

Assisted Suicide: a Caspase- and Engulfment-dependent Cell Death

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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 and caspase-dependent, and can occur even in engulfment-defective animals.

During development of 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 undergoes programmed cell death, 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 we have found that the decision is made 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 cell death is engulfment-dependent; we and others have found that 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. We found that 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 cells that are about to die, the undead cell looks unusually round by Nomarski and electron microscopy and exposes phosphatidylserine on its surface. By contrast, the undead cell in *ced-3* mutants appears healthy, suggesting that the cell-death pathway fails at a point after caspase activation in engulfment mutants. *egl-1* and *ced-3* are expressed in the undead cell and are required for the B.al/rapaav cell death, 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

Session topic: 1-4 Cell Death

Second session topic: 1-1 Cell Fate Patterning

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