MODEL ORGANISMS

A fountain of youth (for worms)

A compound for staining amyloid aggregates is found to slow aging and increase lifespan in *Caenorhabditis elegans*.

Thioflavin T, a widely used dye for selectively staining amyloid aggregates, both *in vitro* and *in vivo*, has been applied in laboratories for more than 50 years. A recent report now shows that thioflavin T and structurally related compounds may have a previously unanticipated health benefit: slowing the aging process.

Gordon Lithgow of the Buck Institute for Research on Aging in Novato, California, USA has long been interested in the relationship between protein aggregation and lifespan, especially in the context of age-related diseases such as Alzheimer's and Parkinson's. Silvestre Alavez joined the lab as a postdoc, having had experience with amyloid-binding dyes. Alavez "put two and two together," says Lithgow, and hypothesized that *in vivo*, thioflavin T might have an impact on the rate of protein aggregation.

The researchers decided to test their idea in the model organism *C. elegans*. Their findings were surprising: at the right doses, thioflavin T and related compounds with similar structures but different pharmacological properties extended worm lifespan by an average of 60%. Moreover, as the worms aged, they continued to behave like much younger worms for longer than untreated worms. In addition, thioflavin T decreased paralysis in worm models of Alzheimer's disease.

The researchers found that the beneficial effects of thioflavin T depended on certain protein homeostasis network regulators responsible for maintaining proper protein folding in the cell, such as molecular chaperones and proteasomal components. "My idea is that these compounds, maybe by direct interaction with soluble oligomers, affect the amount or size of protein prone to aggregate, leading to a genetic response that affects the protein homeostasis machinery," explains Alavez.

Could such compounds be developed to slow or reverse the effects of age-related diseases in humans? "There's some evidence that the same genes [involved in protein homeostasis] in *C. elegans* are important in human longevity," notes Lithgow. "Plus, protein aggregation is a facet of neurological disease, so that gives me hope that there's some translatability, and the fact that thioflavin T has been used in humans to visualize amyloids makes me think that there's a clinical infrastructure there." He hopes that others in the field will build on their proof-of-principle results in the search for new human therapeutics for aging diseases.

Allison Doerr

RESEARCH PAPERS

Alavez, S. *et al.* Amyloid-binding compounds maintain protein homeostasis during ageing and extend lifespan. *Nature* advance online publication (30 March 2011).