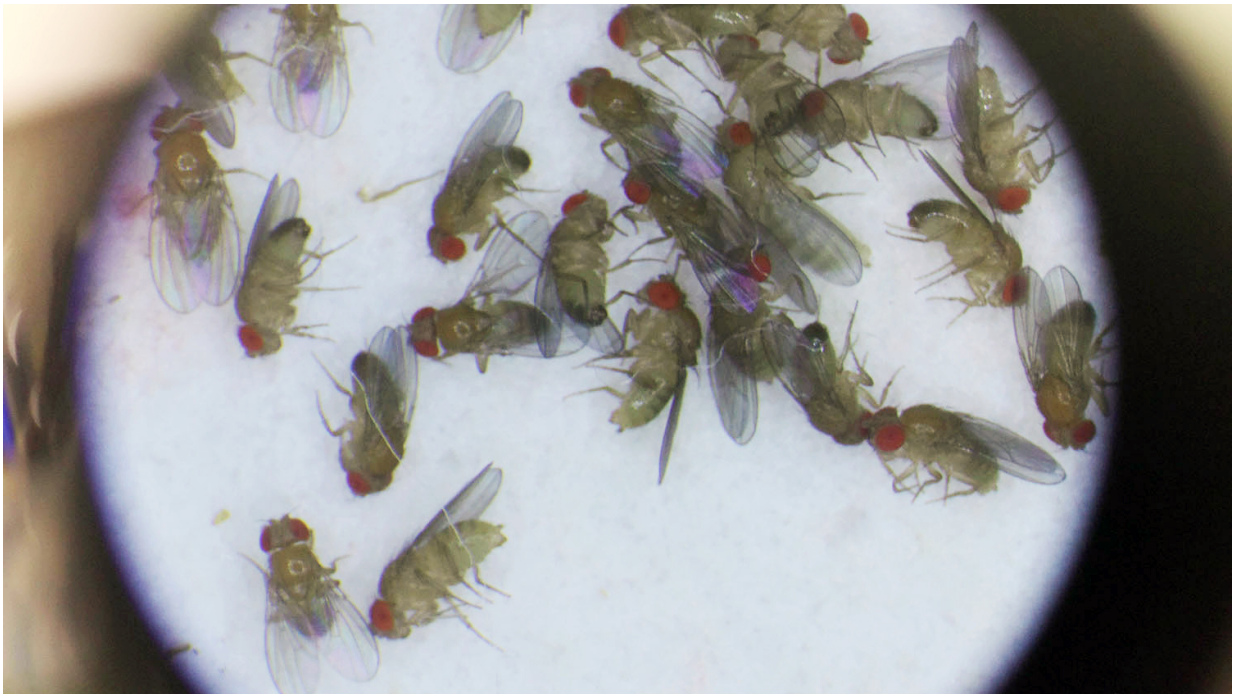


Variation at a central metabolic gene influences male fruit fly lifespan

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Lifespans of male and female fruit flies differ due to variation at an important metabolic gene. Credit: NC State University

The overexpression of an important gene that regulates energy metabolism can cause a severe shortening of lifespan in male fruit flies but has only a small negative effect on lifespans of female fruit flies, according to new research from North Carolina State University. The findings, which involve metabolic genes and pathways that are important

in humans and other animals, shed more light on sex-specific differences between male and female lifespans.

NC State biologists experimented with either inhibiting or overexpressing the bellwether gene, which gives rise to a protein that helps convert nutrients into metabolic energy. Small variations in regions of that gene that regulate its expression were suspected to be correlated with differences in [lifespan](#) based on a previous study, said Robert Anholt, William Neal Reynolds Distinguished Professor of Biological Sciences at NC State and the corresponding author on a paper describing the research, published in *Scientific Reports*.

In the study, Julia Frankenberg Garcia, a visiting student from the University of Surrey in the UK, and Mary Anna Carbone, a research assistant professor of [biological sciences](#) at NC State, suppressed expression of the bellwether gene and found that the gene is required for [fruit](#) fly development and viability.

"Knocking down the expression of this gene is lethal for fruit flies - male and female," said Anholt, who also directs NC State's W.M. Keck Center for Behavioral Biology.

The researchers then examined a number of DNA variants in the protein production-control region of the bellwether gene in cell cultures. Some DNA variants worked better than others and some of those differences were also replicated in vivo - in living fruit flies.

Finally, the researchers overexpressed DNA variants in [fruit flies](#) that were genetically identical except for these different DNA variants. They found that one particular DNA variant shortened male fruit fly lifespan by nearly two-thirds. Females with that DNA variant had shorter lifespans, but this effect was much smaller than in males.

"This is a powerful demonstration of how we can link variation in the genome that controls expression of a central metabolic enzyme to variation in individual lifespan," Anholt said. "There are different gene-gene interactions even though the flies are genetically the same, so that the female genetic background seems to become more protective."

Anholt said that the dramatic effect on male lifespan was unexpected.

"It speaks to the importance of the gene, which is required for development but when overexpressed becomes more lethal for males," Anholt said, "Moreover, the same gene has conserved counterparts in all animals, including people."

More information: Júlia Frankenberg Garcia et al, Regulation of *Drosophila* Lifespan by bellwether Promoter Alleles, *Scientific Reports* (2017). [DOI: 10.1038/s41598-017-04530-x](https://doi.org/10.1038/s41598-017-04530-x)

Provided by North Carolina State University

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