

The role of Nrf2 in the anti-cell senescence effect of rapamycin

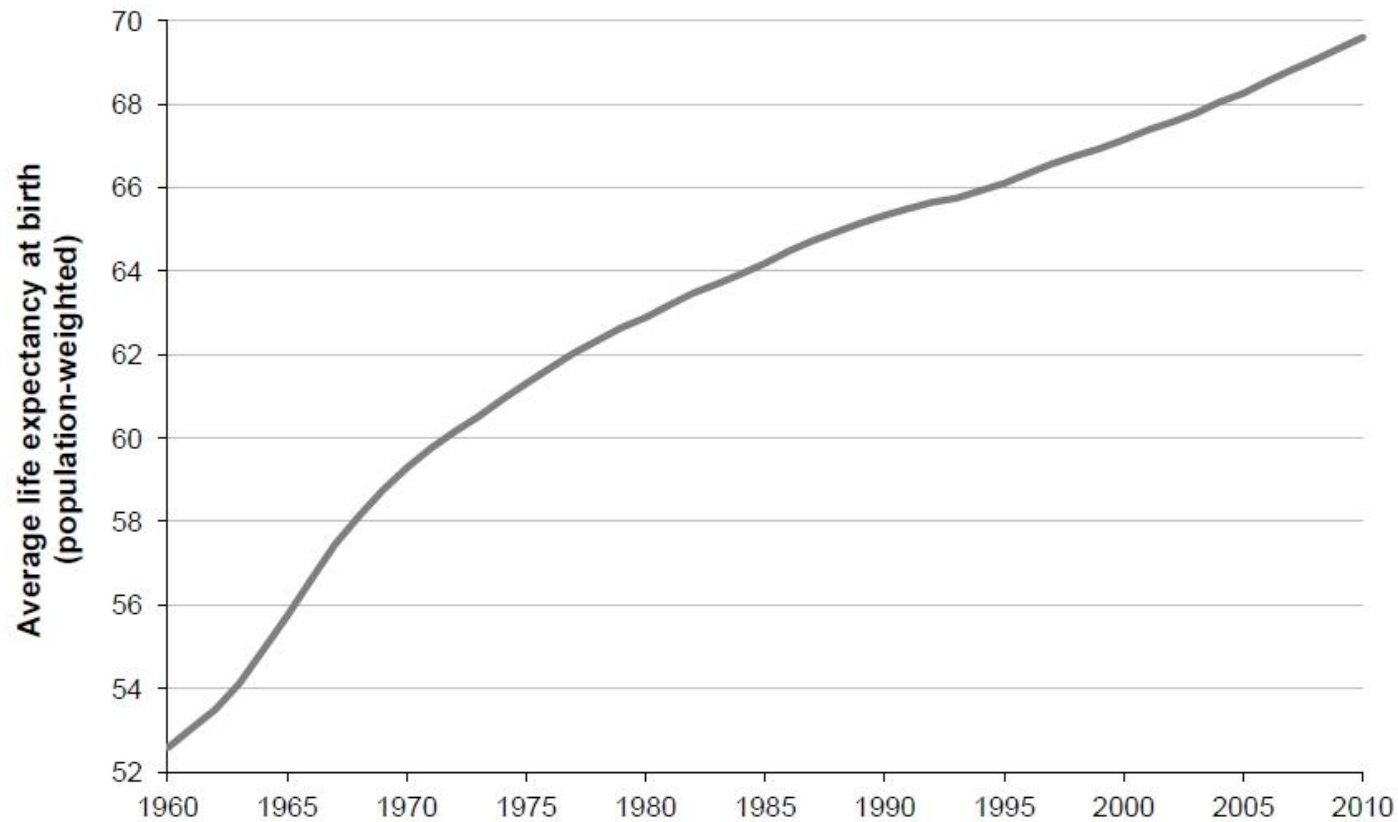
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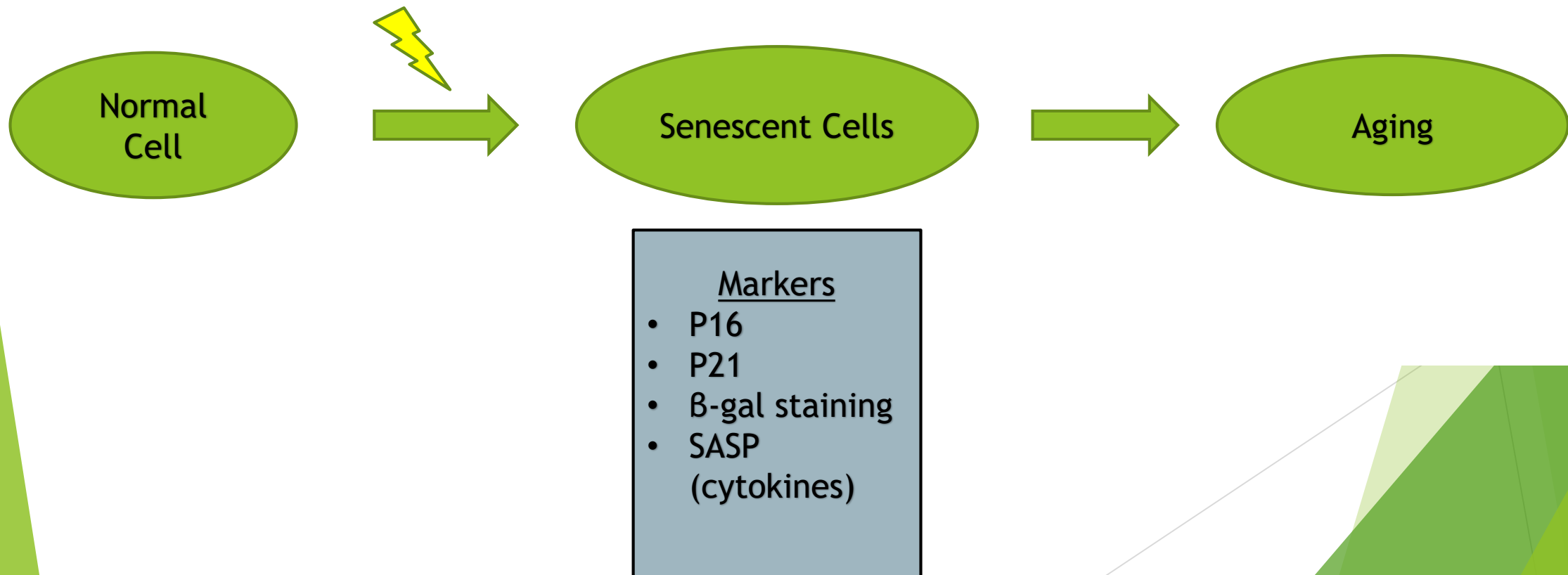
Aging

- ▶ Aging is a universal process
- ▶ Lifespan has increased but with this comes age related diseases



Cellular Senescence

- ▶ Cellular senescence is a cell cycle arrest state in which cells cannot divide
- ▶ Cellular senescence has been associated with many age-related diseases



Rapamycin and Nrf2

- ▶ Rapamycin is a mTOR inhibitor that can improve health in several animal models as well as inhibit cellular senescence in multiple types of cells
- ▶ Rapamycin activates the Nrf2 pathway
- ▶ Nrf2 is a pro-longevity signaling pathway
- ▶ Inverse correlation between aging and Nrf2 expression
- ▶ Silencing the Nrf2 gene induces premature senescence



We investigated whether Nrf2 is involved
in the mechanism by which rapamycin
delays cell senescence

Methods

- ▶ Fat tissues were obtained from WT and Nrf2 KO mice with or without rapamycin (ip injection with rapa)
- ▶ β -gal staining
- ▶ Western Blot
 - ▶ ATF4
 - ▶ STAT3



β -gal Staining

WT

Nrf2 KO

2 Mo



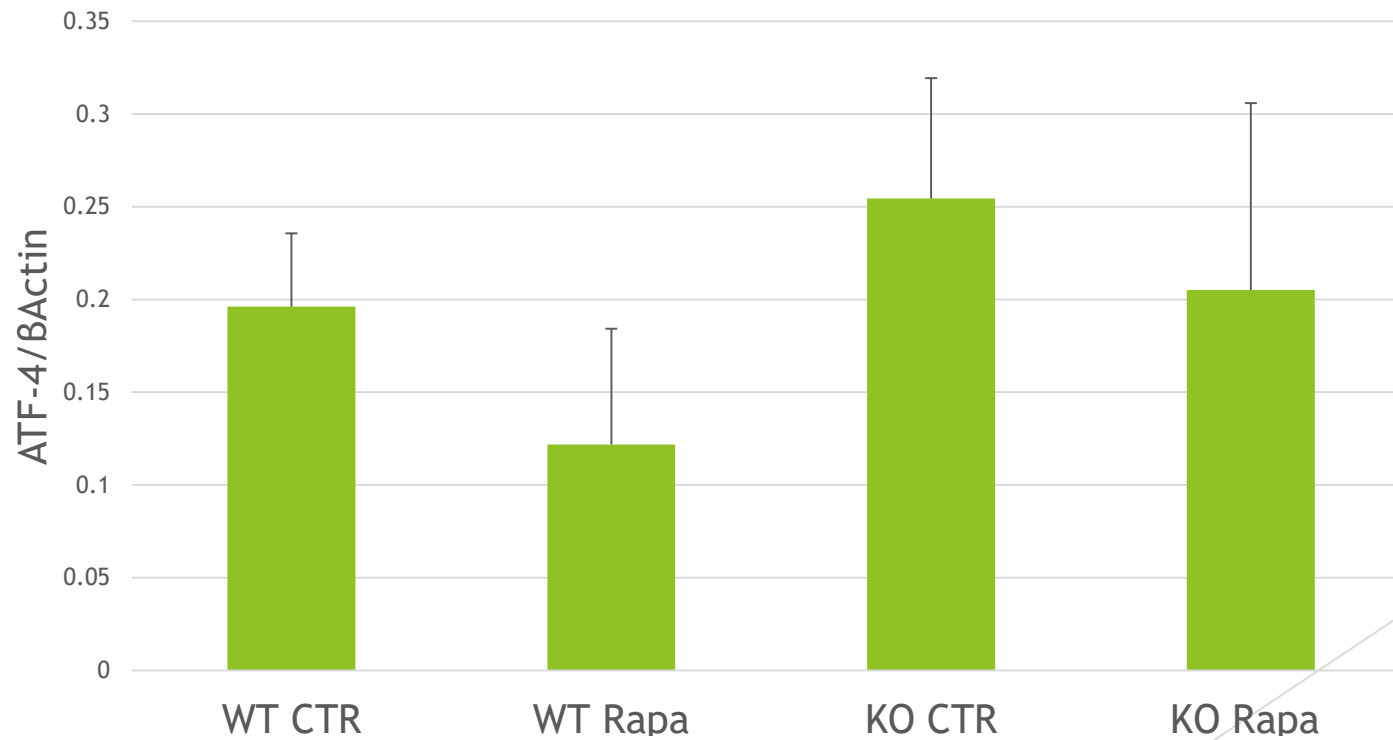
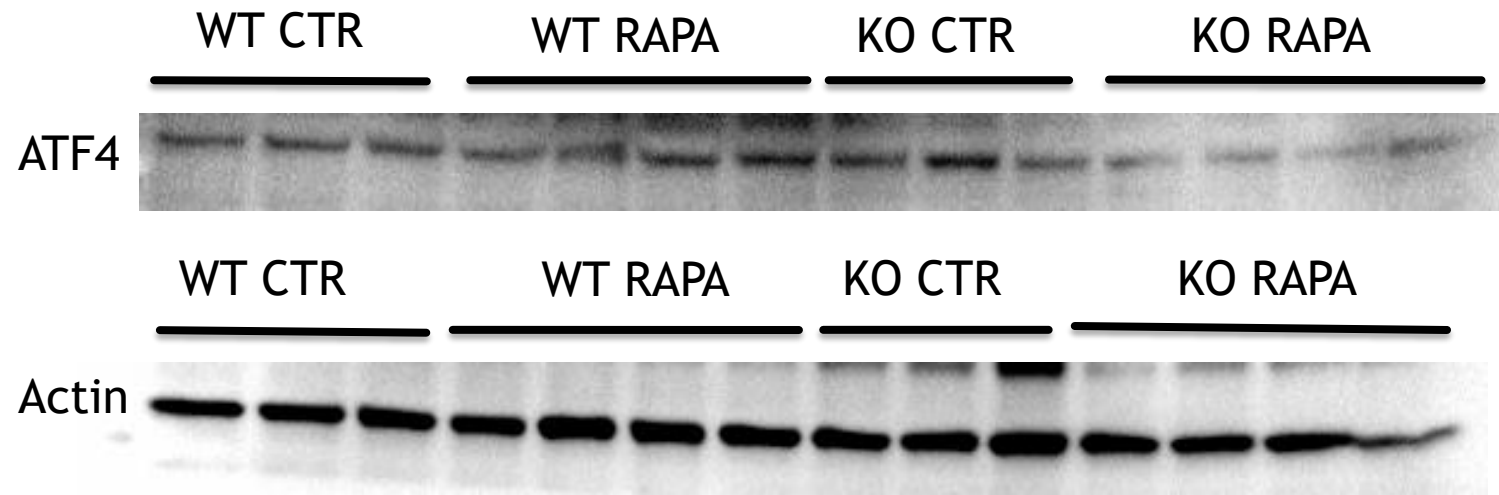
3¹/₂ Mo



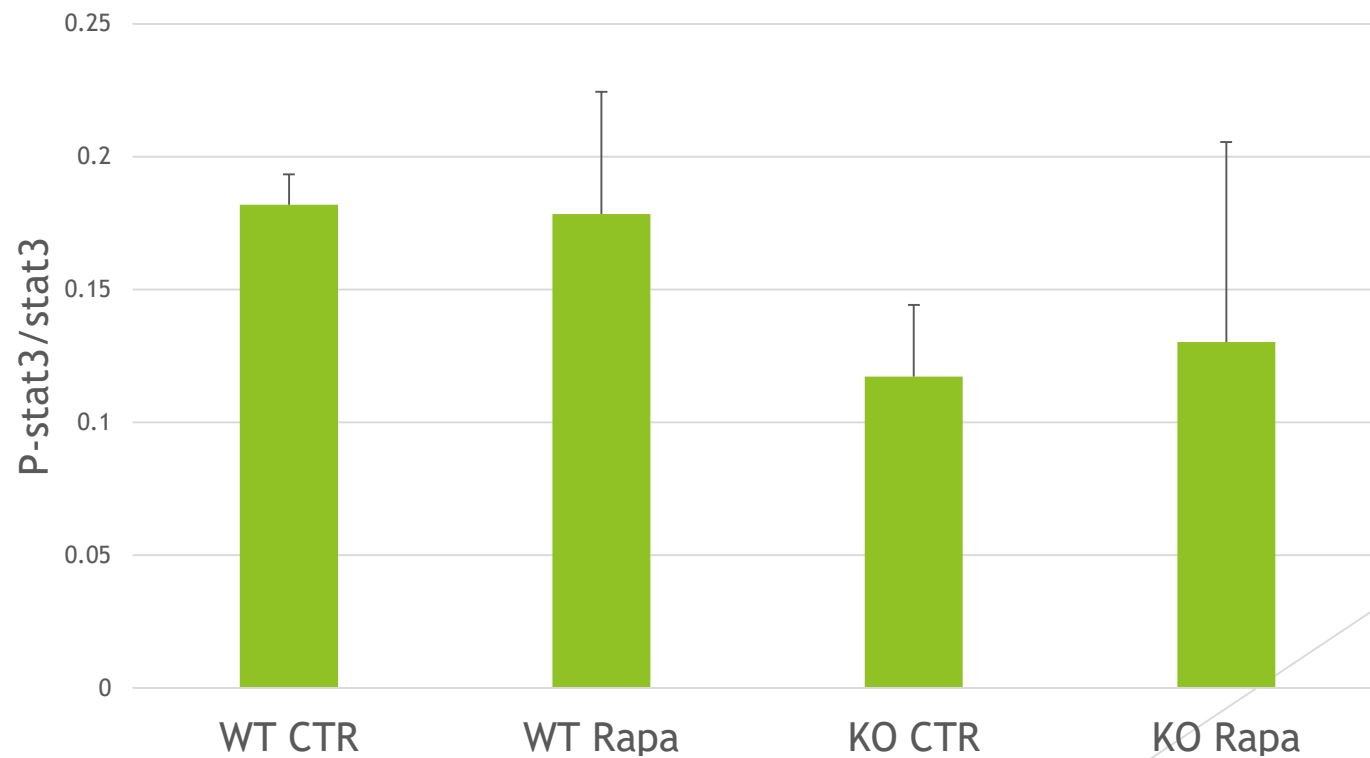
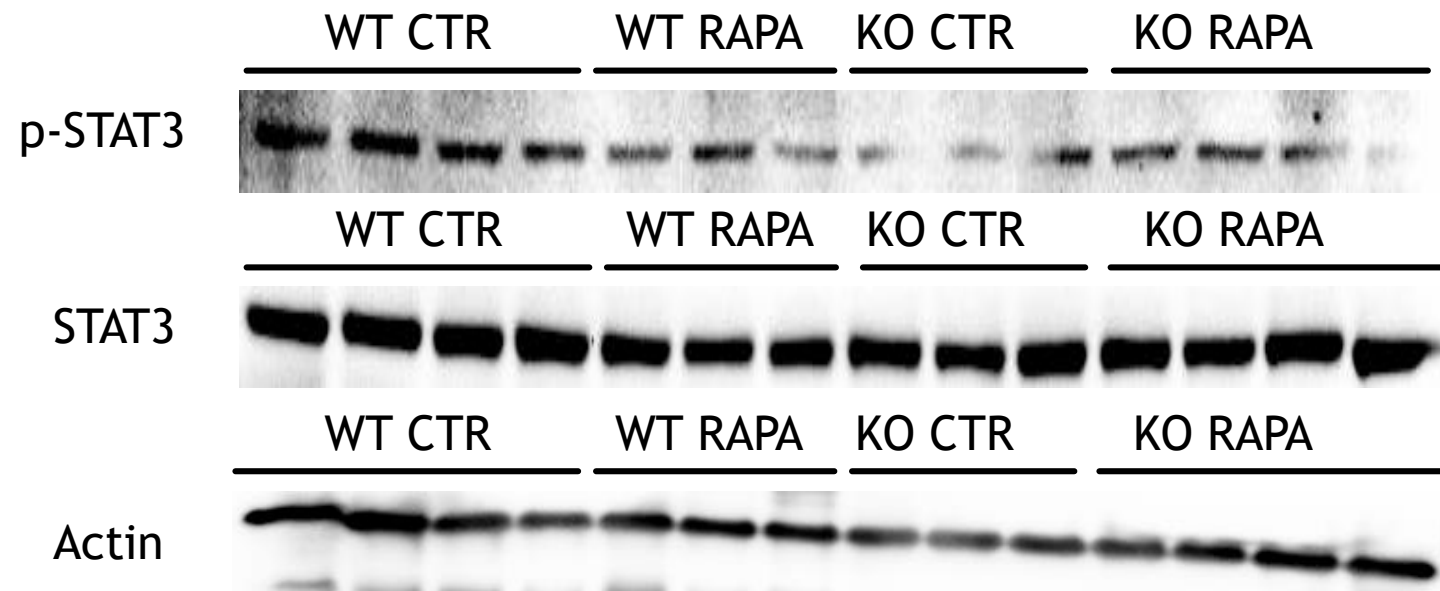
3¹/₂ Mo
+ rapa



ATF4



STAT p-STAT3



Conclusions & Future Studies

- ▶ Rapamycin decreases β -gal staining in Nrf2KO mice
- ▶ Rapamycin inhibits the ATF4 pathways in a Nrf2-independent manner but not STAT3
- ▶ Replicate these experiments in other animal models
- ▶ Use inhibitors and observe the pathways

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