

CELLS AND GENES THAT FUNCTION IN THE REPRODUCTIVE SYSTEM OF C.ELEGANS TO PROMOTE LONGEVITY

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In *C. elegans* signals from the reproductive system influence life span. If germline stem cells are killed by laser ablation, lifespan increases strikingly. This phenomenon can be reproduced genetically in *glp-1* mutants, which lack the germline, and therefore have an extended lifespan. For germline ablation to extend life span, a normal somatic gonad is required. Our findings suggest the model that the reproductive system produces two kinds of counterbalancing cues: the germline provides signals that reduce lifespan while the somatic gonad produces signal(s) that enhance lifespan. The ability of the animals to live longer in the absence of germ line is dependent on DAF-16 (a forkhead transcription factor) as well as on DAF-12 (a putative nuclear hormone receptor). But the molecular mechanism(s) underlying this complex regulatory network are unknown. We've used a combination of laser ablations and RNAi screening to identify cells of the somatic gonad that produce the longevity signal, and genes involved in this pathway. Cells of the somatic gonad that promote longevity: To identify specific cells of the somatic gonad that produce longevity- promoting signal(s), we've devised a 'Twin Ablation' scheme that involves elimination of the germ cells followed by elimination of specific precursors of somatic gonad structures. Using Twin Ablations we've systematically eliminated specific cell types of the somatic gonad, in germline ablated animals, and examined their effect on lifespan. We find that multiple cell types of the somatic gonad are required for the extended lifespan of animals that lack a germline. The implications of these somewhat surprising observations will be discussed.

Genes of the somatic gonad that promote longevity: To identify genes that influence lifespan via the reproductive system we have fed *glp-1* worms with bacteria expressing dsRNA of *C. elegans* genes. We've looked for rare individuals that have a shortened lifespan due to loss of a positive mediator of longevity. We have identified three transcription factors, each of which acts in a unique fashion to promote longevity. The molecular mechanisms underlying the action of these genes will be discussed.