Eliminating germline lengthens fly lifespan, study shows

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New research by Brown University biologists shows that fruit flies live longer when they don't produce germline stem cells – the cells that create eggs and sperm.

The work suggests a provocative general principle at work: Signals from reproductive tissue directly control lifespan and metabolism in the whole organism. The work, which appears in the Proceedings of the National Academy of Sciences, also offers a first glimpse of how this control in the fly might occur at the molecular level.

"For more than 50 years, scientists have known that there is a link between reproduction and lifespan," said Thomas Flatt, a postdoctoral research fellow in the Department of Ecology and Evolutionary Biology at Brown and the lead author of the research article. "When reproduction is delayed, animals live longer. Why? Our research suggests that signals from the reproductive system can regulate aging in animals – including, possibly, humans."

The Brown findings follow a seminal discovery made 10 years ago by acclaimed aging biologist Cynthia Kenyon at the University of California, San Francisco. Kenyon found that eliminating germline stem cells in roundworms extended their lifespan.

"We wanted to see if Kenyon's findings could be duplicated in the fly," said Marc Tatar, the senior scientist on the project and a professor in the Department of Ecology and Evolutionary Biology. "If so, we'd know that

reproductive control of lifespan was a general principle in biology."

In their experiments, Flatt and Tatar over-activated a gene that controls germline stem cells in flies, a move that eliminated the cells' production. They found that these sterile flies lived 20 to 50 percent longer than typical flies – results that matched Kenyon's finding in worms.

Flatt and Tatar speculated that these flies might live longer because they are insensitive to the effects of insulin. Past research at Brown, and other universities, shows that when animals such as flies, worms and mice live longer when they produce or receive less insulin.

Yet, to their surprise, Flatt and Tatar found that when germline cells were eliminated, and flies lived longer, insulin-producing cells in the fly brain actually make more – not less – insulin. These results posed a paradox: How can flies be longer-lived when they're making more of a life-shortening hormone? When the researchers studied the flies' tissues, they discovered something intriguing: Even though the brains were making more insulin, the bodies were responding were responding as if there was less insulin present.

Tatar said the team found a possible explanation for the paradox. In reaction to the flies' brains boosting insulin production, the insects' gonads – their ovaries or testes – produce a protein that acts like a sponge, binding to the insulin and blocking its signals throughout the body. So the flies respond as if there is low, not high, insulin circulation inside their bodies.

"This suggests that the gonad and the brain are in a synchronized hormonal feedback loop," Tatar said. "It's not just the brain affecting the gonad – but also the other way around."

"We think that in mammals, a similar communication occurs between

the brain and the gonad, communication which controls insulin signaling," Flatt said. "And when insulin signaling is re-duced, the body goes into a state of high repair. The body becomes more stress resistant. Tissues protect themselves really well – and that increases longevity."

Source: Brown University