Identification of new genes shows a complex path to cell death

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Can a tiny winged insect's salivary glands really tell us about processes relevant to human disease" Yes, according to a new study by researchers at the University of Massachusetts Medical School (UMMS), who gained new insights into autophagy—a cellular degradation process associated with a form of programmed cell death—by studying the salivary gland cells of the fruit fly.

Since its initial discovery in the 1960s, programmed cell death has been a primary focus of studies for investigators across a wide array of scientific disciplines. An essential mechanism in development and homeostasis, programmed cell death allows for the clean intracellular destruction of unnecessary or damaged cells. While apoptosis is the most understood type of programmed cell death, recently scientists have begun to take a closer look at autophagy— a highly regulated, catabolic process that essentially allows a cell to eat itself. Paradoxically, autophagy is not only a major mechanism by which a starving cell reallocates nutrients to ensure survival, scientists are now demonstrating that autophagy also provides cells that cannot undergo apoptosis with an alternate form of self-destruction.

In "Growth arrest and autophagy are required for salivary gland cell degradation in Drosophila," published in the December 14 issue of *Cell*, Eric Baehrecke, PhD, UMMS Associate Professor of Cancer Biology, and colleagues examined fly salivary glands, which contain all of the machinery required to dismantle and recycle their own cellular components and thus provide a genetic model system for elucidating the

complex functions of autophagy. The paper describes the cellular components required for autophagic cell death and defines multiple pathways that cooperate in the clearance of cells during fly development. Further, their findings demonstrate a critical relationship between growth and this form of cell death.

“When cells keep growing, they don’t die well,” Dr. Baehrecke explained. “We show that an arrest of growth preceded the death of these cells. If we maintain growth by turning on certain genes, we can block the death of these cells, and this has potential clinical implications. Therapies directed at apoptotic mechanisms have resulted in limited success; we hope that further studies of autophagy could lead to new approaches to the treatment of human disease.”

“It’s becoming increasingly important to understand how the various cell death pathways connect and how they affect development, the stress response, and disease,” said Marion Zatz, PhD, who oversees cell death grants at the National Institute of General Medical Sciences, which funded the work. “While this research was done in fruit flies, findings made in model organisms are often the first step in understanding what goes on in humans. By shedding light on autophagic cell death, this work may help explain the pathway’s role in human diseases such as cancer, Alzheimer’s and Parkinson’s.”

“The role of autophagy during cell death remains controversial but is important to our understanding and treatment of many human disorders including cancer and neurodegeneration,” Baehrecke said. “It is important to understand the relationship between autophagy and cell death, as the association of autophagy with cell growth, nutrient utilization, survival and death indicates that this catabolic process is relevant to the treatment of many human disorders including cancer.”

Source: University of Massachusetts