Scientists unlock possible aging secret in genetically altered fruit fly

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Brown University researchers have identified a cellular mechanism that could someday help fight the aging process.

The finding by Stephen Helfand and Nicola Neretti and others adds another piece to the puzzle that Helfand, a professor of biology, molecular biology, cell biology and biochemistry, first discovered in 2000. Back then, he identified a mutation in the Indy ("I'm Not Dead Yet") gene that can extend the life span of fruit flies.

Subsequent studies of the Indy flies have led to the new finding that a mechanism in those genetically altered fruit flies appears to reduce significantly the production of free radicals, a cellular byproduct that can contribute to the aging process. This intervention takes place with few or no side effects on the quality of life for the fruit fly. The discovery could lead to the development of new anti-aging treatments.

"There are very few, if any, interventions that are known to dramatically extend healthy lifespan," Helfand said. "Understanding how … the Indy mutation alters the metabolic state of the fruit fly would allow someone to come up with pharmacological interventions that could mimic it and give you the benefit of genetic manipulation without having to do genetics."

The findings are detailed in new research published Jan. 21 in the online Early Edition of the *Proceedings of the National Academy of Sciences*. Titled "Long-lived Indy reduced mitochondrial reactive oxygen species

production and oxidative damage," the piece includes a number of collaborators. Helfand served as senior author and Neretti, assistant professor (research) in Brown's Institute for Brain and Neural Systems, served as lead author. Other researchers collaborated from the University of Chicago and the University of Connecticut Health Center.

With Helfand having established that the mutated Indy gene helped fruit flies live longer, he now wanted to explore what mechanisms lead to the longer life of the fruit fly. (Indy flies' life span increased from an average life span of about 35 days to 70 days.

The researchers decided the best way to try to understand how the Indy mutation might extend life span would be to study the differences in molecular changes between the Indy flies and normal flies throughout their entire life. By comparing the expression level of all genes in the Indy flies to that of normal flies, they made an important finding. Some of the genes involved in generating the power necessary for normal cell life were expressed at lower levels in the Indy flies.

This led to a decrease in free radicals and the damage they normally cause in the cell, but it surprisingly did not decrease the overall amount of energy in the cell. These studies provide evidence for possible interventions that can alter metabolism in a way that reduces free-radical or oxidative damage and extends life span, without some of the negative consequences normally associated with a change in metabolism.

Source: Brown University