Communication between neighboring cells triggers autophagy

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An immune-related protein deployed between neighboring cells in Drosophila plays an essential role in the cell degradation process known as autophagy, according to new research by Eric H. Baehrecke, PhD, at UMass Medical School. This extracellular molecular link raises the possibility that the breakdown between an immune system signal and autophagy could contribute to human diseases. The study appears online in *Cell*.

"Autophagy, a natural and highly regulated degradation process, appears to be influenced by systemic, body-wide signals, such as malnutrition," said Dr. Baehrecke, professor of molecular, cell & cancer biology. "But the proteins that control this process are largely thought to function autonomously, inside individual cells. Our studies revealed an unexpected finding where one cell triggers autophagy in neighboring cells."

Autophagy is the process cells use to degrade used or damaged components inside the cell for recycling. Normally autophagy acts as a cellular quality-control mechanism. A breakdown in autophagy is associated with diseases such as cancer, immune disorders and neurodegeneration, but little is known about the system-wide signals between cells that control autophagy in complex, multicellular animals.

Using the development of the salivary gland in Drosophila, which degrades as flies mature, to isolate and study the components of autophagy, Baehrecke theorized that a rise in a protein called Mcr in the glands prior to cell death was somehow connected to its degradation. When Baehrecke and colleagues turned off the Mcrgene in Drosophila salivary gland cells, fragments consistent with a breakdown in autophagy appeared, indicating that Mcr played a role in the clearance of cellular debris by activating autophagy.

The Mcr gene is part of the immune response's complement system; it enhances (or complements) the ability of antibodies and phagocytic cells to clear microbes and damaged cells from an organism, promotes inflammation, and attacks the pathogen's plasma membrane. Baehrecke and colleagues also showed that Mcr interacts with the receptor named Draper that resides on the outside of neighboring cells. They also demonstrated that the interaction of the Mcr and Draper is critical for the inflammatory response, as it triggers the recruitment of macrophages to the site of epithelial wounds.

"The relationship between Mcr and Draper is likely an ancient mechanism for activation of the Draper immune receptor," said Baehrecke. "The complement system has mostly been studied in the context of pathogen clearance, but recent studies have also highlighted its importance in other contexts, including synapse pruning in mice with Alzheimer's disease. This study suggests a potential role of autophagy in complement-associated processes that are associated with human diseases."

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