Space-raised flies show weakened immunity to fungus

January 24 2014

A *Drosophila* fly was infected with a fungus. UC Davis experiments with flies raised on the Space Shuttle, on Earth and under high gravity in a centrifuge show that gravity affects the Toll receptor pathway responsible for fighting this infection. Toll receptors are also important for immunity in mammals including humans. Credit: Deborah Kimbrell/UC Davis

Venturing into space might be a bold adventure, but it may not be good for your immune system. Now a study by researchers at the University of California, Davis and published Jan. 24 in the journal *PLOS ONE* shows how growing up on the Space Shuttle weakened a key arm of the immune system in *Drosophila* flies.

It's well-established that spaceflight affects immune responses, said Deborah Kimbrell, a researcher in the Department of Molecular and Cellular Biology in the UC Davis College of Biological Sciences, who lead the study. *Drosophila* share many fundamentals of the immune system with mammals such as mice and humans. With funding from NASA, Kimbrell and colleagues initiated the first study of *Drosophila* immunity and gravity, using first hypergravity (increased gravity), and then microgravity, the decreased gravity of spaceflight.

The flies were sent into space as eggs on a 12-day mission aboard the Space Shuttle Discovery. The flies take about 10 days to develop into adults. After they returned to Earth, Kimbrell and colleagues tested their responses to two different infections: a fungus, which flies fight off through a pathway mediated by the Toll receptor, and a bacterial infection that flies resist through a gene called imd ("Immune deficiency").

Both the Toll and Imd pathways have counterparts in humans and other mammals: The 2011 Nobel Prize for Physiology and Medicine was awarded for discovery of Toll receptor activation of innate immunity in flies and mammals.

While the response through the Imd pathway was robust, the Toll pathway was "non-functional" in space-raised flies, Kimbrell said.

In Earth-based experiments, the researchers found that when flies were tested in a centrifuge under hypergravity conditions, their resistance to

the fungus was improved, suggesting that their Toll pathway was boosted. However, for the mutant yuri gagarin, which lacks normal responses to gravitational fields, resistance was the same at normal and hypergravity, further demonstrating a link between gravity and the immune response.

Future spacecraft designed for long missions could already include centrifuges that crew could use to keep up bone and muscle mass: it turns out that this might also have a beneficial effect on astronauts' immune systems, Kimbrell said.

How does microgravity affect the immune system? Kimbrell said they have two hypotheses in mind, which are testable both in humans and flies.

Firstly, the space flies also showed high expression of genes for heat-shock proteins, which are produced in response to physiological stress. Heat shock proteins bind directly with mammalian Toll receptors, Kimbrell said, and may also moderate Toll activation in *Drosophila*. Another possibility is that microgravity interferes with the behavior of proteins outside the cell—an area which is more important for Toll than for imd signaling, she said.

The team hopes to carry out future research with flies on the International Space Station.

Provided by UC Davis