Boston OAIC

Significant interactions and collaborations with other aging initiatives

Paul F. Glenn Center for Biology of Aging Research
Harvard Medical School

MISSION: The Paul F. Glenn Center for the Biology of Aging is dedicated to understanding the mechanisms of normal aging and the development of interventions to delay its onset and progression, thereby extending the healthy years of human life.

Research:

YANKNER LAB
Epigenetics, Brain Aging
Alzheimer's disease

SINCLAIR LAB
Sirtuins, Aging
DNA Damage

HAIGIS LAB
Sirtuins, Mitochondria
Metabolism, Cancer

WAGERS LAB
Aging, Stem Cells
Organ Regeneration

Teaching and dissemination of ideas: Aging courses for graduate students, undergrads and lay audiences

Upcoming events: Harvard Glenn Symposium (May 20, 2019!), Boston Aging Data Club (monthly)

Blood-borne factors impact multiple age-related phenotypes

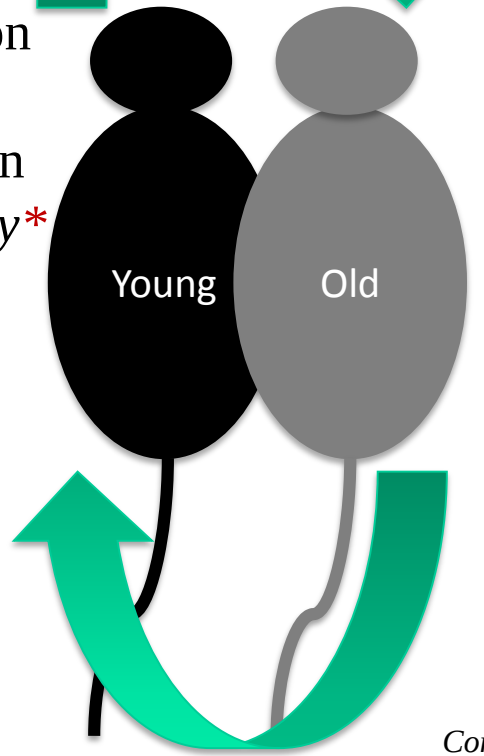
Benjamin Alman
Andrew Brack
Irina Conboy

Yuval Dor
Robin Franklin
Richard Lee
Janko Nikolich-Zugich

Heterochronic parabiosis

Tom Rando
Lee Rubin
Tom Serwold
Saul Villeda

Amy Wagers
Clifford Woolf
Tony Wyss-Coray
Elaine Fuchs



- ↓Muscle regeneration
- ↓Neurogenesis
- ↓Beta cell replication
- ≈*Cardiac hypertrophy**
- ≈*Remyelination**
- ≈*Bone healing*
- ≈*Peripheral nerve regeneration**
- ≈*Hair regeneration*
- ≈*Thymic atrophy**

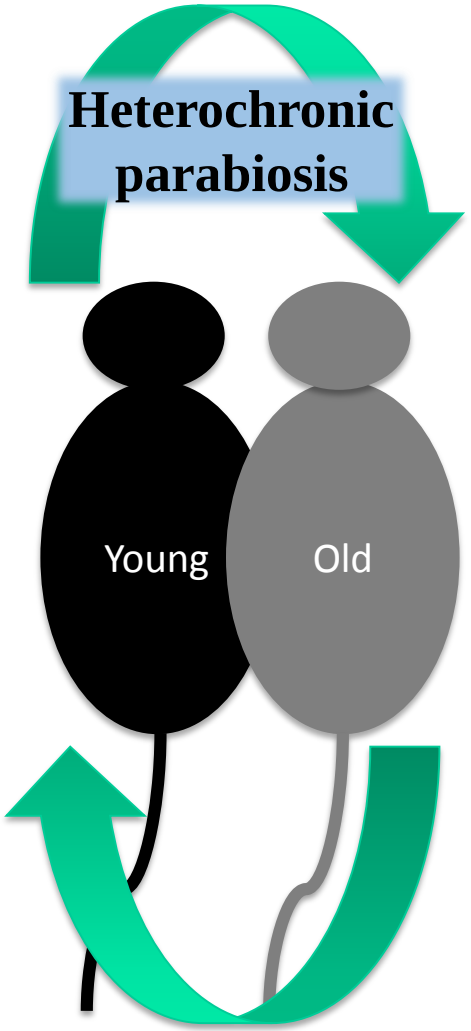
- ↓Cardiac hypertrophy*
- ↑Muscle regeneration*
- ↑NMJ and muscle ultrastructure*
- ↑Neurogenesis and neural function*
- ↑Remyelination*
- ↑Beta cell replication
- ↑Bone healing
- ≈*Peripheral nerve regeneration**
- ≈*Hair regeneration*
- ↑*Thymic atrophy**

*Wagers lab contributions

Brack et al., 2007; Villeda et al., 2011; Ruckh et al., 2012 Salpeter et al., 2013; Loffredo et al. 2013; Keyes et al., 2013; Painter et al., 2014 Kim et al., 2015; Davies et al., 2018

Conboy et al., 2005; Brack et al., 2007; Villeda et al., 2014; Ruckh et al., 2012; Loffredo et al. 2013; Salpeter et al., 2013; Keyes et al., 2013; Sinha, Jang et al., 2014; Katsimpardi et al., 2014, Painter et al., 2014; Kim et al., 2015; Baht et al., 2015

Multiple blood-borne factors impact age-related phenotypes



Macrophages (spinal cord)
Activin A (spinal cord)
GDF11 (muscle, heart, brain)
Oxytocin (muscle)
TIMP2 (brain)
Ostocalcin (brain)

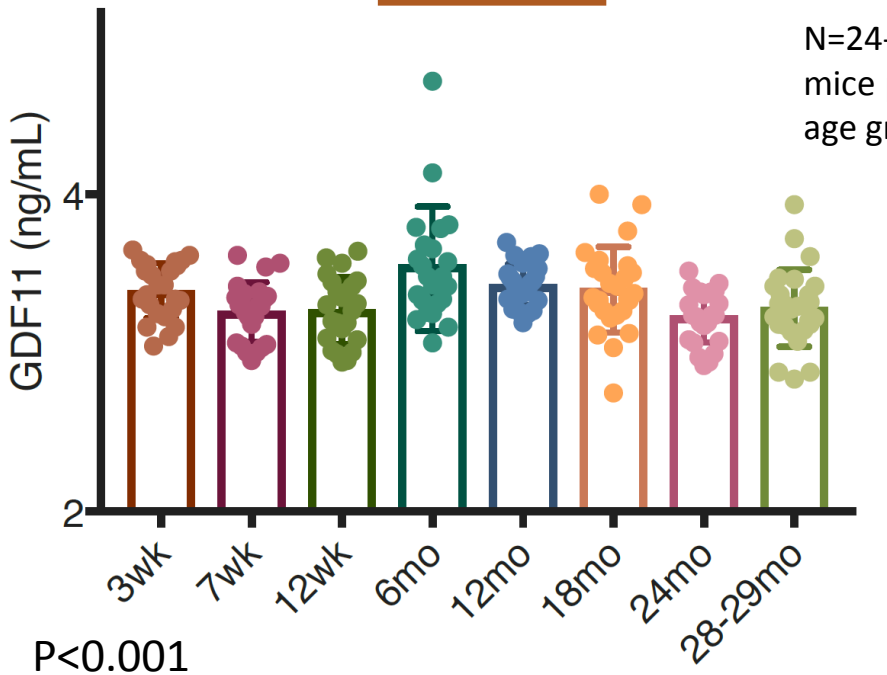
Wnt (muscle)
CCL11 (brain)
B2-microglobulin (brain)

Brack et al., 2007; Villeda et al., 2011; Smith et al., 2015

Conboy et al., 2005; Brack et al., 2007; Villeda et al., 2011; Ruckh et al., 2012; Loffredo et al. 2013; Sinha, Jang et al., 2014; Katsimpardi et al., 2014; Elabd et al., 2015; Castellano et al., 2017; Khrimian et al., 2017

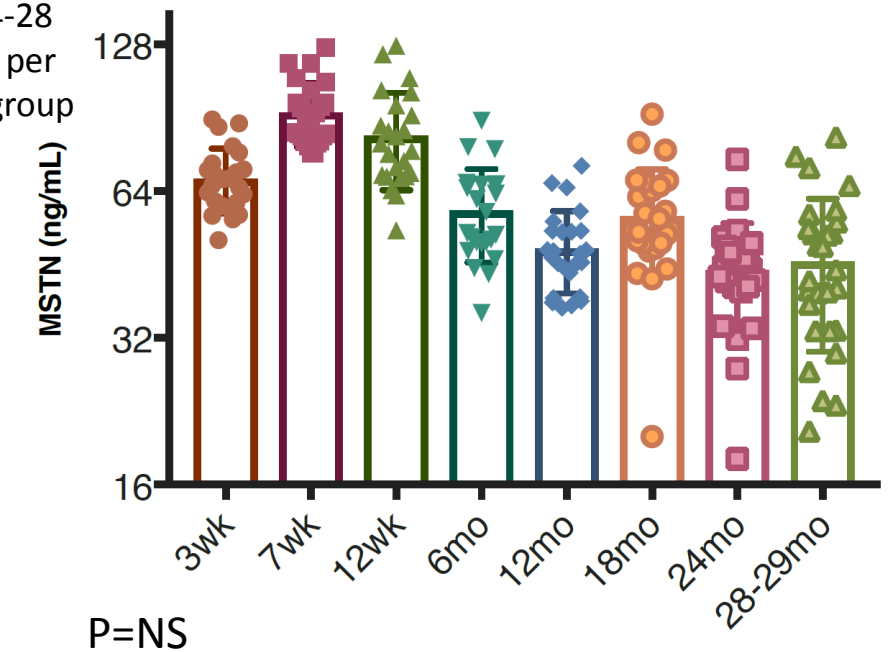
Age-related changes in circulating GDF11 protein

N=24-28 mice per age group



P<0.001

7wk. V. 6 m.	6m. v. 24m./28m.
12 wk. V. 6m.	



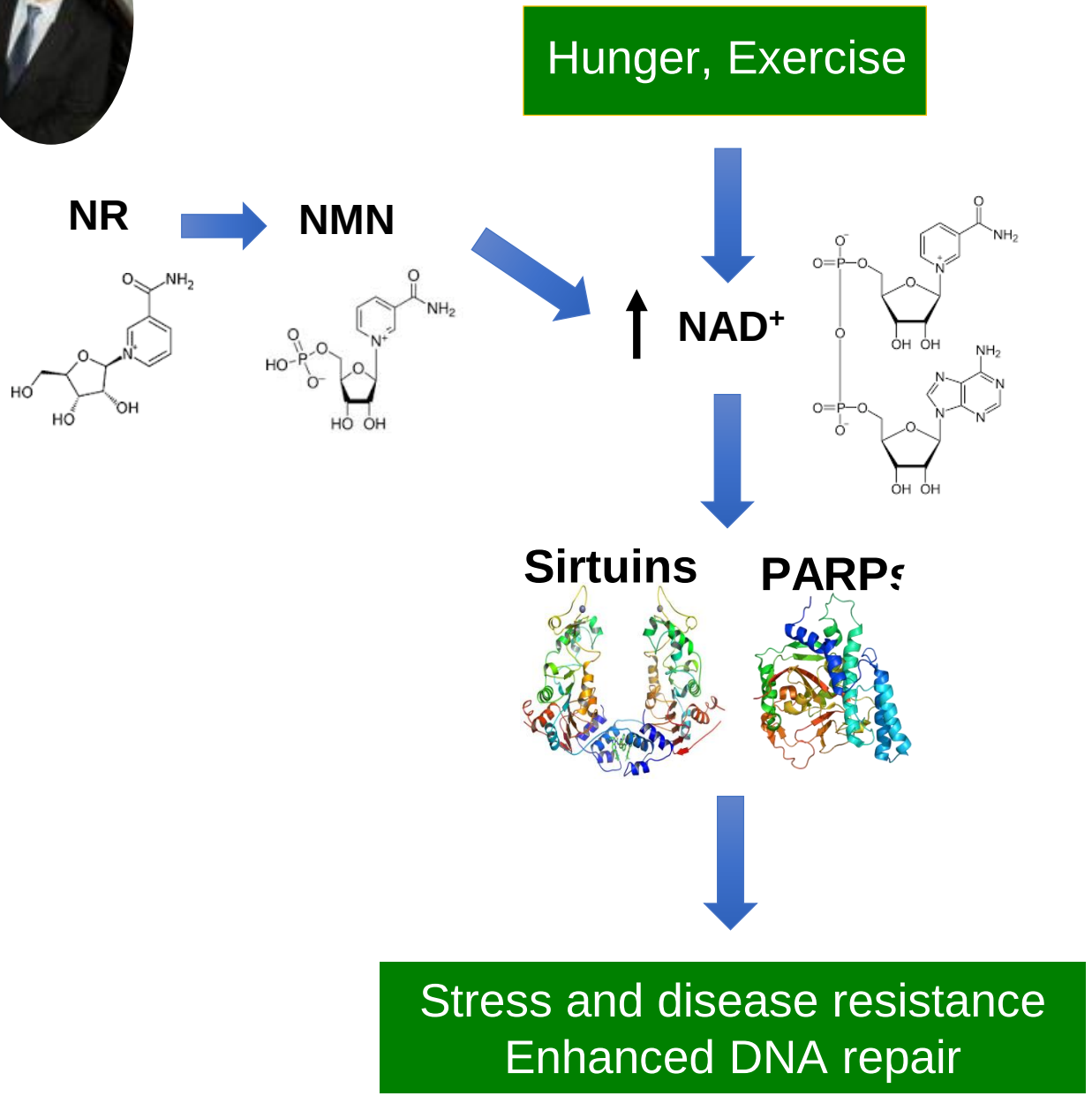
P=NS

3wk v. 6m./18m.	12m. v. 18m./24m./28m.
7wk. V. 12wk.	18m. V. 28m.
6mo. V. 12 mo./18mo.	24m. V. 28m.

Kathleen Messemer, Miook Cho, collaboration with Shally Bhasin and Limeng Peng

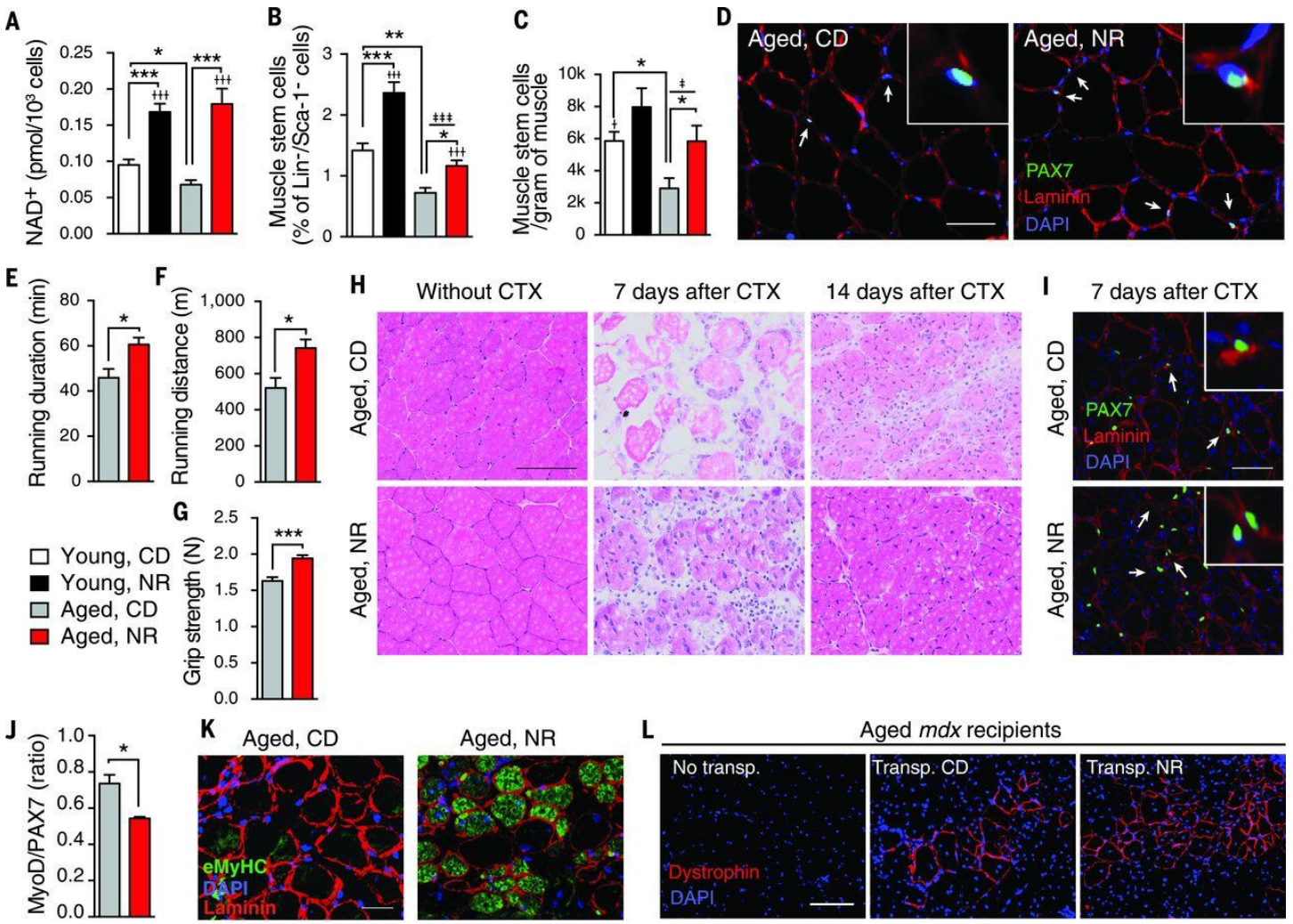
etary

Central role of NAD+ in cellular homeostasis



- NAD levels decline in mice and humans with age.
- NAD levels can be ”boosted” by:
  - providing substrates that can be converted to NAD+ (nicotinamide riboside or nicotinamide mononucleotide),
  - increasing the activity of the NAD salvage pathway enzymes (recycles NAD+ from nicotinamide),
  - inhibiting proteins that degrade NAD+ (CD38, CD157).
- This can activate all 7 Sirtuins at once.
- Increased NAD levels can increase lifespan in yeast, and upregulation of the NAD salvage pathway by stressors (CR, heat, osmotic stress, etc.) may explain in part hormetic effects.

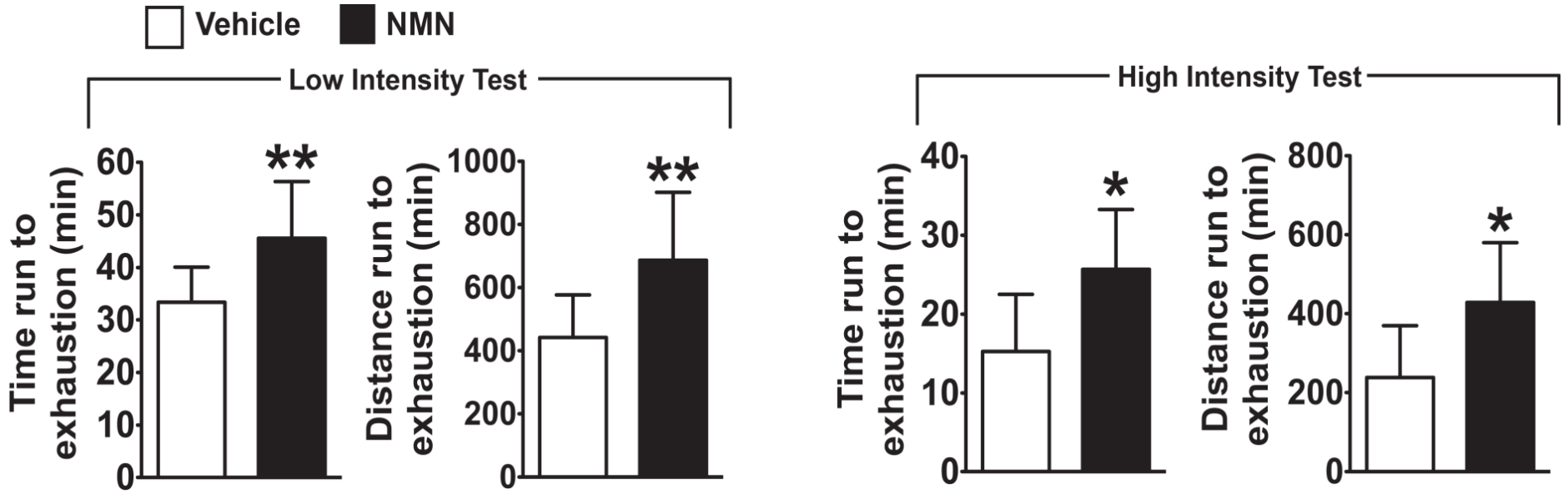
Improved muscle stem cell numbers and muscle function in NR-treated aged mice.



Published by AAAS

Hongbo Zhang et al. Science 2016;352:1436-1443

NMN increases muscle capillarization and endurance



20 month old mice +NMN in drinking water for 4 wks.

Abhi Das, George Huang et al., 2017

Human clinical trials of NMN currently recruiting

HARVARD MEDICAL SCHOOL

Harvard Initiative on Aging (HIA)

Funding for Planning Activities for future Innovation Grants in Healthy Aging

Dean's Innovation Pilot Awards in Healthy Aging