

Genes that regulate the programmed cell deaths of the sisters of the RIM/RIC neurons

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Programmed cell death is a widespread and crucial process that eliminates unwanted cells during development. *C. elegans* produces 1,090 somatic cells during development, 131 of which undergo programmed cell death. Most of the cells that undergo cell death during early *C. elegans* development are sisters of neurons. Studies of *C. elegans* have identified evolutionarily conserved components of the central pathway of programmed cell death: EGL-1/BH3 (Bcl-2 homology region 3), CED-9/Bcl-2, CED-4/APAF-1, and CED-3/caspase. However, how the deaths of specific neuronal sister cells are regulated is less understood. We are using genetic screens to identify genes that regulate the embryonic deaths of the sisters of the RIM and RIC neurons. Transgenic worms that express GFP specifically in the two RIM and two RIC neurons display four GFP positive cells in the head, while mutations in genes in the canonical cell-death pathway lead to eight or more GFP positive cells, suggesting that surviving RIM and RIC sister cells differentiate into RIM-like and RIC-like cells, respectively. To identify regulators of RIM/RIC sister death, we screened approximately 45,000 genomes and isolated 31 mutations that result in extra GFP-positive cells. Among the 31 isolates, six complemented components of the canonical cell-death pathway, and the six isolates themselves define four complementation groups. Two of the four genes likely regulate the death of the RIC sister cells, and the other two genes seem to control the death of the RIM sister cells. These data suggest that we have potentially identified four novel factors that specifically regulate the deaths of the RIM or the RIC sisters but not both. Currently we are mapping and characterizing the mutations that prevent the deaths of RIM or RIC sister cells. This work should define novel factors and pathways that regulate programmed cell death.