insulin-signalling pathway in mammals. Specifically, activation of DAF-2 influences the rate of synthesis and degradation of a second messenger called phosphatidylinositol-1,4,5-trisphosphate, PtdIns(1,4,5)P_3 (refs 5,6). The resulting increase in the level of PtdIns(1,4,5)P_3 activates a protein-kinase cascade[7,8]. One output of this insulin-signalling pathway, which was first discovered in *C. elegans*, occurs via the forkhead-like transcription factor DAF-16 (refs 9,10). Mutations that result in activation of DAF-16 lead to a dramatic extension of lifespan (and increased dauer formation), and loss of DAF-16 function prevents this extension.

One gap in our understanding has been what acts upstream of the DAF-2 insulin receptor to regulate its activity. The answer is presumably insulin-like ligands[11], but what regulates their synthesis and secretion? Dauer formation involves sensory transduction, and the roles of several specific ciliated sensory neurons in dauer formation have been described[12]. Many genes have been identified in *C. elegans* that affect the structure and function of broad sets of sensory neurons, and Apfeld and Kenyon[1] now show that mutations in nearly all of these genes cause increased lifespan, although this effect is much weaker than that caused by mutations in *daf-2*. These sensory mutations do not seem to influence feeding rate, timing of development or fertility, suggesting that their effect on lifespan is relatively direct.

In *C. elegans*, lifespan can also be increased if the germ line is eliminated by laser microsurgery[13]. When Apfeld and Kenyon did this in the sensory-deficient mutants they found that the extension of lifespan was roughly additive, suggesting that the two pathways act independently. Finally, the authors showed that sensory-deficient mutations do not further extend the lifespan of worms mutated in the *daf-2* gene. Moreover, the extended-lifespan effect in sensory-deficient worms is partially suppressed by mutations in the *daf-16* gene. These results indicate that the extension of lifespan caused by the sensory defects results, at least in part, from effects on the insulin-signalling pathway.

What do these striking results mean for the normal process of ageing? The authors' interpretation is simple and sexy — they assert that environmental signals act through sensory neurons to control lifespan. Supporting this view is the fact that there are many insulin-like proteins in *C. elegans*[11]. By analogy with vertebrate insulins, the worm insulins are presumably packaged into secretory vesicles for release from excitable cells. These proteins are a potential mechanistic link between sensory processes and the *daf-2* insulin-signalling pathway. It is possible that insulin release is regulated by sensory neurons that respond to environmental cues, and that sensory defects reduce this release. The result is a partial failure in activation of the DAF-2 receptor.

But is the link between sensory processes and insulin signalling as direct as a failure to respond to specific sensory cues, as Apfeld and Kenyon suggest? There is reason to doubt this simple idea. In the sensory-deficient mutants, the affected sensory neurons don't just fail to function — they adopt physiologically abnormal states. In particular, the neurons that regulate dauer formation are in an abnormal state that influences dauer formation in ways not characteristic of the wild type[14]. For example, in these sensory mutants affecting the structure of cilia, at least one of the dauer-regulating neurons is thought to release the transforming growth factor-β-related protein DAF-7 constitutively[12]. This activity accounts for the dauer-defective phenotype of these mutants. A morphological correlate to this abnormal state is the growth of aberrant axonal processes by many of these neurons[15]. Considering the complexity and variety of the defects, simple interpretations of these results would be incautious.

Nevertheless, Apfeld and Kenyon provide excellent evidence that physiologically abnormal sensory neurons can exert a strong influence on the lifespan of *C. elegans*. This evidence is consistent with a key function for these neurons in the related process of dauer formation, and with the regulation of insulin release by neurons. What it does not provide is specific information about what the normal sensory involvement might be. Discovering whether there are specific environmental modulators of lifespan and, if so, what they are and how they act, is a challenge for the future. ■

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