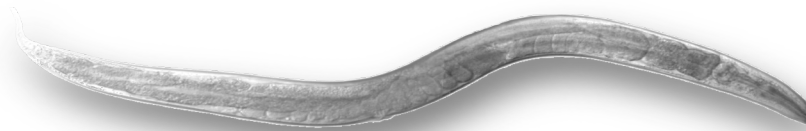


HISTONE DEUBIQUITINATION IN MITOCHONDRIAL STRESS AND LONGEVITY



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The importance of understanding ageing



Ageing associated diseases

- Alzheimer
- Parkinson
- Huntington
- Diabetes
- Obesity
- Cancer

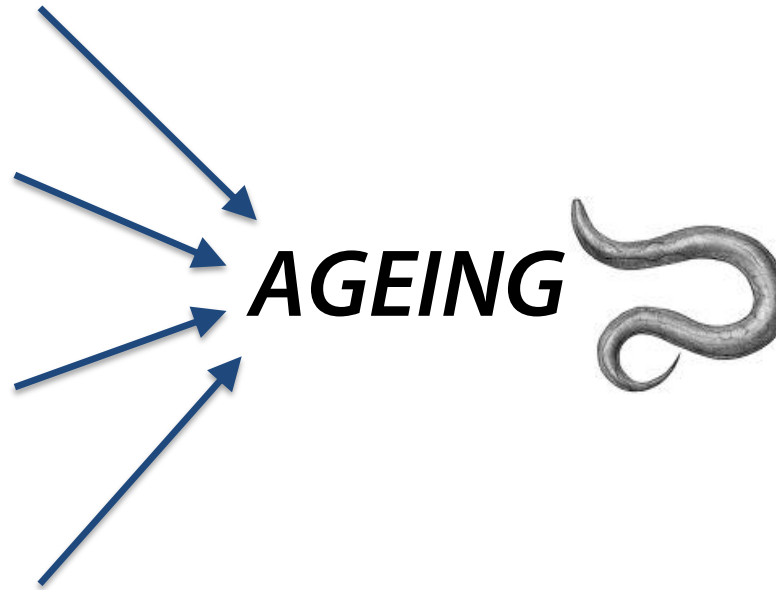
The genetics of ageing

*Insulin/IGF-1
signalling (IIS)*

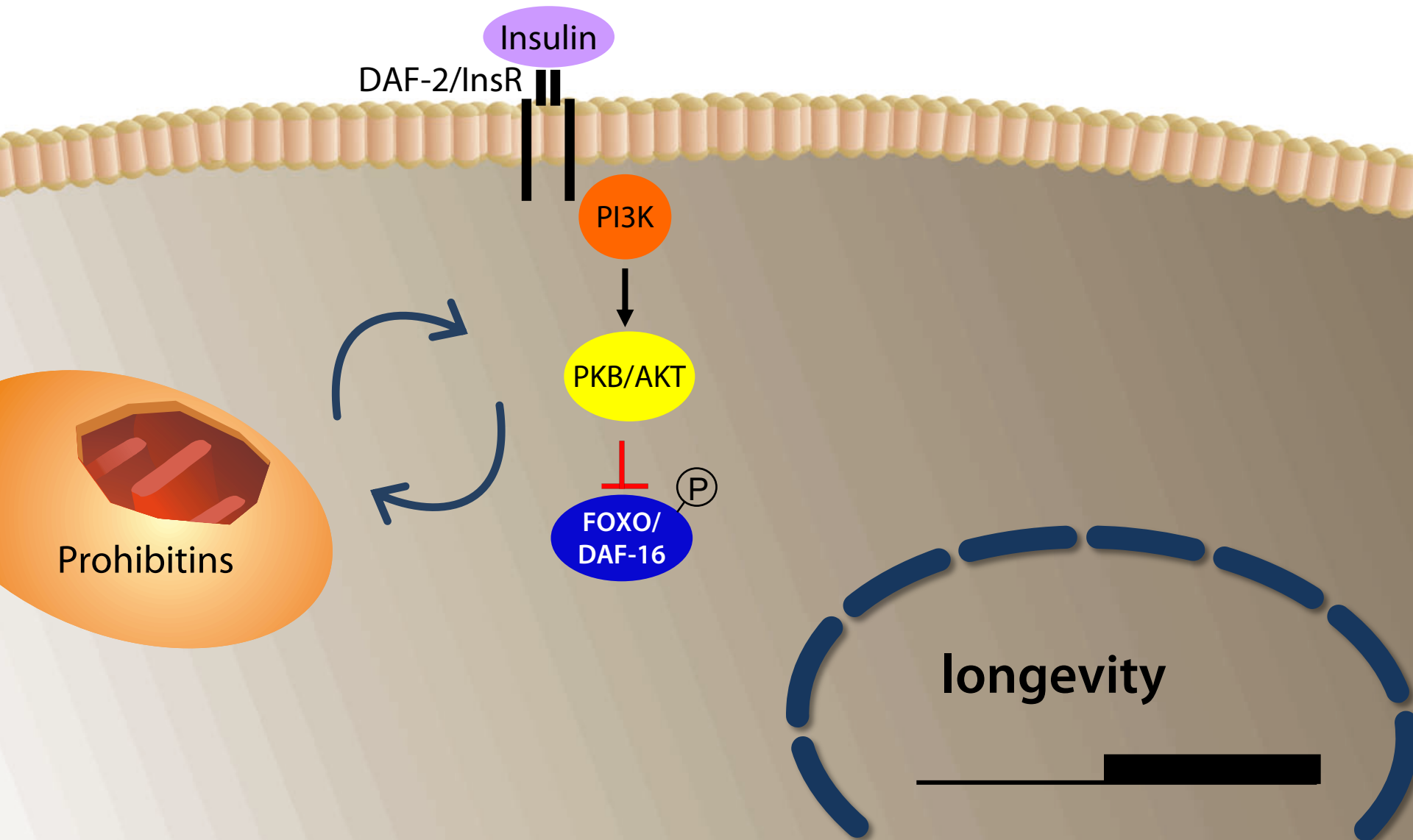
TOR signalling

*Dietary
restriction*

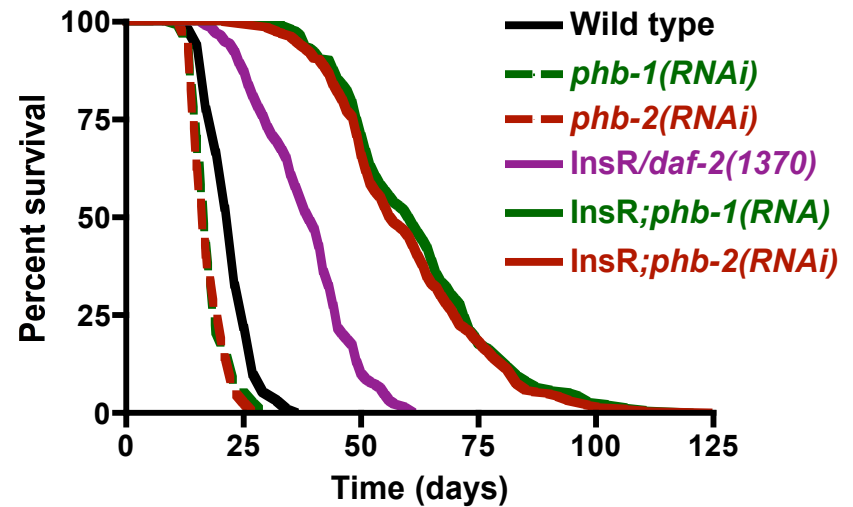
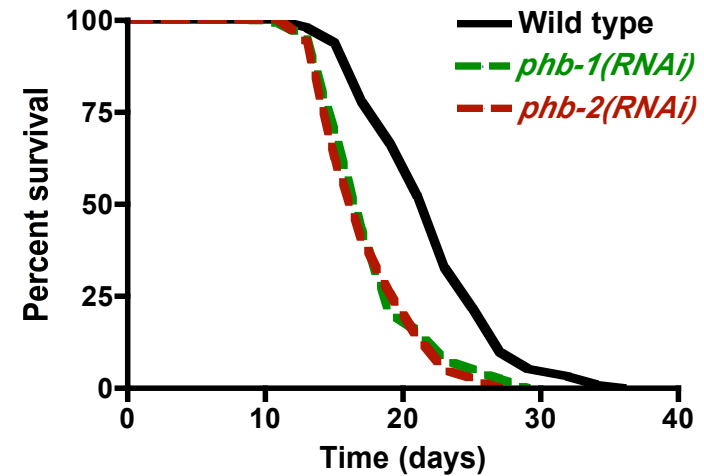
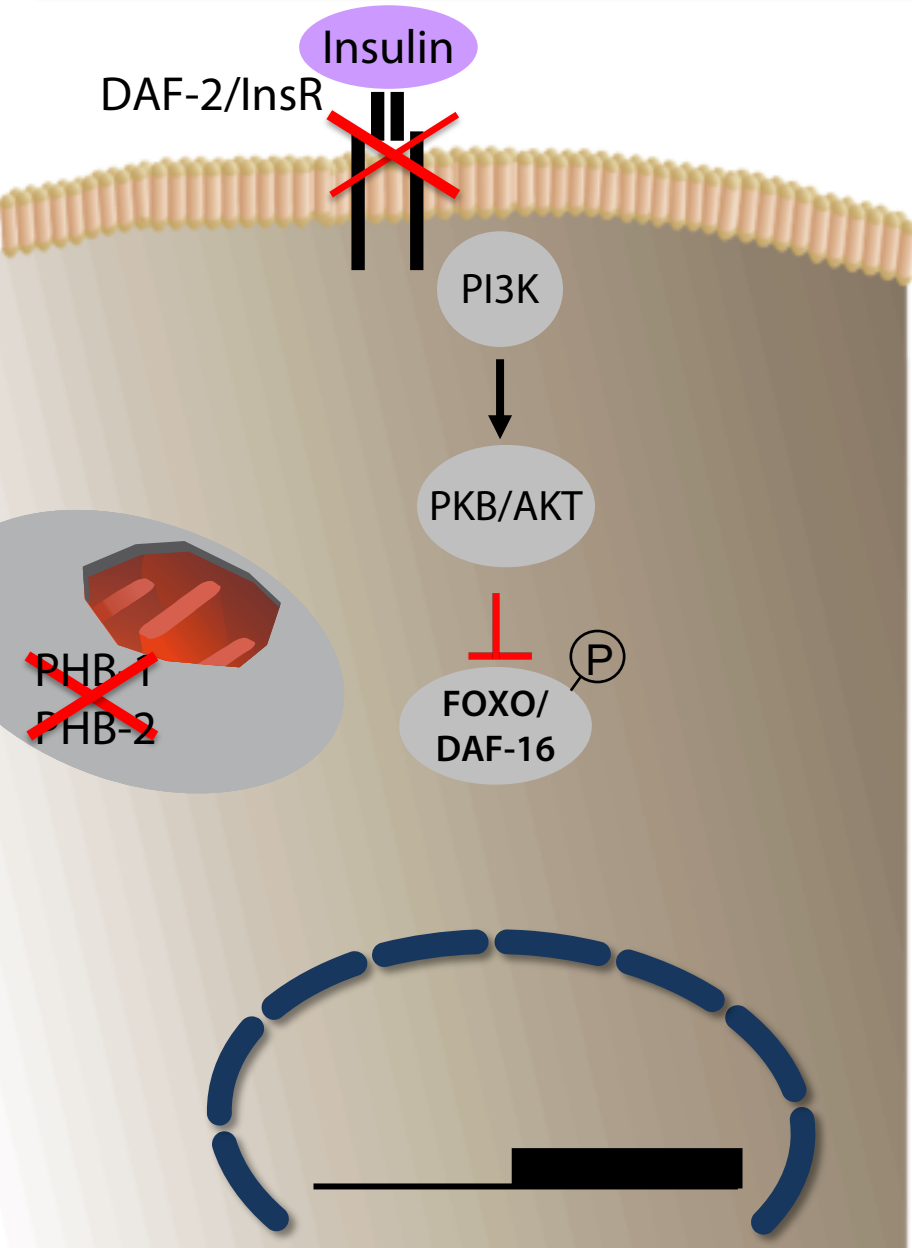
*Mitochondrial
function*



Mitochondrial crosstalk in ageing

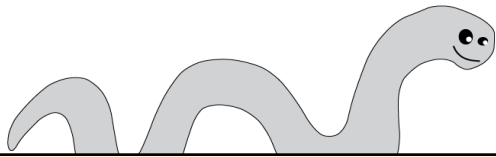


Mitochondrial prohibitins in ageing



Artal-Sanz and Tavernarakis (2009) *Nature*

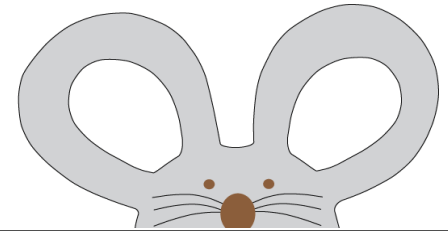
A conserved role for prohibitins in ageing



Artal-Sanz and Tavernarakis.
2009, *Nature*

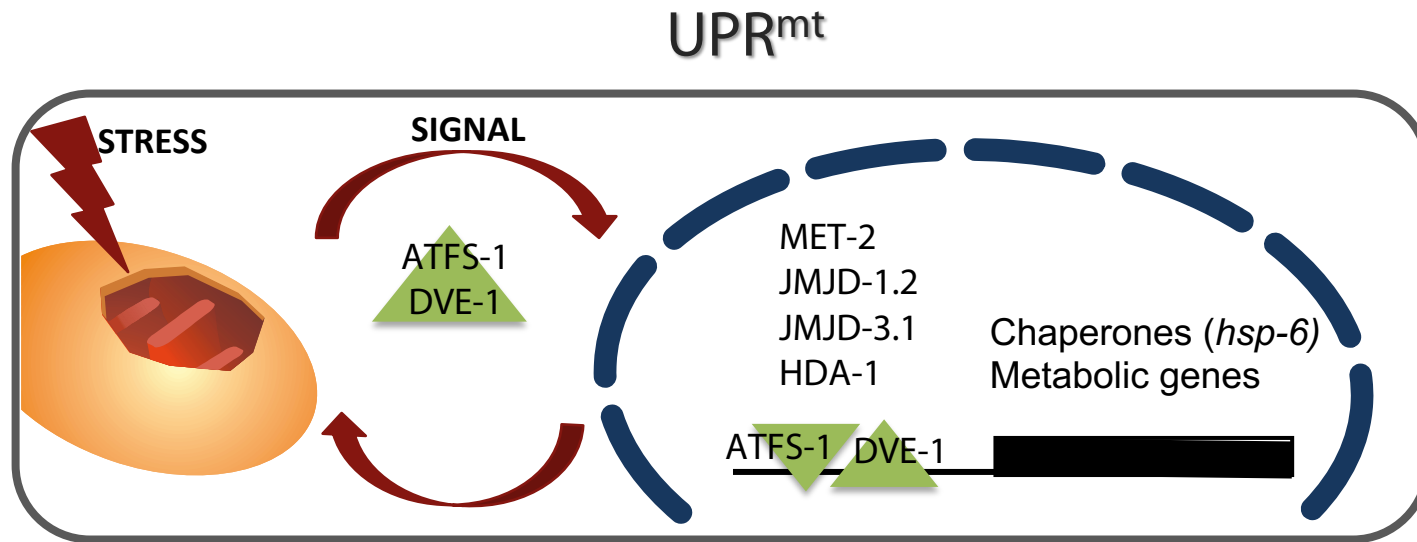


Schleit et al.
2013, *Aging Cell*

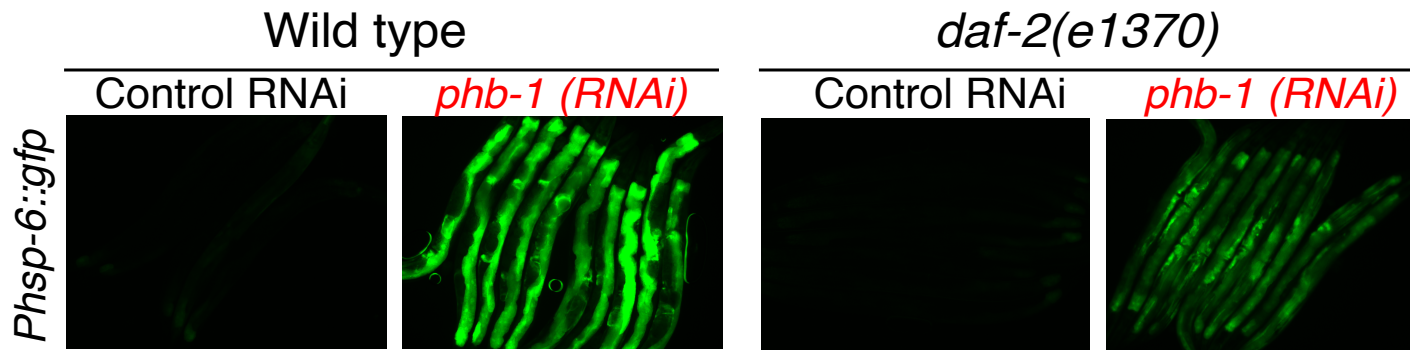


Ising et al.
2015, *EMBO Mol. Med.*

PHB depletion induces the mitochondrial unfolded protein response (UPR^{mt})

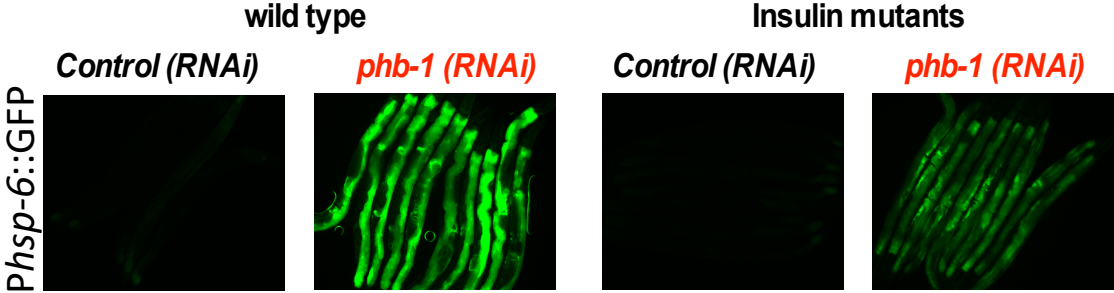


Adapted from Merkwirth et al. 2016.

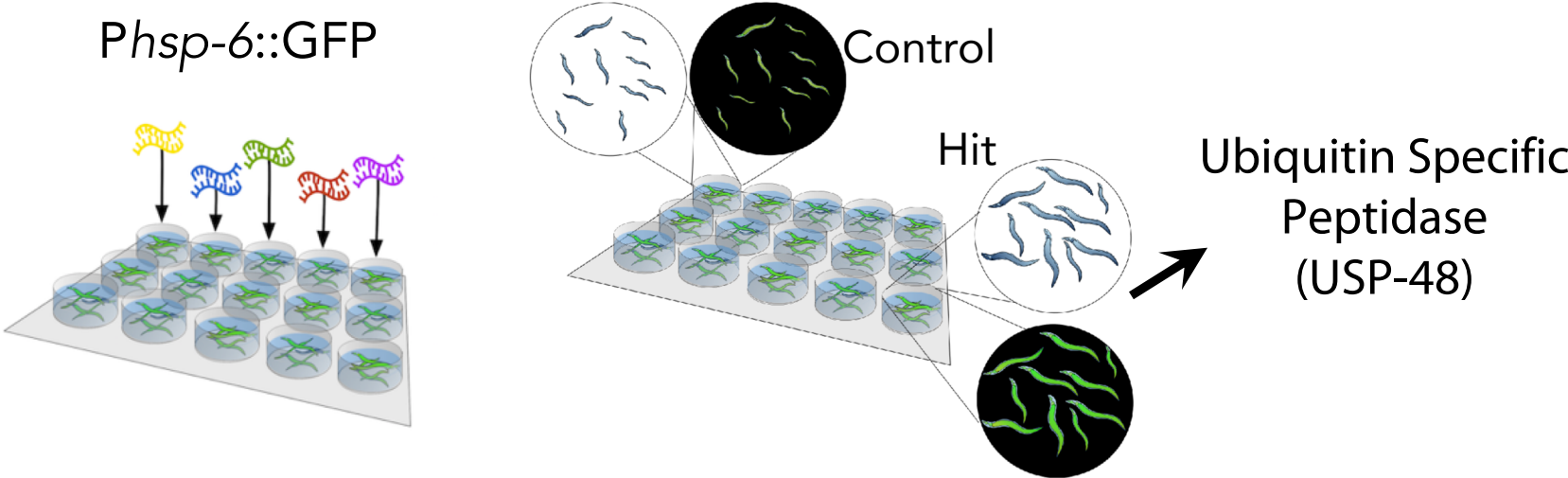


Gatsi et al. 2014. *PLoS One*

An RNAi screen uncovers USP-48 as a new UPR^{mt} regulator

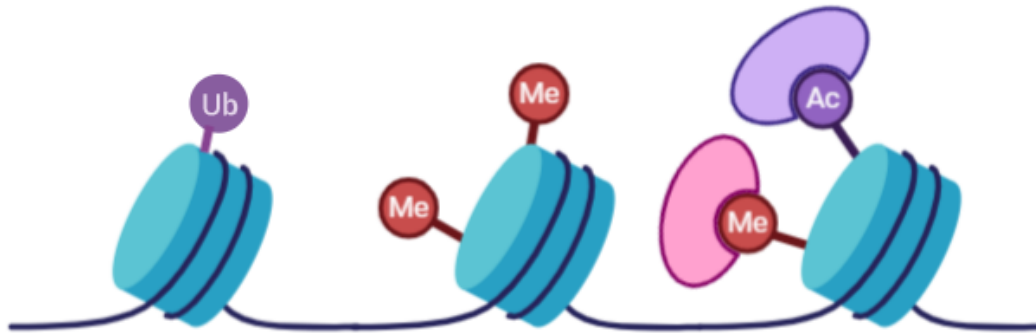


Genome-wide RNAi screen



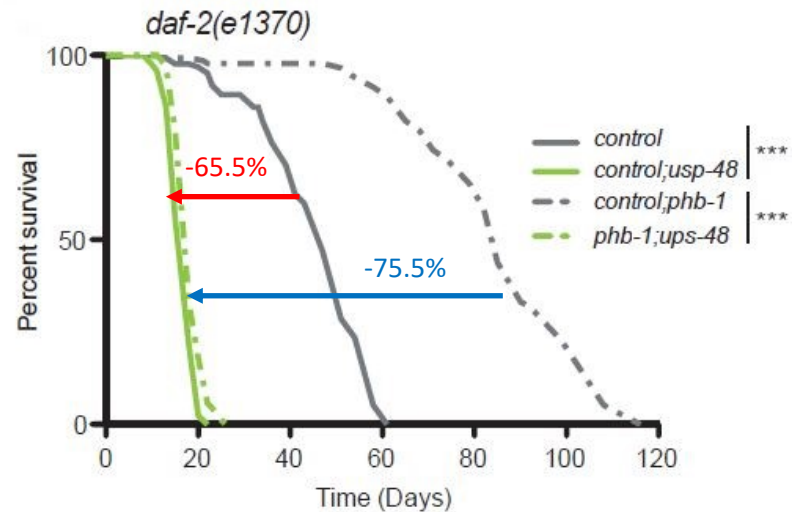
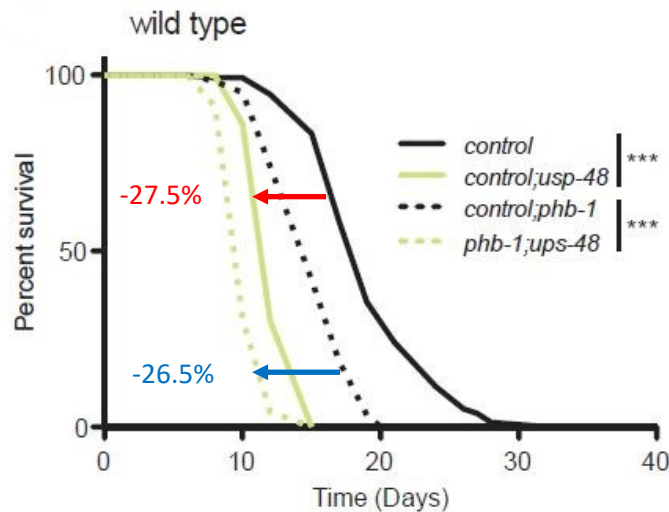
Histone deubiquitination in mitochondrial stress and longevity

Histone ubiquitination



USP-48 reduces histone ubiquitination levels and affects gene expression

USP-48 depletion suppresses lifespan extension conferred by *daf-2* loss of function



What will you do?

Worm physiology

Analyse the mitochondrial functionality of *usp-48* mutants.

Microscopy

Using endogenously (CRISPR) tagged USP-48, analyse USP-48 expression

Determine the role of H2A and H2B ubiquitin ligases in the UPRmt.

Molecular Biology

Western blot analysis of Histone Ubiquitination levels under different stress conditions

CRISPR tag USP-48 for biochemical applications. Cloning and injection