

Recent aging discoveries



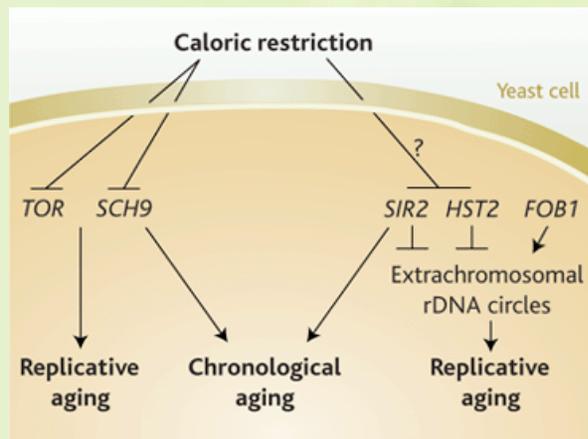
A&S300-002 Jim Lund

Yeast aging and CR

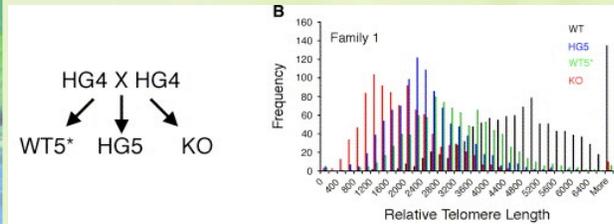
Regulation of Yeast Replicative Life Span by TOR and Sch9 in Response to Nutrients. (Kaeberlein et al., 2005)

HST2 Mediates SIR2-Independent Life-Span Extension by Calorie Restriction. (Lamming et al., 2005)

Yeast aging and CR



Wild type mice with short telomeres have germ cell defects



HG heterozygote telomerase RNA mutants.
WT wild type offspring of the hets.
KO $-/-$ knock-out offspring of the hets.

Hao et al., 2005

Regulation of Lifespan in Drosophila by Modulation of Genes in the TOR Signaling Pathway.

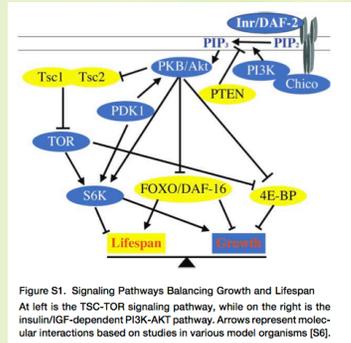


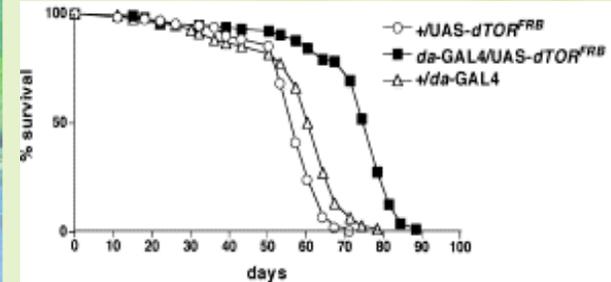
Figure S1. Signaling Pathways Balancing Growth and Lifespan
At left is the TSC-TOR signaling pathway, while on the right is the insulin/IGF-dependent PI3K-AKT pathway. Arrows represent molecular interactions based on studies in various model organisms [56].

(Kapahi et al., 2004)

TOR=Target Of Rapamycin

(rapamycin is a product of the bacterium *Streptomyces hygroscopicus* found in a soil sample from the island Rapa Nui, better known as Easter Island!)

Mutations in fly TOR extend lifespan



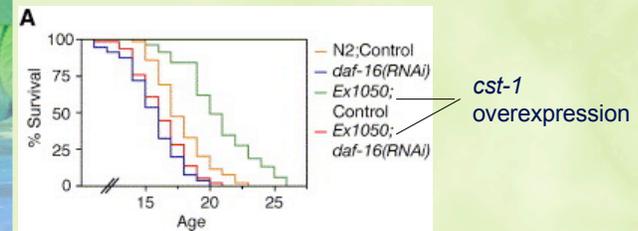
A Conserved MST-FOXO Signaling Pathway Mediates Oxidative-Stress Responses and Extends Life Span

•Protein kinases in the Ste20(yeast)/MST (mammals)/hippo(flies)/CST(worms) regulate cellular responses to oxidative stress.

•FOXO3(mammals)/daf-16(worms) is activated by the MST kinases in response to oxidative stress.

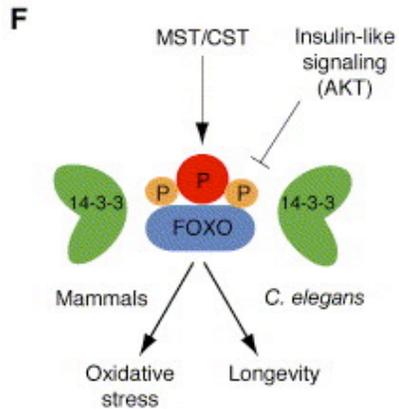
(Lehtinen et al., 2006)

Overexpression of *cst-1* in worms extends lifespan



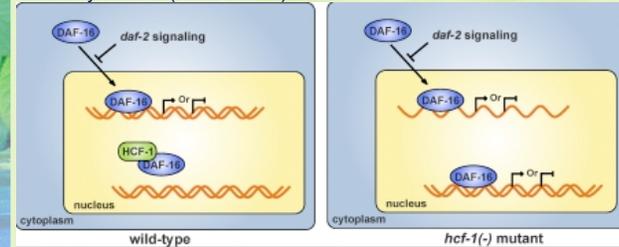
cst-1 is a STET-20-like kinase (a signaling pathway gene)
-This is the first study on *cst-1*, nothing else is known about it.

MST/*cst-1* signals (in part) through FOXO/*daf-16*



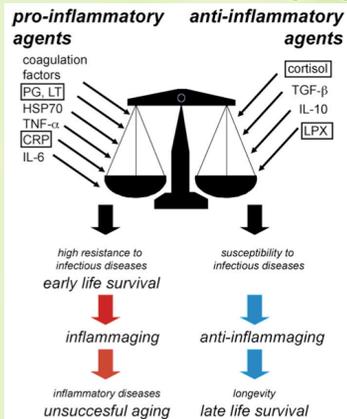
Caenorhabditis elegans HCF-1 Functions in Longevity Maintenance as a DAF-16 Regulator

Ji Li, Atsushi Ebata, Yuqing Dong, Gizem Rizki, Terri Iwata, and Siu Sylvania Lee (Cornell Univ)

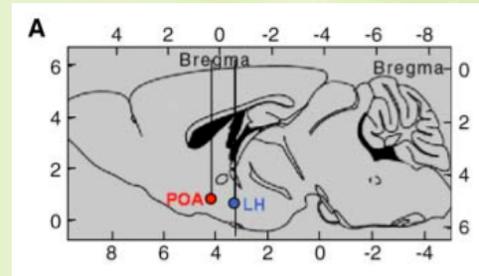


- * *hcf-1* worms are long-lived.
- * HCF-1 is nuclear localized and physically associated with DAF-16, and prevents DAF-16 from binding to promoters of genes.

Growing evidence of the role of inflammation in aging



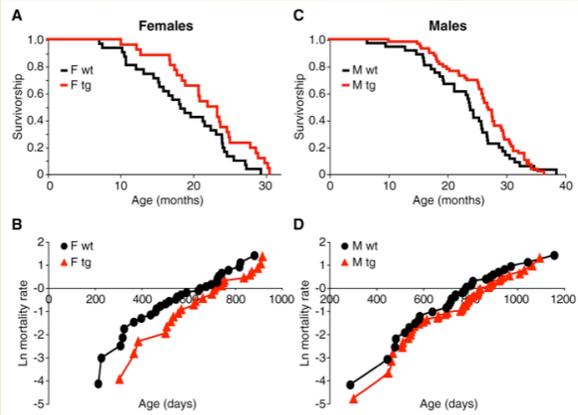
Transgenic Mice with a Reduced Core Body Temperature Have an Increased Life Span



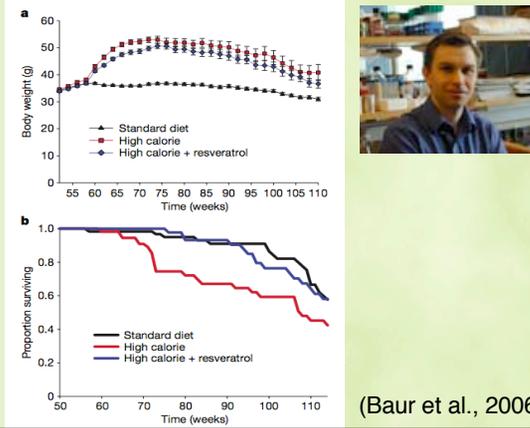
Expressed uncoupling protein UCP2 in the lateral hypothalamus.

(Conti et al., 2006)

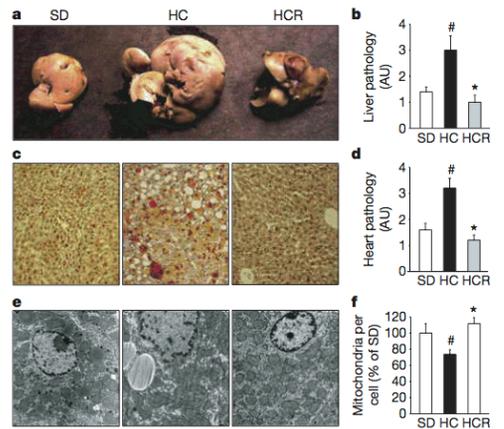
Reduced body temperature extends lifespan in mice



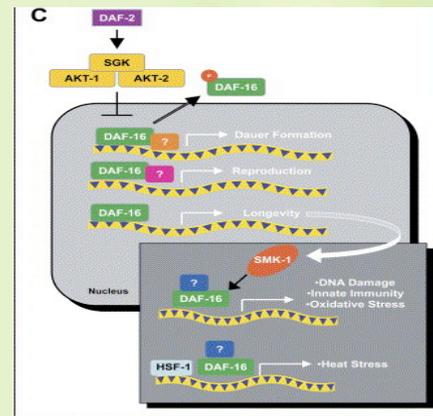
Resveratrol improves health and survival of mice on a high-calorie diet



Organ pathology improved on resveratrol

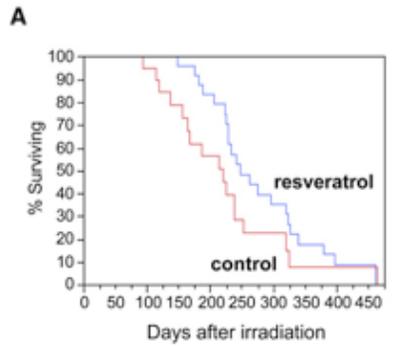


Discoveries in the insulin-like signaling pathway



SIRT1 Redistribution on Chromatin Promotes Genomic Stability but Alters Gene Expression during Aging.

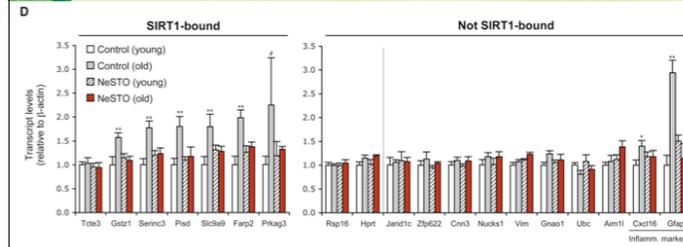
Oberdoerffer *et al.*, 2008 (Sinclair lab)



A. Survival of irradiated p53^{+/+} mice fed normal or resveratrol-supplemented chow.

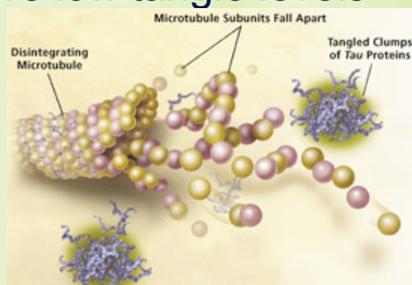
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Oberdoerffer *et al.*, 2008 (Sinclair lab)



D. q-RT-PCR analysis of SIRT1-bound genes (left) and non-SIRT1-bound genes (right) including housekeeping genes (*rps16*, *hprt*) and genes upregulated in 30-month-old mice by microarray.

High cognitive function elderly have low tangle levels



- * Resistant to tangle formation
- Tangles main component is tau protein.

Changiz Geula (Northwestern University)