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Nature study shows common lab dye is a wonder drug -- for worms

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Basic Yellow 1, a dye used in neuroscience laboratories around the world to detect damaged protein in Alzheimer's disease, is a wonder drug for nematode worms. In a study appearing in the March 30, online edition of *Nature*, the dye, also known as Thioflavin T, (ThT) extended lifespan in healthy nematode worms by more than 50 percent and slowed the disease process in worms bred to mimic aspects of Alzheimer's. The research, conducted at the Buck Institute for Research on Aging, could open new ways to intervene in aging and age-related disease.

The study highlights a process called protein homeostasis – the ability of an organism to maintain the proper structure and balance of its proteins, which are the building blocks of life. Genetic studies have long indicated that protein homeostasis is a major contributor to longevity in complex animals. Many degenerative diseases have been linked to a breakdown in the process. Buck faculty member Gordon Lithgow, PhD, who led the research, said this study points to the use of compounds to support protein homeostasis, something that ThT, did as the worms aged.

ThT works as a marker of neurodegenerative diseases because it binds amyloid plaques – the toxic aggregated protein fragments associated with Alzheimer's. In the nematodes ThT's ability to not only bind, but also slow the clumping of toxic protein fragments, may be key to the compound's ability to extend lifespan, according to Lithgow. "We have been looking for compounds that slow aging for more than ten years and ThT is the best we have seen so far," said Lithgow. "But more exciting is the discovery that ThT so dramatically improves nematode models of

disease-related pathology as well," said Lithgow, who said the discovery brings together three crucial concepts in the search for compounds that could extend healthspan, the healthy years of life. "ThT allows us to manipulate the aging process, it has the potential to be active in multiple disease states and it enhances the animal's innate ability to deal with changes in its proteins."

The research was the brainchild of Silvestre Alavez, PhD, a staff scientist in the Lithgow lab. Alavez was trained in neuroscience and knew about the use of these compounds to detect disease-related proteins. With the idea that small molecules could impact protein aggregation, he looked at 10 compounds and found five that were effective in increasing lifespan in the worms. Alavez said curcumin, the active ingredient in the popular Indian spice turmeric, also had a significant positive impact on both healthy worms and those bred to express a gene associated with Alzheimer's. "People have been making claims about the health benefits of curcumin for many years. Maybe slowing aging is part of its mechanism of action," said Alavez. Curcumin is currently being tested in several human clinical trials for conditions ranging from colon cancer to rheumatoid arthritis to depression. Alavez says the study supports the concept that protein homeostasis should be the focus of future research. "We now have an exciting new avenue in the search for compounds that both extend lifespan and slow disease processes," said Alavez. "Any small molecule that maintains protein homeostasis during aging could be active against multiple disease states." Follow up research on ThT is now underway in mice bred to have Alzheimer's.

Provided by Buck Institute for Age Research