Assisted Suicide: a Caspase- and Engulfment-Dependent Cell Death Holly Johnsen, Bob Horvitz. HHMI, Biology, MIT, Cambridge, MA.

Programmed cell death occurs during the development of many organisms. The *C. elegans* cell-death pathway has been extensively studied and is evolutionarily conserved. During programmed cell death, caspases are activated in the dying cell. The cell corpse is engulfed by a neighboring cell and degraded. Almost all cell deaths are "suicides"—they are cell-autonomous, caspase-dependent and can occur even in engulfment-defective animals.

In the *C. elegans* male, the cells B.alapaav and B.arapaav are generated during the late L3 stage. During the early L4 stage one of these cells dies, and the other survives and adopts an epithelial fate. These two cells form an equivalence group; the decision of which cell dies and which survives is stochastic and takes place during the L3/L4 lethargus. The cell that dies is engulfed by the neighboring cell P12.pa. In contrast to most *C. elegans* cell deaths, the B.al/rapaav death is engulfment-dependent; if engulfment is blocked by a mutation in one of the genes in the engulfment pathway, both B.alapaav and B.arapaav survive. Furthermore, we have found that if the engulfing cell P12.pa is ablated, the B.al/rapaav death fails to occur in approximately 60% of animals. These observations suggest that cell interactions between B.alapaav and B.arapaav as well as between B.al/rapaav and P12.pa are involved in this cell death, leading some to suggest that P12.pa "murders" B.al/rapaav.

We are investigating the control and execution of the B.al/rapaav cell death. When the B.al/rapaav cell death is blocked by engulfment defects or P12.pa ablation, the undead cell still initiates the cell-death pathway. Similar to other dying cells, the undead cell looks round by Nomarski and EM and exposes phosphatidylserine on its surface. *egl-1* and *ced-3* are required for the B.al/rapaav cell death and are expressed in the undead cell, suggesting that the core cell-death pathway is required but not sufficient for this cell death, i.e. that this death is an assisted suicide. We hope our studies will provide insight into new mechanisms of programmed cell death, cell-cell signaling, and fate determination within equivalence groups.

Poster
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