

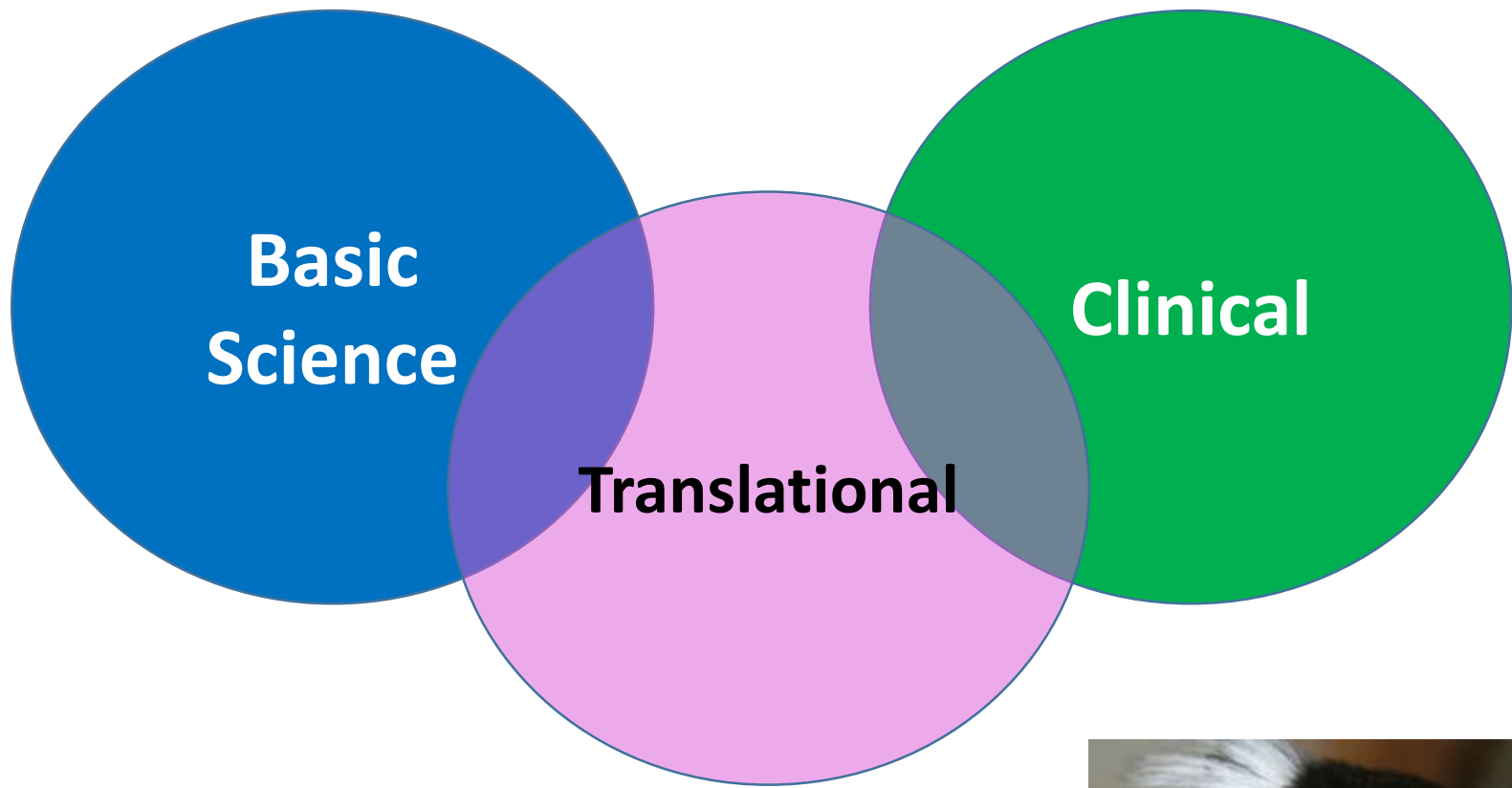
Marmosets as translational models for aging research



Corinna N. Ross, PhD



Aging Research

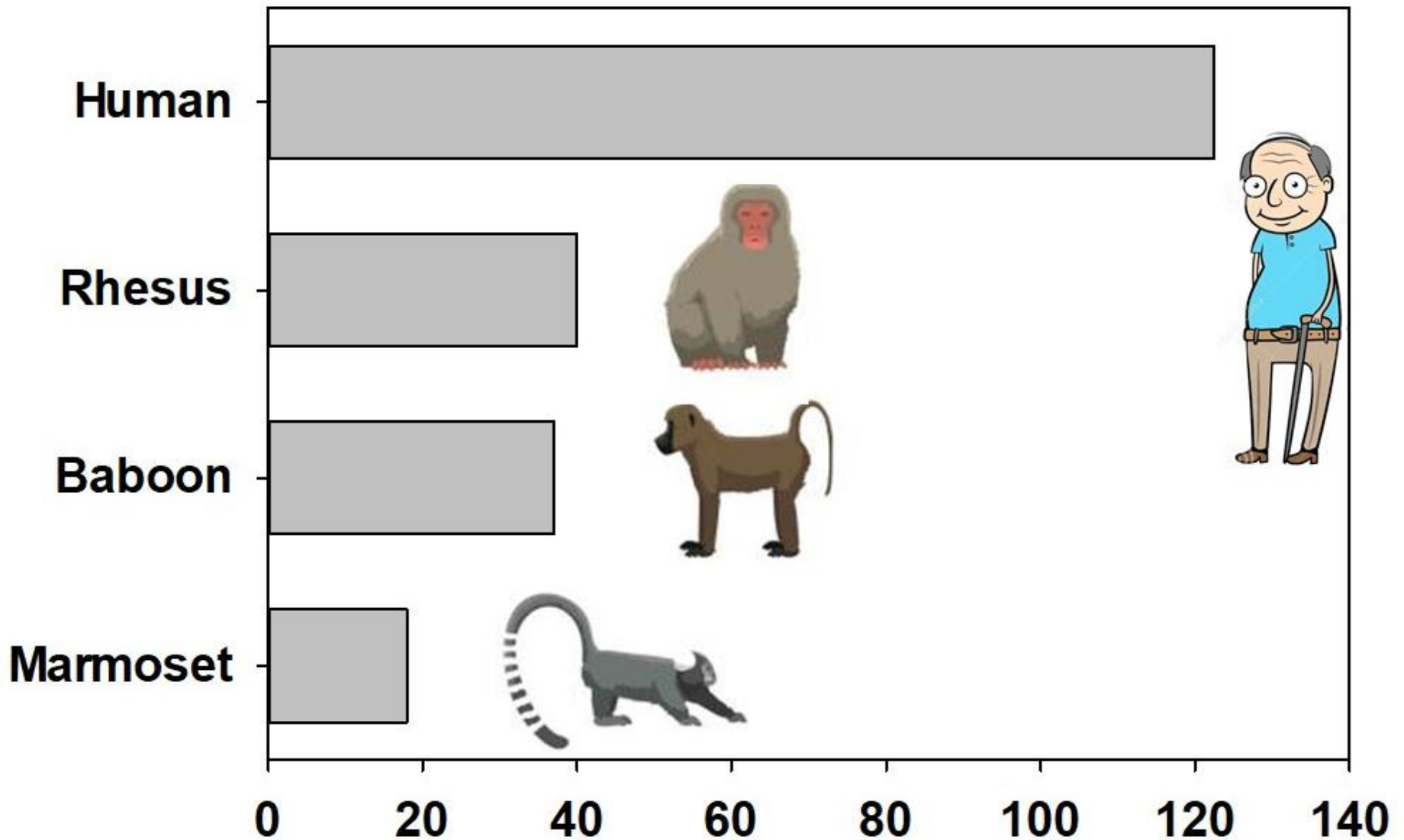


Marmosets

- 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

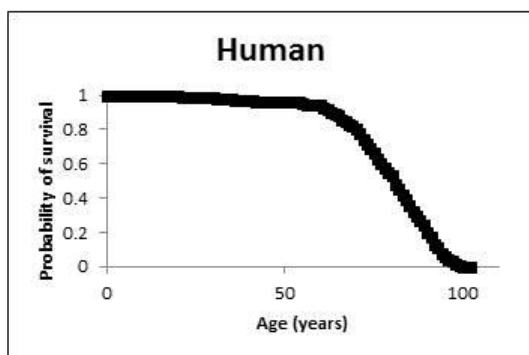


Longevity

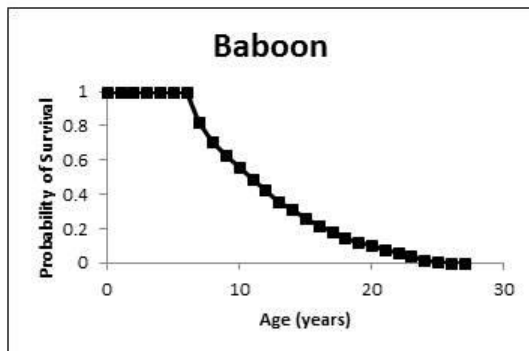


(Ross & Salmon 2018)

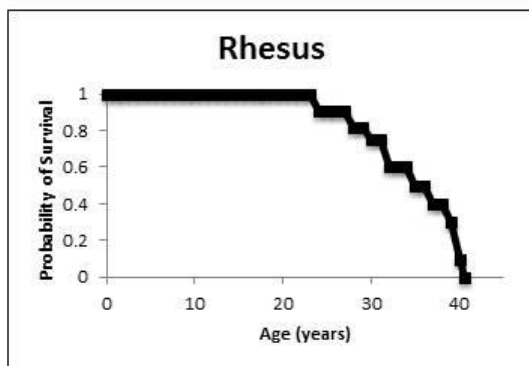
A



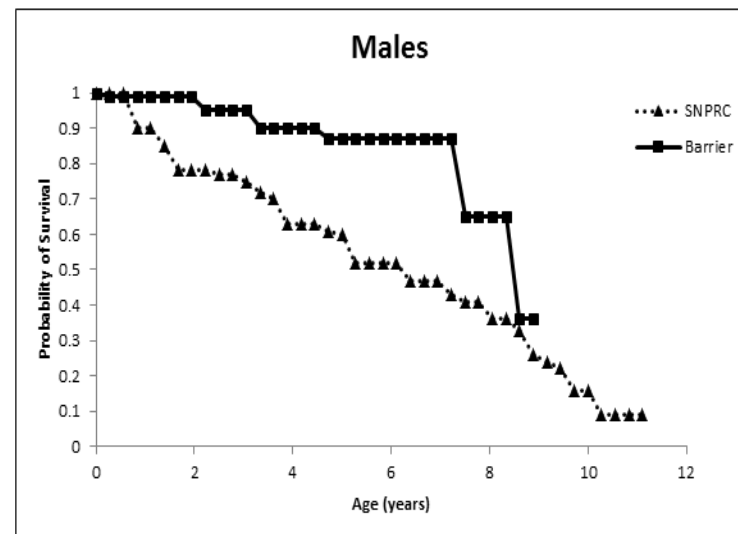
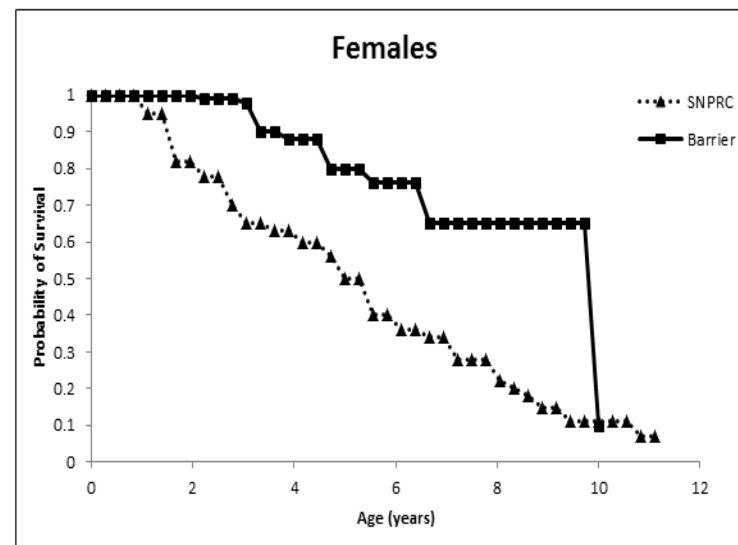
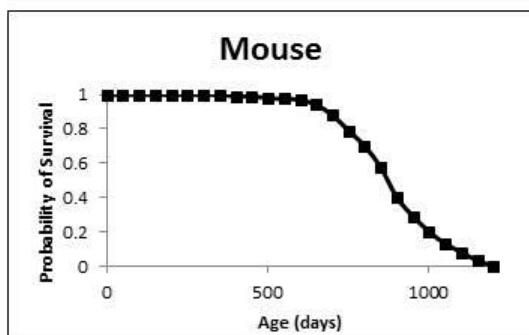
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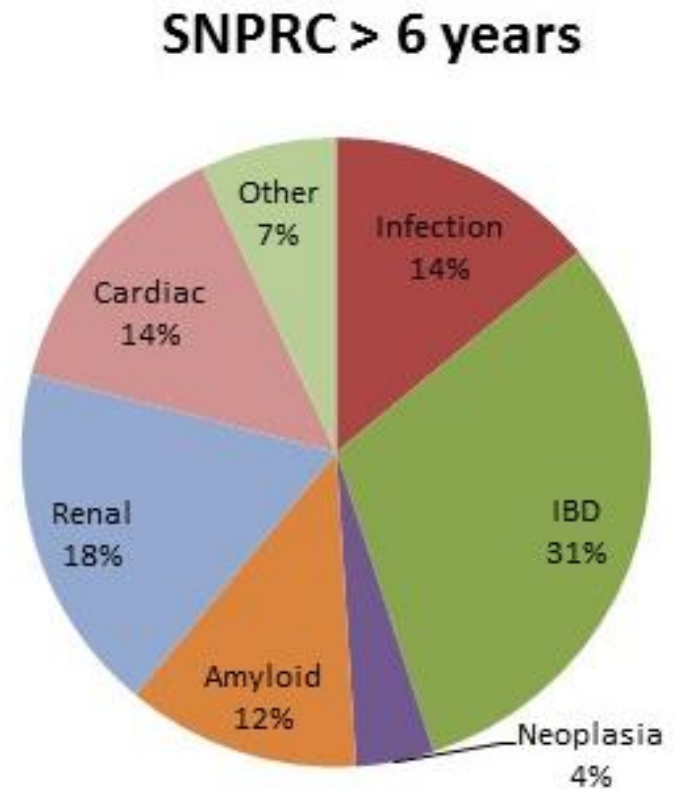
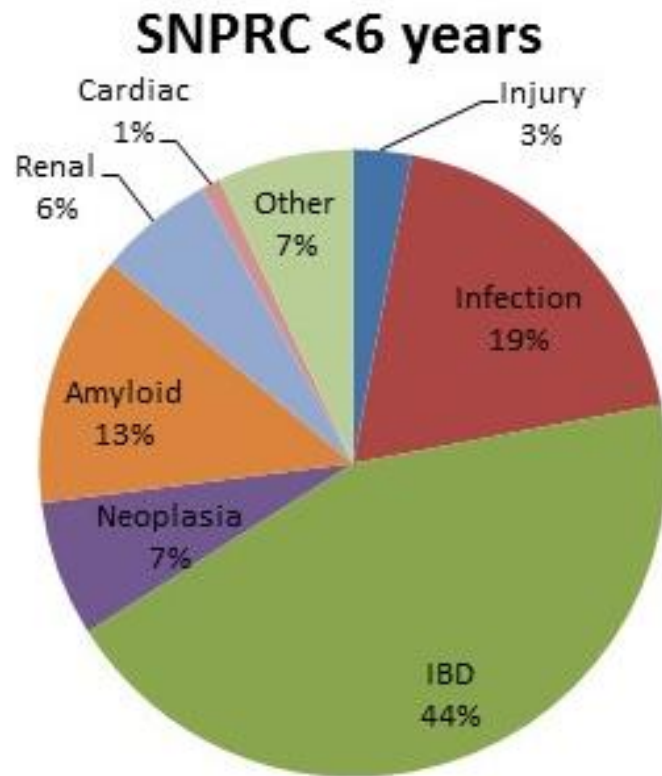


D



(Ross 2018)
(Ross et al 2017)

Causes of Death



Characterizing Marmoset Aging – 5 domains

- Metabolic
- Homeostatic
- Immune
- Mobility
- Cognition

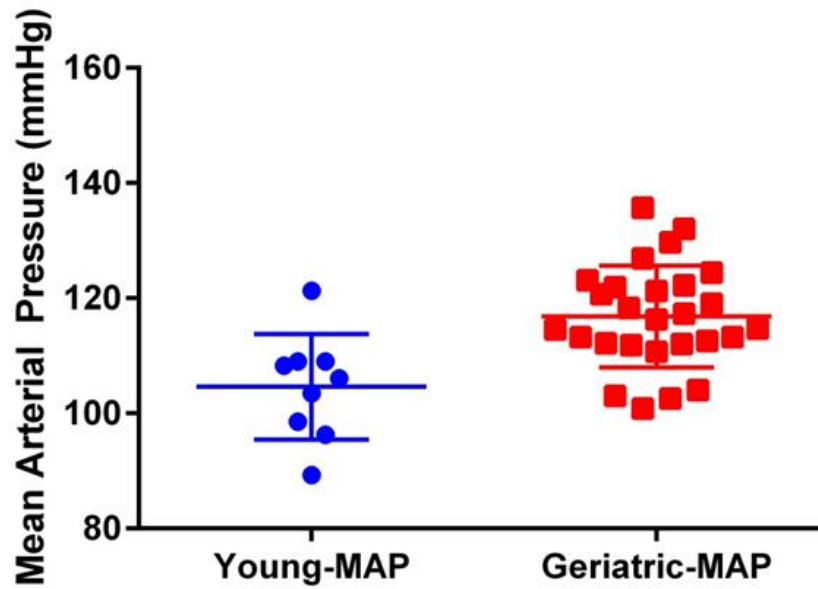


Metabolic Aging

- 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

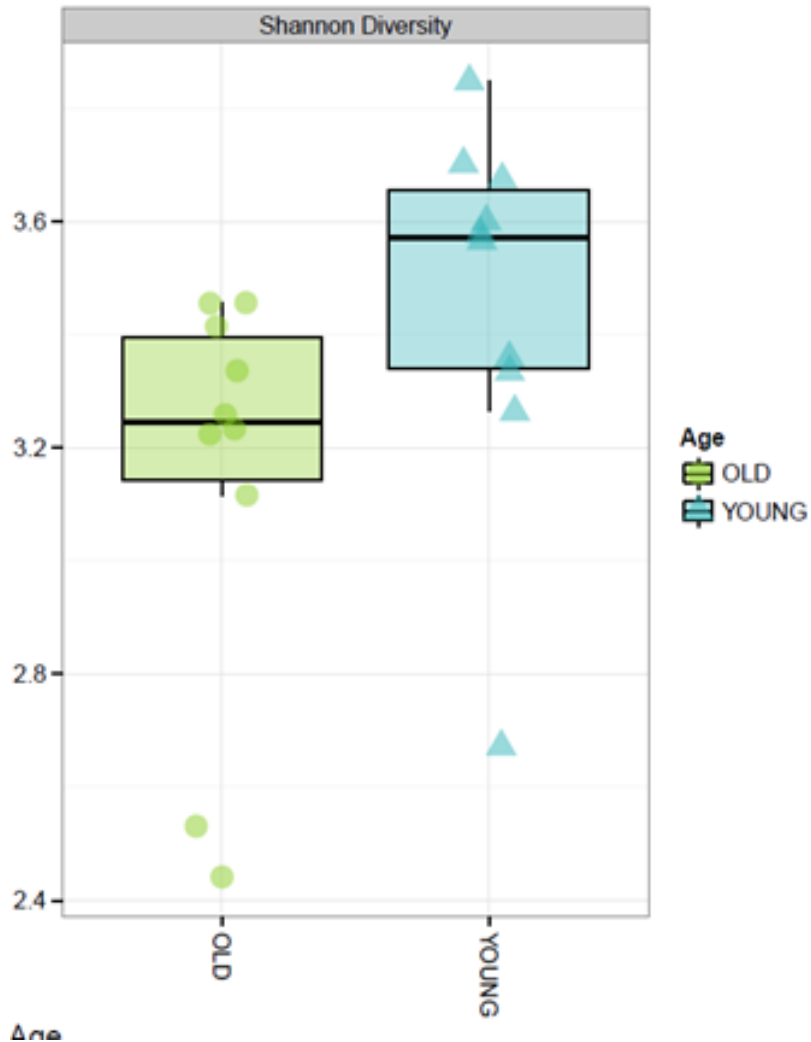
Homeostatic Aging

- Geriatric marmosets have significantly higher diastolic and mean arterial pressure



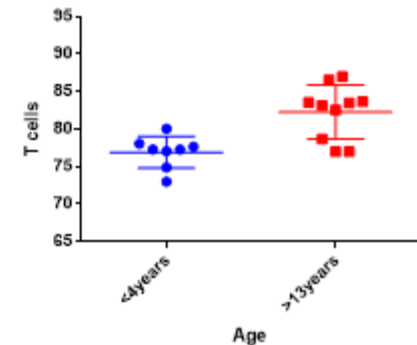
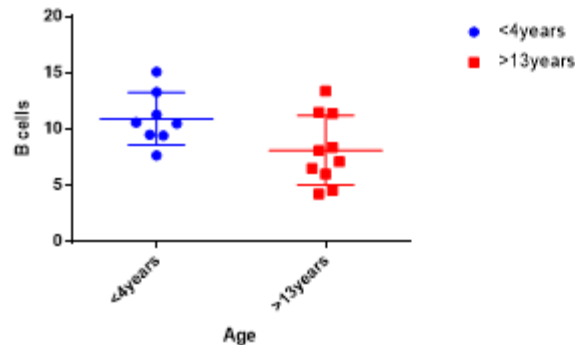
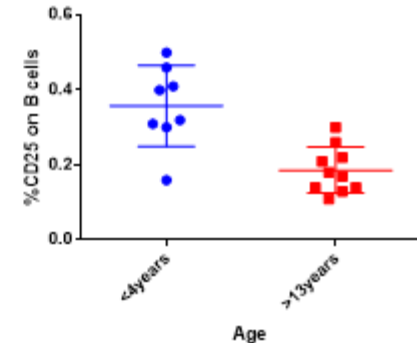
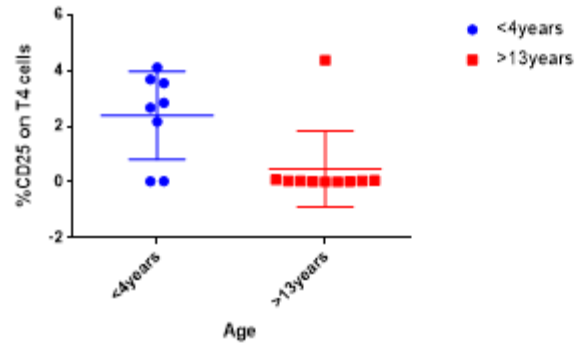
Homeostatic Aging

- Geriatric marmosets have significantly less diverse gut microbiome

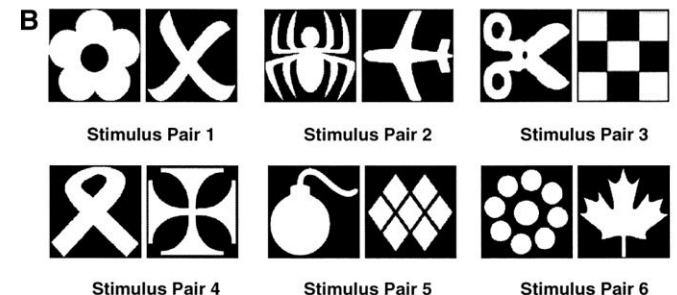
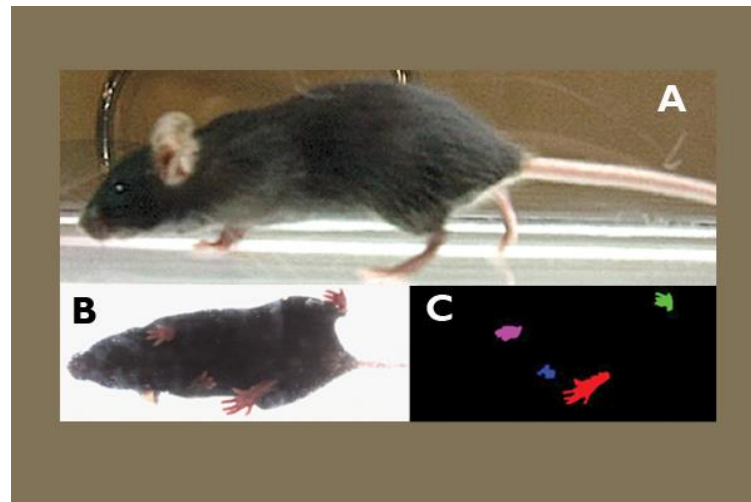
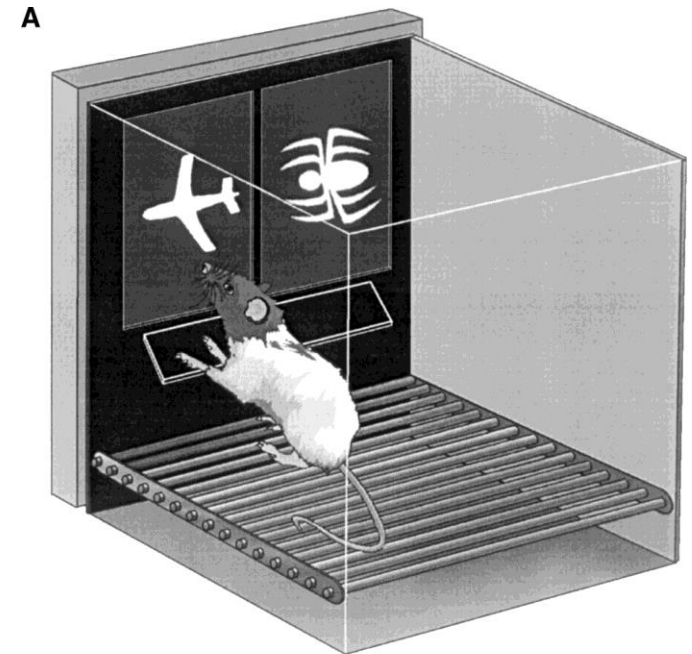
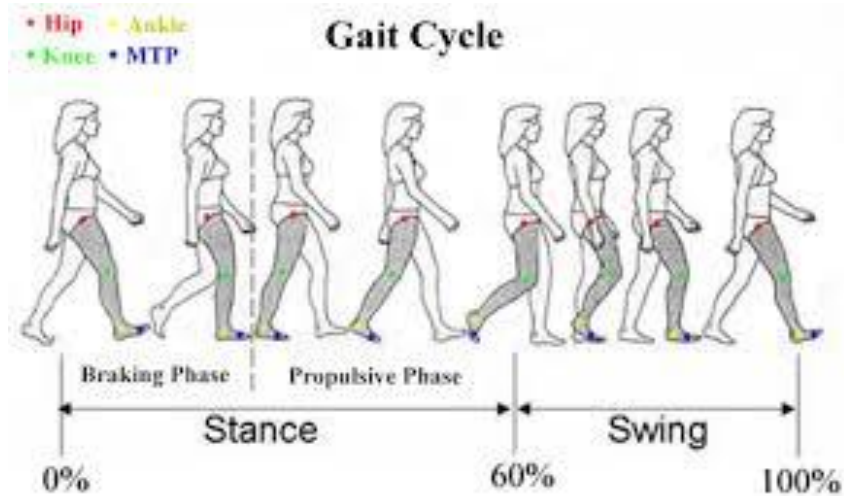


Immune Aging

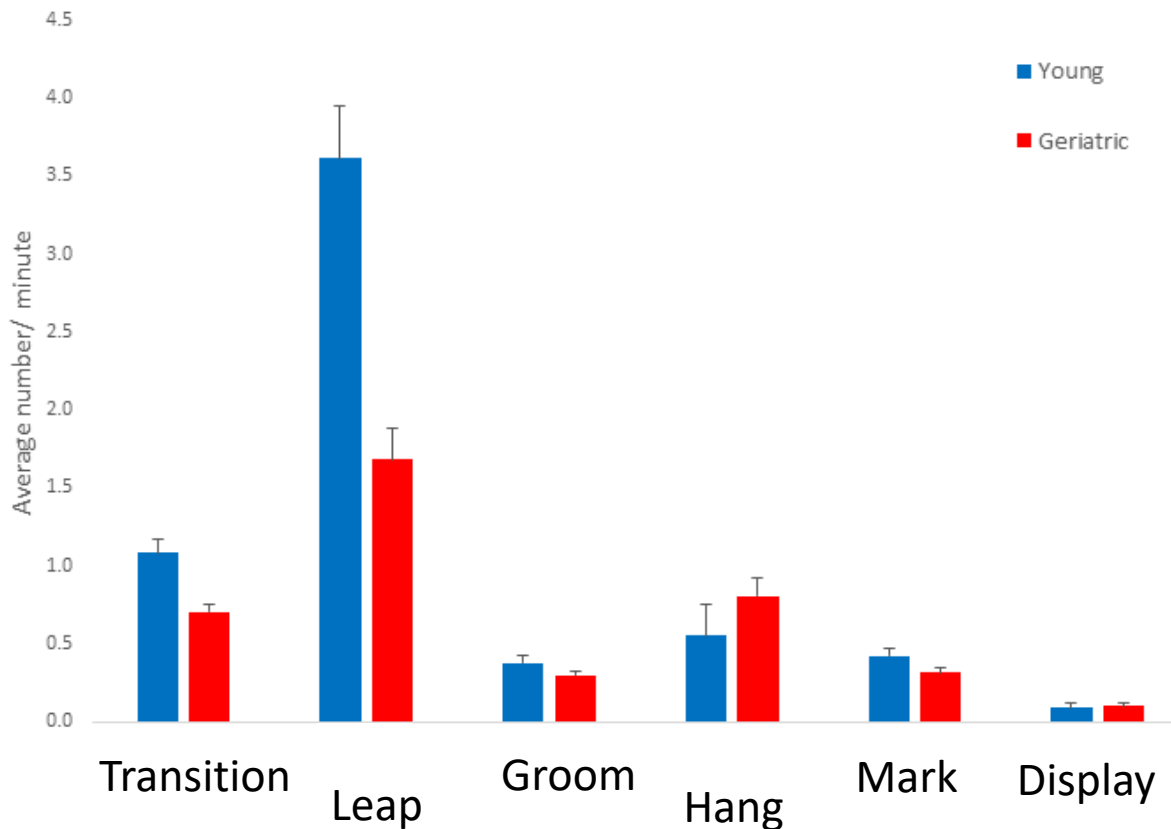
- Serum albumin concentrations decrease with age (Ross et al 2012)
- Older animals express increased inflammatory states



Translational Phenotyping – from mouse & human to marmoset



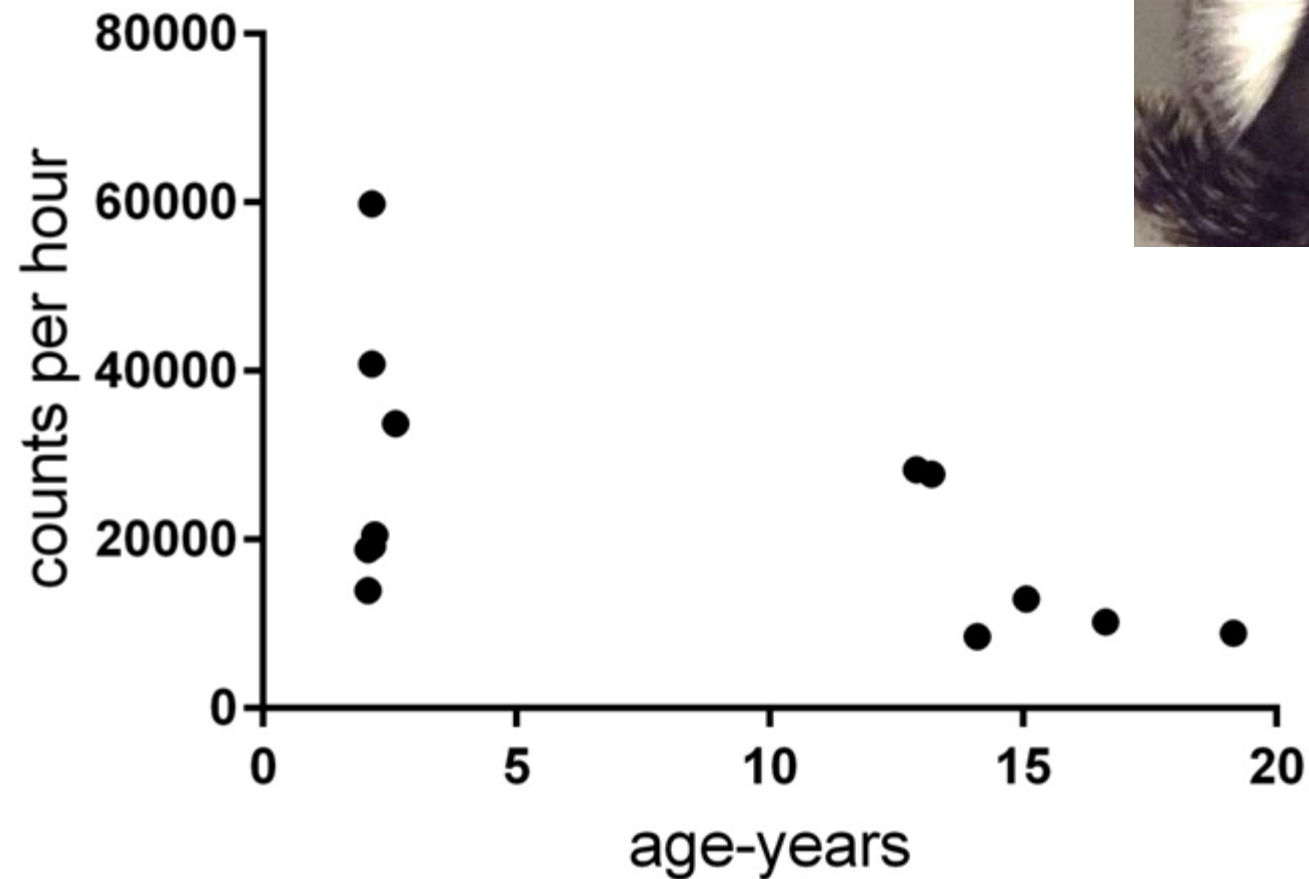
Mobility



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



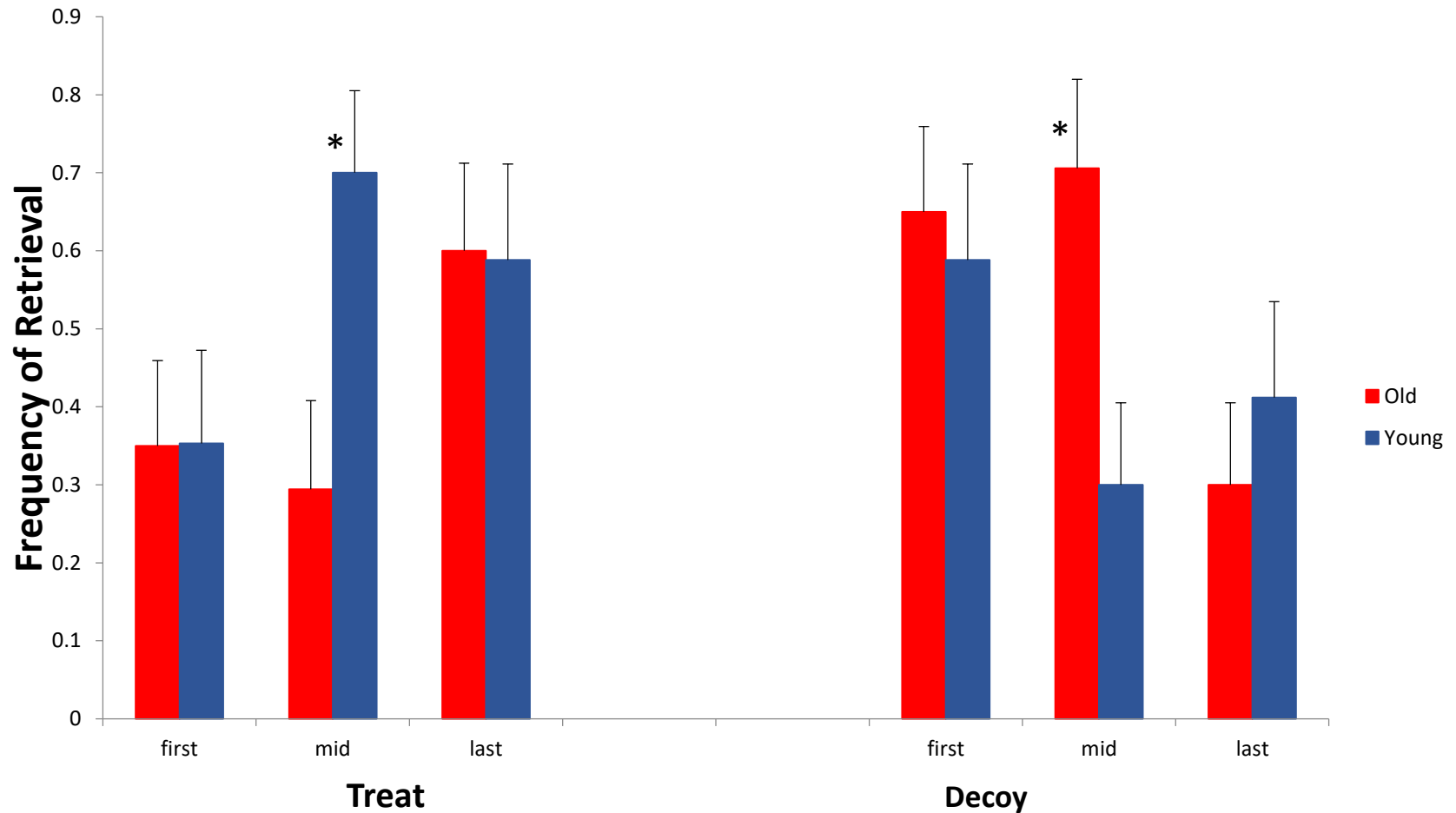
Marmoset Conveyor

Single Treat

Marmoset Conveyor

First Dual Treat

Marmoset Conveyor



Subjects :39

Older 8+ years, n = 21

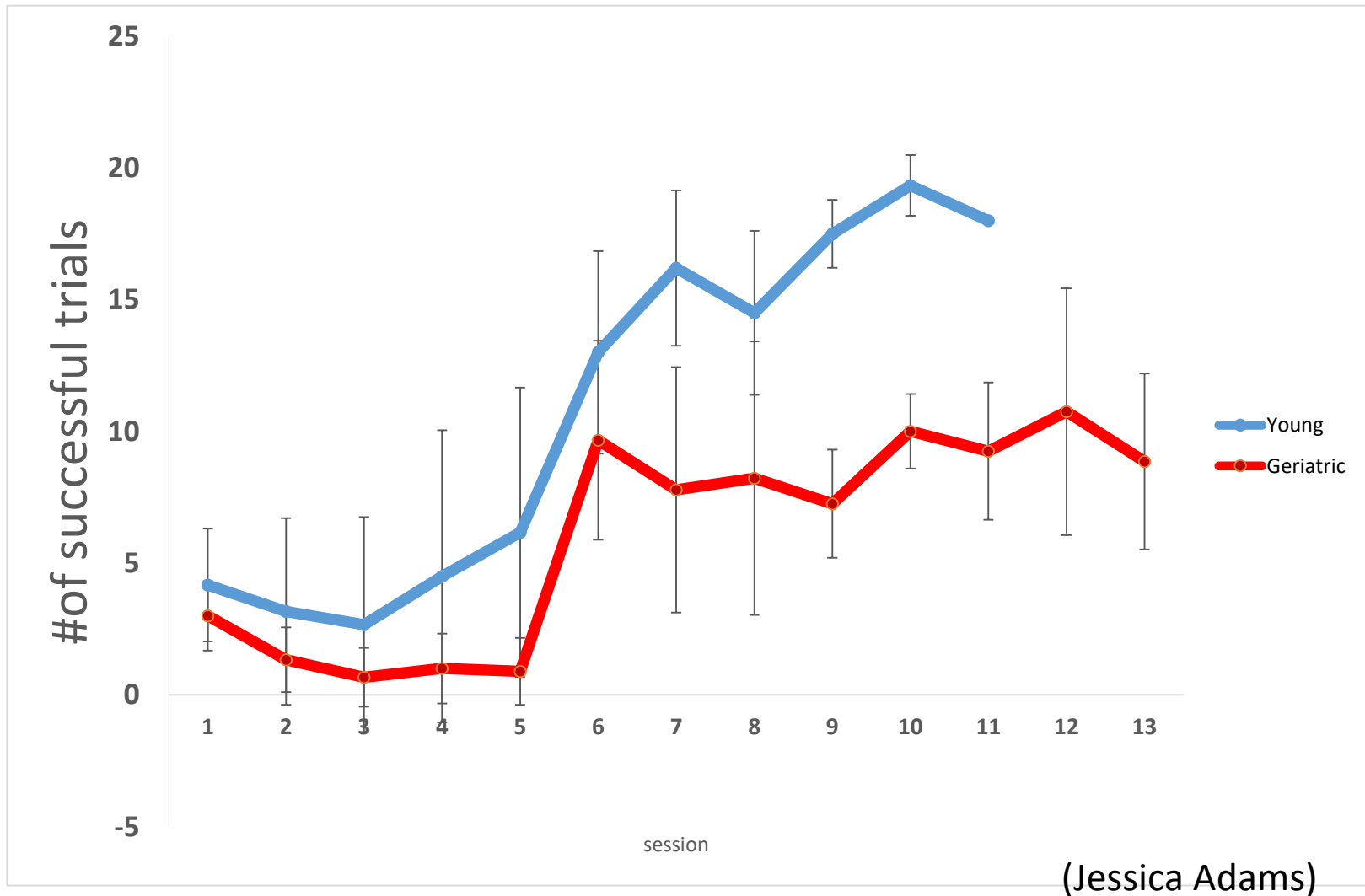
Young <8, n= 18

(Alex Greig)

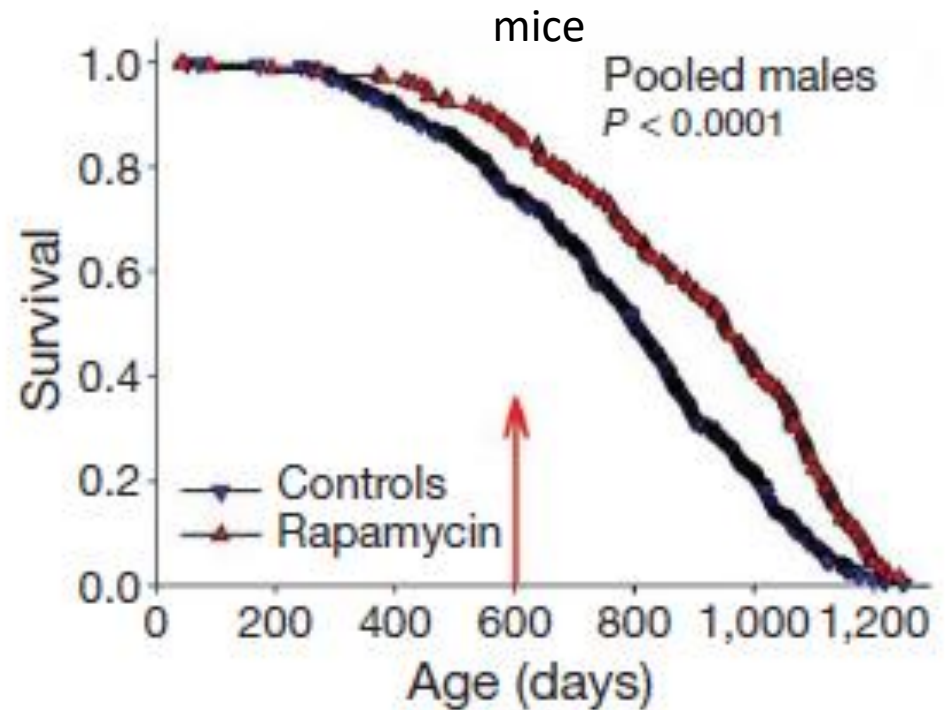
Detoured Reach

Detoured Reach Task

Detoured Reach



Intervention testing - Rapamycin

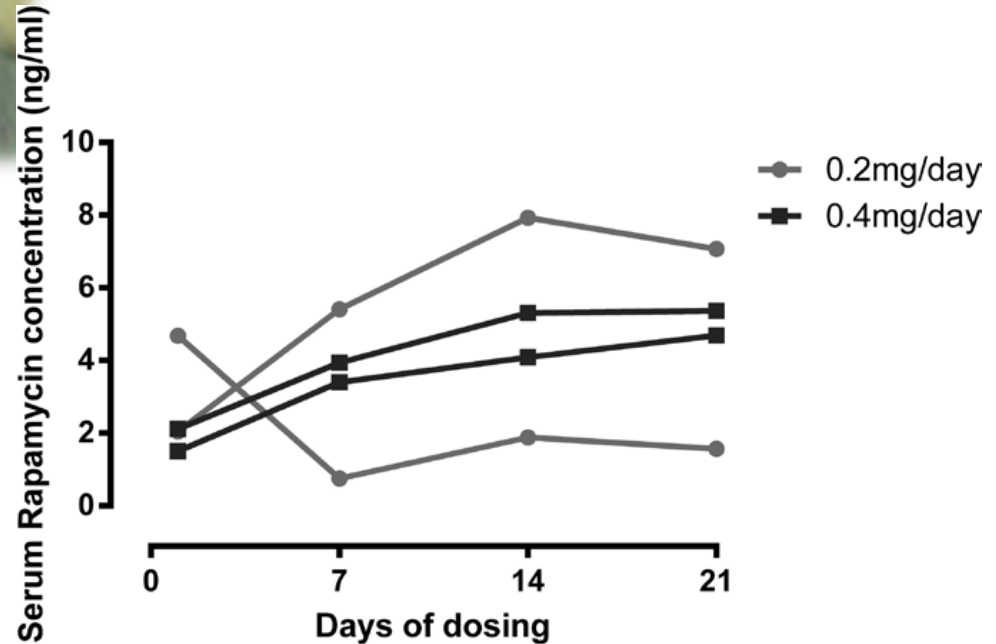


(Harrison et al 2009 *Nature*)

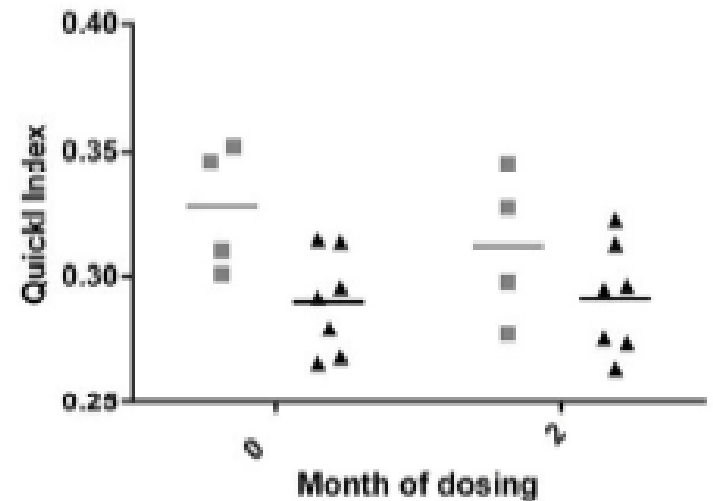
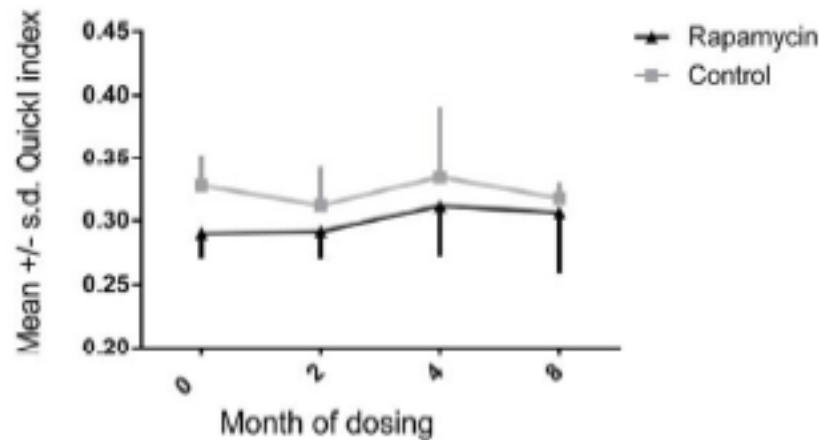
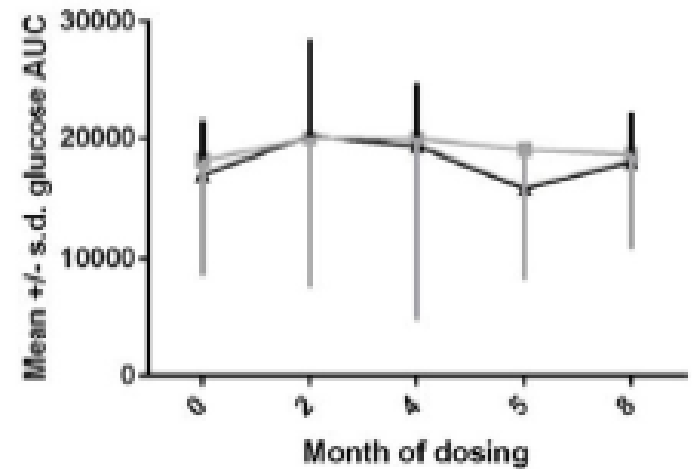
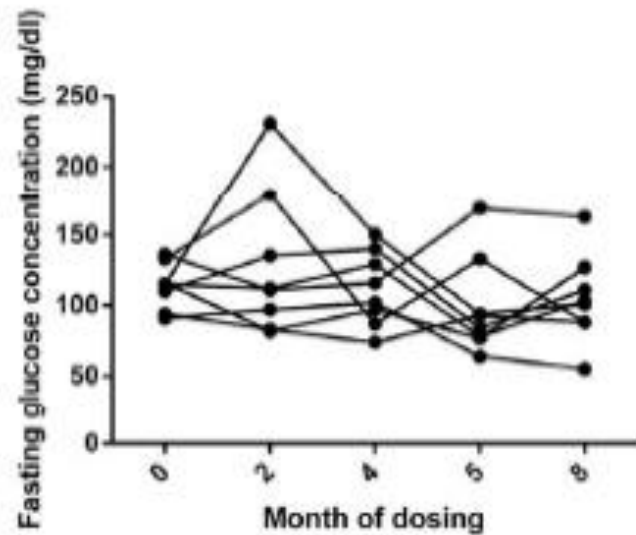
Marmoset Rapamycin



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



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

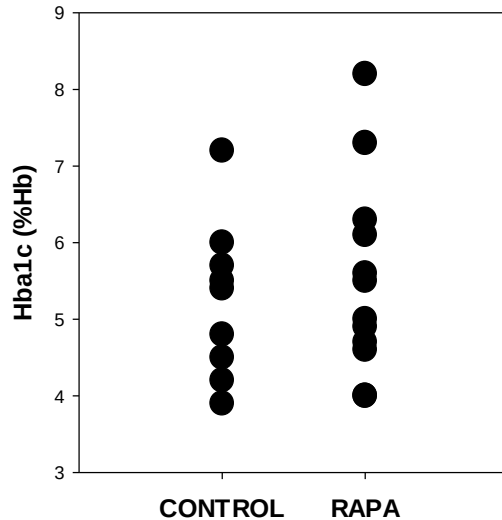


Marmosets receiving rapa do not exhibit significantly altered glucose metabolism

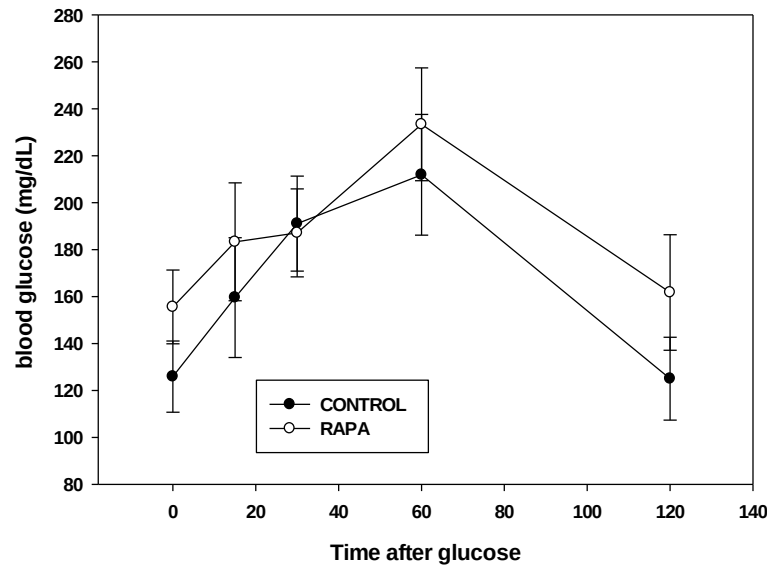
(Ross et al 2015)

Longitudinal follow - No significant detriment in glucose metabolism with 12 months treatment

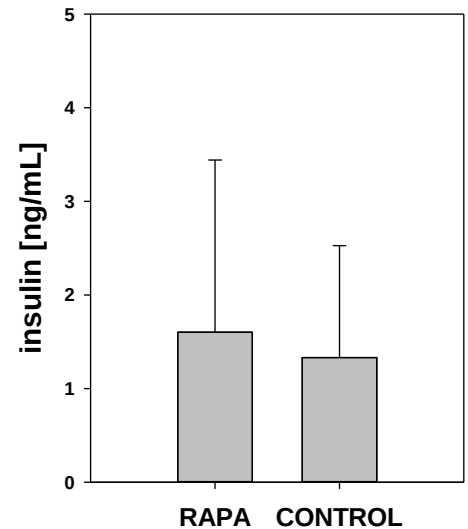
Hba1c



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

Acknowledgements

SNPRC

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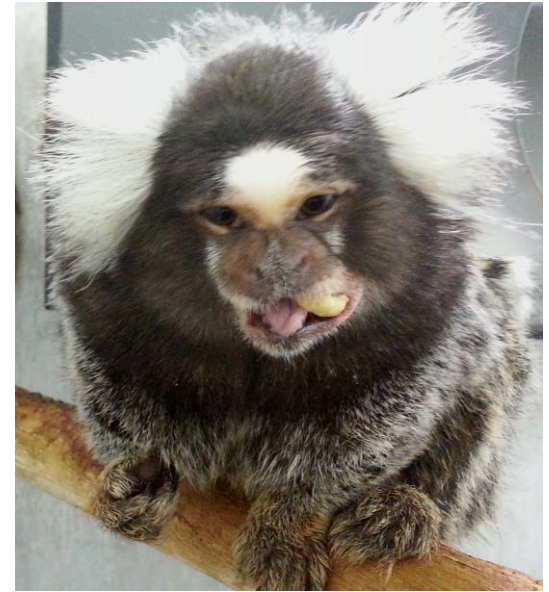
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