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Bacteria help *Drosophila*

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When *Drosophila melanogaster* are shielded from bacteria during their first week of adulthood, their lives are shortened by a third, says a study published in PNAS this week. Eliminating the same bacteria late in adulthood, however, increases the flies' longevity. The authors also show that genetic mutations associated with longevity can modulate the effects of bacteria on lifespan.

"I wasn't surprised, but I was excited," Daniel Promislow of the University of Georgia said of the results. "I think this is just the beginning. A few years from now, we're going to look back and have a lot of really interesting data on the roles that parasites play" in organism lifespan, said Promislow, who was not involved in the study.

Ted Brummel of Sam Houston State University in Texas and his former colleagues at CalTech raised *Drosophila* in axenic conditions by treating eggs with bleach and ethanol and then keeping the flies in a germ-free environment with sterilized food. Flies that live under these conditions suffer lifespans shortened by about 30%. In a parallel set of experiments, *Drosophila* with bacteria eliminated from their bodies by antibiotic treatment lived 35% shorter lives.

To pin down a critical period for bacterial exposure, the researchers then raised flies in sterile conditions and exposed them to bacteria at various time points after metamorphosis. Conversely, they also raised flies in normal conditions and then transferred them to antibiotic-containing food after adult emergence.

If flies were exposed to bacteria within the first 4 to 7 days of adulthood, they lived normal-length lives. If they were kept axenic for this first week, subsequent addition of bacteria made no difference - longevity was reduced by 30%.

At metamorphosis, a pulse of the steroid hormone ecdysone initiates the shift from larval to adult structures, resulting in fat body transition, upregulation of immune genes, and gut remodeling. Most larval bacteria are destroyed during this process, according to Brummel. "The window at which the bacteria are important is actually the period in which the fly would re-expose itself to bacteria," Brummel told *The Scientist.*

The critical bacterial exposure period also overlaps nicely with the transition from larval to adult fat, Brummel said, and the *Drosophila* fat body has been shown to regulate longevity through insulin-related signaling pathways. It makes sense that bacteria could feed into these pathways, Brummel said, but "at this point, it's just a correlation."

Brummel's group found the opposite effect on longevity when bacteria were removed late in fly life. Flies fed antibiotic-containing food during the fourth week of adulthood lived about 10% longer than those that ate normal food.

"What we think is the case there is simply that the animal's fitness has been reduced to a point where bacteria that are normally not a big threat to the animal become more dangerous," Brummel said.

"These results are fantastic," said Margaret McFall-Ngai of the University of Wisconsin-Madison. Because most animals evolved in microbe-rich seas, "the selection pressure by bacteria has been intense," McFall-Ngai said. "It's not surprising to me that the presence of environmental bacteria would be incorporated into the biological program of an animal."

Brummel's team also looked at bacteria deprivation in longevity mutants. The *Drosophila* mutant EcR, which has a mutation in the ecdysone receptor gene, is long-lived as a heterozygote. Unlike normal flies, these mutants did not suffer reduced longevity with lifelong antibiotic treatment.

Out of a series of other long-lived mutants, one called DJ817 showed different effects from either wildtype or EcR flies: They lived 30% longer than wildtype flies when bacteria were present, but were no different from wildtype in the absence of bacteria. The genetic basis of the DJ817 phenotype has not been fully characterized.

"The idea of putting together parasites and aging in a genetic or evolutionary context is a pretty new one," said Promislow. "In the equation that puts together genes and longevity, it may turn out that parasites are a critical variable that we haven't considered until now."

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