Fruit Flies, Death, and Immunity

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University of Arkansas scientists have found 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.

Biology professor Michael Lehmann, graduate student Chike Cao and research assistant Yanling Liu recently published their findings in the *Journal of Cell Biology*.

Lehmann and his colleagues examined the expression of different proteins during the development and demise of larval salivary glands in Drosophila melanogaster, a common fruit fly. Previous studies have shown that steroids and other hormones trigger programmed cell death during normal development, such as the destruction of the tadpole tail during frog metamorphosis. However, little was known about what tells these hormones to act on a specific tissue at a given time.

"We wanted to know why one cell dies during steroid hormone release, while another one doesn't," Lehmann said.

Cell death, it turns out, is essential to life - without it, normal development can't take place, and this sometimes results in premature death. Lehmann points out that cancer cells have a defect in their cell death program, which is why they grow unchecked. Thus, understanding the mechanisms that control cell death can give scientists insights into how such deaths preserve life.

While investigating the Drosophila model, the researchers found that the life and death of the salivary gland cells depend upon a member of the Fork head protein family. This protein first protects the salivary glands from steroid-triggered death by acting as a "traffic cop," preventing the activation of two key genes responsible for cell death. However, the protein then disappears after a particular steroid pulse in a sequence of pulses. A subsequent steroid pulse triggers the death of the salivary gland cells.

To determine the extent of involvement of this protein, the researchers removed this protein at an earlier stage in development, which led to the activation of the cell-killing genes by an earlier steroid pulse and to premature cell death. Further, when the scientists caused the continued presence of the Fork head protein, the cell death genes remained inactive and the cells continued to live past their normal life span.

These findings have implications beyond fruit flies, as the molecular machinery that controls cell death is largely similar for invertebrates and vertebrates. The Fork head protein in Drosophila has homologs in humans, called FOXAs. These FOXAs are known to work together with corticosteroids, which control cell death in the immune system and are in therapeutic use to suppress allergic and inflammatory responses.

"Our research suggests that the FOXAs might have a similar role in cell death control in the immune system," Lehmann said. "This gives medical researchers a direction in which they might want to look."

Source: University of Arkansas