AGEING, STRESS, AND TRADE-OFFS IN *CAENORHABDITIS ELEGANS*

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Extending life of the nematode *C. elegans* by a variety of interventions has greatly increased our understanding of the basic biology of ageing. Genetic analysis indicates that one principal determinant is a signaling pathway resembling the mammalian insulin or insulin-like growth factor-I (INS/IGF) pathway. This pathway also controls progression through normal development and determines adult stress resistance. Recent evidence suggests that INS/IGF effects have been conserved across taxa.

Ageing has been postulated to result from late life detrimental effects of genes that act beneficially early in life. Evidence to support this hypothesis has been provided by the competitive fitness of a single-gene mutant in the INS/IGF pathway that increases *Caenorhabditis elegans* mean and maximum lifespan by up to 80%. When grown at 20^{o}C, adults with the mutation *age-1(hx546)* have increased lifespan, thought due to a reduced rate of ageing, but otherwise are essentially identical to wild type worms suggesting, that this lifespan extension comes without a fitness cost. However, we demonstrated that under starvation cycles that may be representative of the nematodes evolutionary history, the wild type *age-1* allele is selected due to beneficial effects on reproductive fitness. This was the first direct evidence of a single gene that acts on early life, ageing, and Darwinian fitness, as predicted by antagonistic pleiotropy. Subsequent laboratory natural selection experiments using *daf-2* long-lived mutants that appear phenotypically similar to *age-1(hx546)* suggest that the mechanisms observed for *age-1* may be generalized to INS/IGF signaling. A number of factors appear to be involved in the trade-off observed under starvation cycling, including the timing of starvation, recovery from starvation and maternal effects on progeny quality.