

Novel genes that regulate RIM/RIC sister cell death

Dongyeop Lee, Takashi Hirose, Lan Qin, and Bob Horvitz

HHMI, Dept. Biology, MIT, Cambridge, MA 02139, USA

Programmed cell death is widespread in animal development. Most of the cells that undergo cell death during early *C. elegans* development are sisters of neurons. Many studies of *C. elegans* have identified evolutionarily conserved components of the core pathway of programmed cell death. However, how the deaths of specific neuronal cells are regulated is incompletely understood. We are using a genetic screen to identify genes that regulate the embryonic deaths of the sisters of the RIM and RIC neurons. *Ptdc-1::GFP* transgenic worms that express GFP specifically in the two RIM and two RIC neurons display four GFP(+) cells in the head, while mutations in genes in the canonical cell-death pathway lead to eight or more GFP(+) cells, indicating that surviving RIM and RIC sister cells differentiate into RIM-like and RIC-like cells. To identify regulators of RIM/RIC death, we screened 45,500 genomes and isolated 31 mutations that result in extra GFP(+) cells. Among the isolates, nine appear to act independently of the canonical cell-death pathway. Interestingly, each of these nine strains displays six GFP(+) cells, suggesting that the mutations permit survival of RIM or RIC sister cells but not both. Currently we are mapping and characterizing the mutations that prevent the deaths of RIM or RIC sister cells. We hope to provide novel insights into the pathways that regulate neuronal cell death.