Marmosets as translational models for aging research

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Marmosets

- NHP models allow control of environment, diet, and medicines
- Small (350-450 g)
- Rapidly reproducing
- Relatively short lifespan and development
  - Reach adult size ~2 years
  - Average lifespan ~6 years in captive colonies
  - Oldest marmoset ~22 years
Longevity

- Human
- Rhesus
- Baboon
- Marmoset

(Ross & Salmon 2018)
(Ross 2018)

(Ross et al 2017)
Causes of Death

(Tardif et al, 2011)
Characterizing Marmoset Aging – 5 domains

- Metabolic
- Homeostatic
- Immune
- Mobility
- Cognition
Metabolic Aging

• Lose weight at an increasing rate above middle age (Power et al 2001, Tardif et al 2011)

• Aging associated with decreased fat mass (longitudinal follow) (Ross et al 2012)

• Response to a glucose challenge is not significantly different for geriatric marmosets

• Geriatric marmosets have significantly reduced VO$_2$ compared to young animals
Homeostatic Aging

- Geriatric marmosets have significantly higher diastolic and mean arterial pressure
Homeostatic Aging

- Geriatric marmosets have significantly less diverse gut microbiome
Immune Aging

• Serum albumin concentrations decrease with age (Ross et al 2012)

• Older animals express increased inflammatory states
Translational Phenotyping – from mouse & human to marmoset
Geriatric marmosets have significantly reduced movement, but retain normal social behaviors.

Hanging (stretching) behavior is significantly associated with risk of death in next 6 months.
Mobility
Cognition

- Tasks to assess visual learning, spatial learning, impulse control, and executive function

Photo: Georgia Tech
Marmoset Conveyor

Single Treat
Marmoset Conveyor

First Dual Treat
Subjects: 39
Older 8+ years, n = 21
Young <8, n = 18

(Alex Greig)
Detoured Reach

Detoured Reach Task

(Khira Wharford)
Detoured Reach

# of successful trials

session

Young
Geriatric

(Jessica Adams)
Intervention testing - Rapamycin

(Harrison et al 2009 Nature)
Marmoset Rapamycin

- Marmosets trained to receive oral daily doses of rapamycin
- Serum rapamycin values similar to those published for rodent and human studies

Pilot study: 14 months
Marmosets aged 7 – 9 yrs
Rapa - 4 male/female pairs
Control – 2 male/female pairs

(Tardif et al 2014)
Marmosets receiving rapa do not exhibit significantly altered glucose metabolism

(Ross et al 2015)
Longitudinal follow - No significant detriment in glucose metabolism with 12 months treatment

**Hba1c**

**Oral GTT**

**Fasting insulin**

Salmon, Unpublished
Cohort 1
Males and females
Rapamycin Conclusions

• Rapamycin is having no negative impacts on metabolic function in marmosets

• There are currently no significant differences between rapamycin and control animals for
  • Activity
  • Locomotion
  • Metabolic function

Continue to follow the progress
Marmoset Aging

• We are able to quantify more than just longevity

• We are able to use techniques from mice and humans to examine marmoset aging behaviors

• We are able to begin testing interventions that may increase health-span
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