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The engulfment of dying cells contributes to the killing process of programmed cell death

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The engulfment of a cell corpse by a neighboring cell typically occurs rapidly after the generation of a cell programmed to die. This engulfment can initiate before the completion of cell division, as shown by electron microscopy (1). Because cell corpses are generated in mutants defective in engulfment, the proposed function of engulfment has long been solely the removal of unwanted apoptotic cell bodies. We have discovered, however, that in addition to functioning in cell-corpse removal, engulfment assists in the killing of dying cells.

Animals with strong loss-of-function mutations in the killer gene *ced-3* lack most if not all programmed cell deaths. However, weaker *ced-3* mutants exist that lack only a small percentage of programmed cell deaths. We found that such a partial block in the execution of programmed cell death is enhanced by mutations in genes that are involved in the engulfment process (*ced-1*, *ced-2*, *ced-5*, *ced-6*, *ced-7*, and *ced-10*). Furthermore, mutations in these engulfment genes alone are sufficient to result in a low-penetrance survival of some cells that normally die in the ventral cord. Lineage analysis shows that cells that fail to die initially show some morphological characteristics of programmed cell deaths but ultimately appear morphologically indistinguishable, using Nomarski optics, from living cells. Surviving Pn.aap cells in these ventral cord lineages are capable of expressing the cell-type specific reporter *lin-11::gfp* (see Cameron, Tsung, and Horvitz, this meeting), suggesting that they are capable of differentiating.

We are analyzing the relative contributions of the different engulfment genes to cell killing, how the engulfment role in killing interacts genetically with *ced-8* and *ced-9*, and the contribution of the killing role of engulfment to the death of different cell types.

1. Sulston, J.E., Albertson, D.G., and Thomson, J.N. (1980). *Dev. Biol.* 78, 542-576.