Researchers develop new system to study trigger of cell death in nervous system

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(Medical Xpress)—Researchers at the University of Arkansas have developed a new model system to study a receptor protein that controls cell death in both humans and fruit flies, a discovery that could lead to a better understanding of neurodegenerative diseases such as Alzheimer's and Parkinson's.

Michael Lehmann, an associate professor of biological sciences, uses fruit fly genetics to study the receptor—N-methyl-D-aspartate receptor, known as the NMDA receptor—that triggers programmed cell death in the human nervous system.

With an aging population, neurodegenerative diseases have become a major public health concern, Lehmann said.

"Whenever brain cells die as a result of neurodegenerative disease, or as a consequence of injuries caused by stroke, exposure to alcohol or neurotoxins, this receptor is involved," he said. "So it's very important to understand how it functions and how it may be possible to influence it."

When larvae of *Drosophila melanogaster*, a common fruit fly, grow from the larval stage into adults, they shed most of their former organs and grow new ones. About 1 ½ years ago, researchers in Lehmann's laboratory discovered that the NMDA receptor is required for cell death in the system that they had used for several years to study basic mechanisms of programmed cell death in fruit flies.

"Our model system for studying programmed cell death is the salivary glands in the fly larvae, which are comparatively large organs that completely disappear during metamorphosis," he said. "Disposal of this tissue by programmed cell death provides us with a very nice system to study the genes that are required for the process. We can use it to identify genes that are required for programmed cell death in humans, as well."

The National Institutes of Health has awarded Lehmann a three-year, $260,530 grant to support the study.

Brandy Ree, a doctoral student in the interdisciplinary graduate program in cell and molecular biology, worked with Lehmann to use a combination of biochemistry and fruit fly genetics in an attempt to define the pathway that leads from activation of the receptor to the cell's eventual death.

"We developed a new system to study the receptor outside the nervous system in a normal developmental context," Lehmann said. "Many of the different components involved in cell death are known in this system. There are more than 30,000 publications about this receptor, but there is still very little known about how the receptor causes cell death. We just have to connect the dots and fit the receptor into the pathway to find out how exactly it contributes to the cell's death."

A mid-career investigator in the Center for Protein Structure and Function at the University of Arkansas, Lehmann has studied programmed cell death in Drosophila melanogaster for more than a decade.

In 2007, Lehmann's research group discovered an important mechanism that regulates the destruction of larval fruit fly salivary glands that could point the way to understanding programmed cell death in the human

immune system. They published their findings in the *Journal of Cell Biology*.

Provided by University of Arkansas