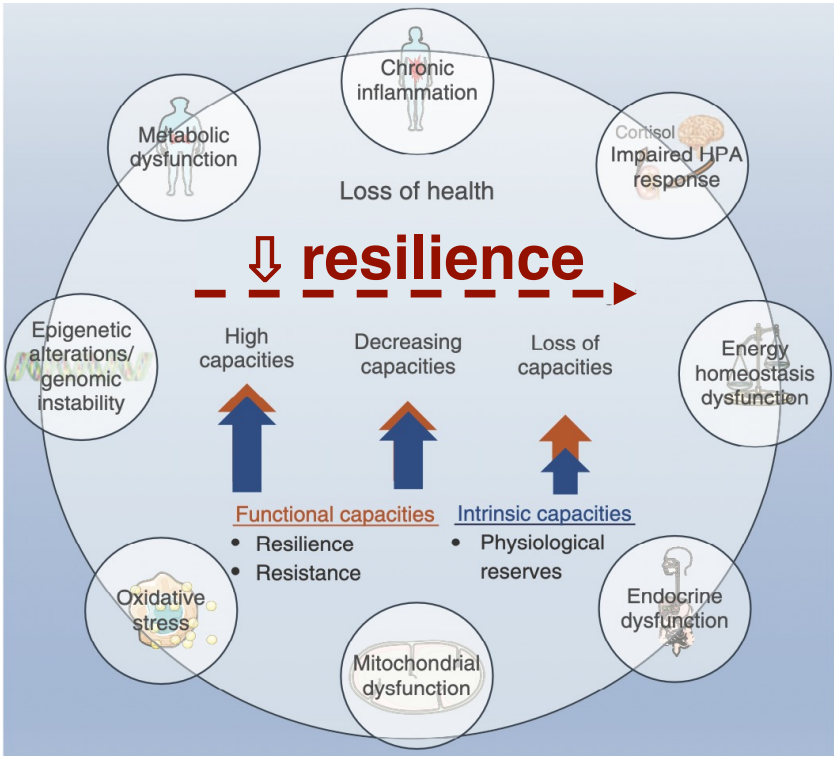
Resilience for a given challenge



R_1: limit decline

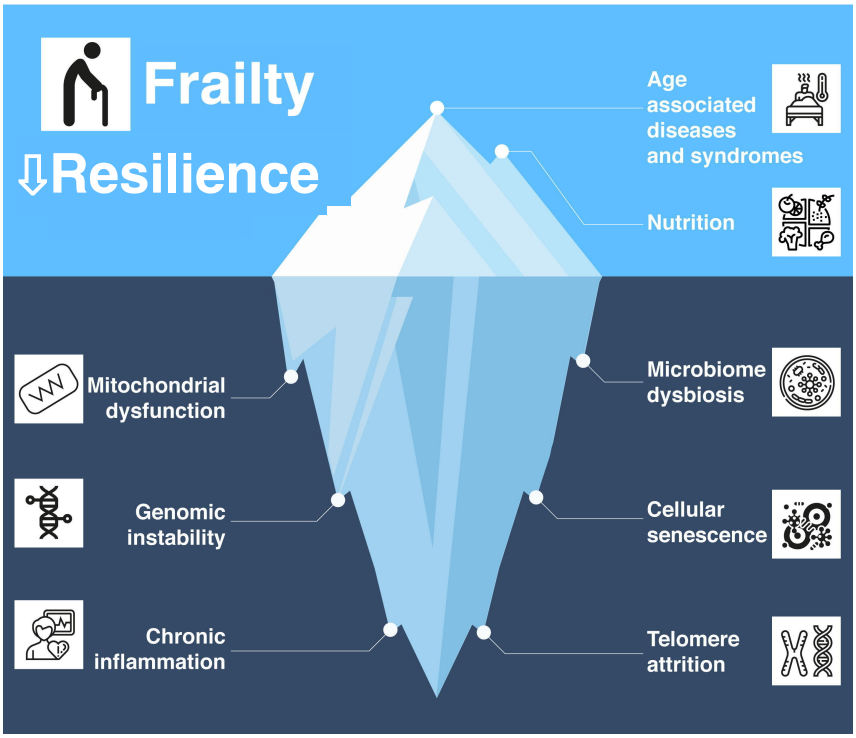
R_2: restore function towards baseline

Mechanistic spectrum (frailty)



Perazza et al. Compr Physiol 2022

Loss of Resilience – Tip of the Iceberg?



Seldeen & Troen 2022

Biomarkers Associated with Physical Resilience After Hip Fracture

- Physical resilience after hip fracture—the expected recovery differential (ERD)
- Used biomarkers associated with physical performance, morbidity, mortality, and hip fracture
- Baltimore Hip Studies (N = 304): biomarkers of inflammation (TNFR-I, TNFR-II, sVCAM-1, and IL-6), metabolic and mitochondrial function (non-esterified fatty acids, lactate, ketones, acylcarnitines, free amino acids, and IGF-1), and epigenetic dysregulation (circulating microRNAs)
- Complete biomarker set explained 37% of the variance in ERD ($p < .001$)
- Biomarker subset ⇒ 27% of the ERD variance and included metabolic factors (aspartate/asparagine, C22, C5:1, lactate, glutamate/mine), TNFR-I, miR-376a- 3p, and miR-16-5p

Parker et al. J Gerontol 2020

Phenotype may be all we need???

GeroScience (2017) 39:83–92
DOI 10.1007/s11357-017-9960-3

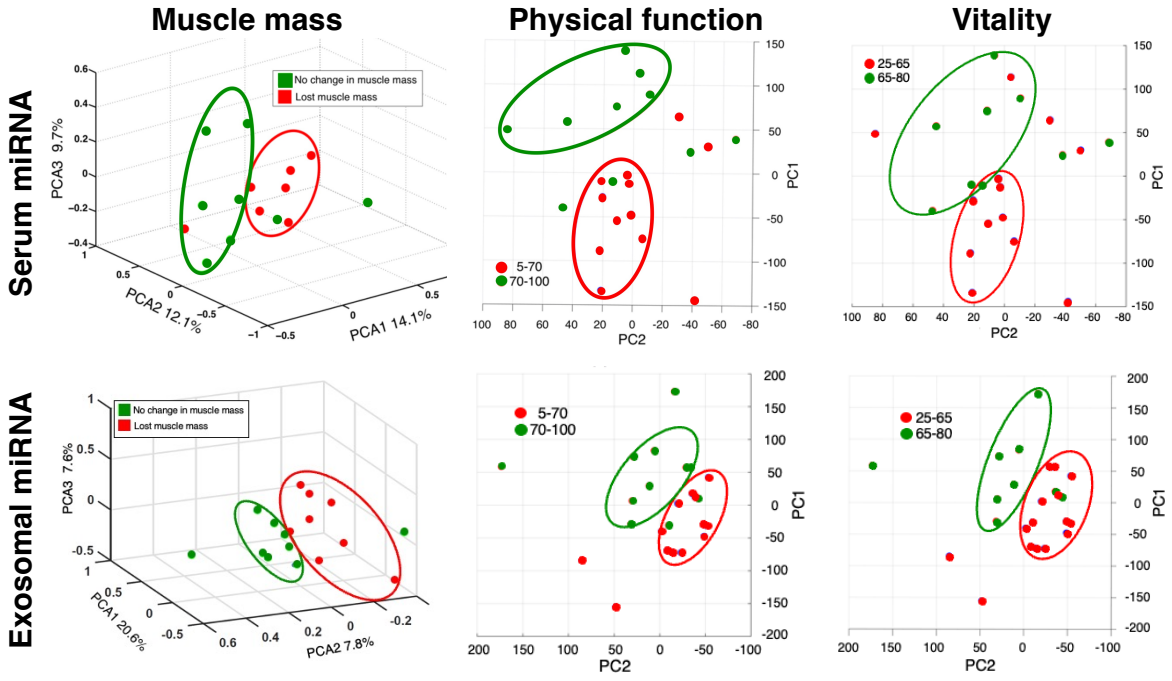
ORIGINAL ARTICLE

The frailty index outperforms DNA methylation age and its derivatives as an indicator of biological age

Sangkyu Kim · Leann Myers · Jennifer Wyckoff · Katie E. Cherry · S. Michal Jazwinski

- FI_{34} was a significant predictor of mortality, whereas none of the DNA methylation age-based metrics were.
- FI_{34} outperformed DNA methylation, remaining significant with chronological age when DNA methylation measures were not.
- FI_{34} is a robust predictor of biological age, while DNA methylation measures are largely a statistical reflection of the passage of chronological time.

Baseline miRNA profiles predict loss of muscle, declines in physical function, and decreased energy 17 years later



Reynolds et al. Preliminary Results

Questions / Future Strategies

- Measures of frailty may be too late – the horse may have left the barn?
- Though, we have demonstrated that frailty (in mice and likely people) can be reduced with HIIT – is resilience modifiable?
- Will resilience measures be specific to pathways and molecular systems and/or correlate to clinical outcomes?
- Need models that permit prognostication and prevention: keep the horse in the barn rather than just bringing it back?

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