



Figure 1 A model for gonadal influences on lifespan arising from the results of Hsin and Kenyon². Arrows, activating signals; T-bars, inhibitory signals. Insulin-like ligands are proposed to activate the DAF-2 receptor, which then deactivates the DAF-16 transcription factor through a phosphorylation cascade. DAF-16 increases longevity (by promoting a process that requires CTL-1 catalase activity) unless inhibited by DAF-2 or by a separate signal from the germ line. Somatic-gonadal cells enhance longevity by reducing the level of DAF-2 inhibition. The role of the DAF-12 protein is uncertain. Destruction of the whole gonad has a similar effect to *daf-12* mutations, so DAF-12 might be required for signalling from both somatic gonad and germ line. However, DAF-12 is not required for somatic-gonad signalling in a wild-type genetic background. Hsin and Kenyon suggest that DAF-12 activity is influenced by DAF-2, an idea that is supported by other genetic data^{5,8}.

long as normal. They stay younger longer, as judged by their movement and appearance^{4,8}. The extended longevity requires the activity of DAF-16, a transcription factor in the forkhead family^{9,10}, and also involves DAF-12 (ref. 5), a nuclear hormone receptor⁶. The *daf-2* mutants overexpress CTL-1, a cytosolic catalase that may prevent oxidative damage, and CTL-1 activity is required for increased longevity¹¹. A *ctl-1* mutant has a 'progeric' (precocious ageing) phenotype. The overall conclusion in this context¹¹ is that the catalase protects the nematode from oxidative damage during dormancy, and increased protection extends adult life.

Hsin and Kenyon² have discovered that DAF-16 and DAF-12 activities are required for germline ablation to extend life. These proteins both appear to be transcription factors regulated by germline signalling. To reveal the hypothesized signals from the somatic gonad, they carried out a series of surgical experiments on animals lacking *daf* gene functions. Germline ablation did not extend the life of *daf-16* mutants, but whole-gonad ablation shortened life relative to that of intact *daf-16* controls, supporting the idea that the somatic gonad promotes longevity. Furthermore, ablation of either the germline precursors alone, or both the germline and somatic-gonadal precursors, extended *daf-2* mutant longevity, indicating that DAF-2 activity is required for the life-shortening response to destruction of the somatic gonad.

Given these results, the authors propose that signals from the normal somatic gonad promote longevity by inhibiting DAF-2 receptor activity. The idea is relatively simple. The germline signal shortens lifespan by downregulating DAF-16 and DAF-12 activities, whereas the somatic gonad produces a signal that lengthens life by inhibiting DAF-2 (Fig. 1). The activities of germ line and soma are opposite, because one acts on DAF-16,

which enhances longevity, and the other acts on DAF-2, which normally acts to shorten life.

One can imagine how gonadal signalling for longevity might be adaptive. Prolonged survival of the adult in response to limited food might improve its chances of reproducing. This is a strategy analogous to dauer arrest, and is apparently controlled by some of the same genes. On the other hand, a healthy germ line associated with maximal reproduction might also be adaptive by limiting a parent's competition with its progeny for food.

The dauer or non-dauer developmental decision, and the trade-offs between reproductive pattern and longevity, are major aspects of *C. elegans* life history. Investigations of how they have co-evolved, and the molecular controls that are responsible for their integration, are addressing one of the most complex issues in evolutionary biology. Perhaps it is not surprising that insights on ageing arise from developmental genetics. It is interesting to consider whether similar gonadal signals affect longevity in mammals, especially in species that hibernate. □ Donald L. Riddle is in the Molecular Biology Program and the Division of Biological Sciences, University of Missouri, Columbia, Missouri 65211, USA.

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- Rose, M. R. *Evolutionary Biology of Aging* (Oxford Univ. Press, 1994).
- Hsin, H. & Kenyon, C. *Nature* **399**, 362–366 (1999).
- Kimura, K., Tissenbaum, H., Liu, Y. & Ruvkun, G. *Science* **277**, 942–946 (1997).
- Kenyon, C., Chang, J., Gensch, E., Rudner, A. & Tabtiang, R. A. *Nature* **366**, 461–464 (1993).
- Larsen, P., Albert, P. & Riddle, D. *Genetics* **139**, 1567–1583 (1995).
- Riddle, D. & Albert, P. in *C. elegans II* (eds Riddle, D., Blumenthal, T., Meyer, B. & Priess, J.) 739–768 (Cold Spring Harbor Laboratory Press, 1997).
- Klass, M. & Hirsh, D. *Nature* **260**, 523–525 (1976).
- Gems, D. et al. *Genetics* **150**, 129–155 (1998).
- Ogg, S. et al. *Nature* **389**, 994–999 (1997).
- Lin, K., Dorman, J., Rodan, A. & Kenyon, C. *Science* **278**, 1319–1322 (1997).
- Taub, J. et al. *Nature* **399**, 162–166 (1999).



100 YEARS AGO

Thirty years ago, a French entomologist, named Leopold Trouvelot, was living at Medford, in Massachusetts. He was engaged in carrying on a series of experiments on rearing moths. ... He imported the Gipsy Moth, and by some accident, some of the insects escaped from his custody into his own or the neighbours' gardens. ... Had prompt measures been taken, the insect might possibly have been exterminated; but it does not seem to have attracted any attention till about 1880, when the people then living in or near M. Trouvelot's former residence began to be troubled with swarms of caterpillars, though what they were, and whence they came, was then unknown. For several years the neighbouring houses suffered severely, apple- and pear-trees and shade-trees being stripped of their leaves and killed, and the caterpillars creeping all over and into the houses. Nevertheless, they spread very slowly along the street, and into surrounding woods till 1889, when the insects multiplied so much that the caterpillars stripped all the trees in the immediate neighbourhood of M. Trouvelot's old house, and then marched forth in armies sufficient to blacken the streets, in search of fresh provender. A terrible account of the ravages of the caterpillars is given by those who witnessed them. From *Nature* 25 May 1899.

50 YEARS AGO

The numbers of university undergraduates, in the technical faculties especially, are to-day greater than ever before, and yet apprehension as to the true worth of university training was never so widespread as at the present time; for modern scholarship has made such strides, particularly in the field of science, that no one subject can be adequately studied without undue specialization and consequent neglect of other points of view. This danger of specialization was the theme of Mr. Oliver Stanley's recent address, on being installed as chancellor of the University of Liverpool, when he said that too many men and women to-day leave a university complete masters of a subject but still incomplete individuals, unable to act as evangelists of that broader culture, that more general philosophy which should be the university's gift to the people. From *Nature* 28 May 1949.