

**IDENTIFICATION OF TWO GENES THAT CONTROL THE SURVIVAL OF THE MALE-SPECIFIC CEM NEURONS**

**Hillel Schwartz, Bob Horvitz**

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

During wild-type hermaphrodite development, 131 somatic cells undergo programmed cell death. While many genes involved in the execution of cell death have been identified, the mechanisms that control the commitment of specific cells to undergo programmed cell death are poorly understood. To date, mutations in four genes, *ces-1*, -2, and -3 (cell death specification), and *egl-1*, have been found to affect specifically the deaths of particular cells. *ces-1* and *ces-2* encode transcription factors. Mutations in a transcriptional regulatory element of *egl-1*, which encodes a protein required for all somatic cell deaths, cause inappropriate expression of *egl-1* in the HSNs in hermaphrodites, resulting in their deaths.

To identify additional genes that act in the specification of cell death, we have performed a genetic screen for hermaphrodites in which the male-specific CEM neurons fail to undergo programmed cell death. The CEM neurons die during normal hermaphrodite development but survive and differentiate in males. The reporter *pkd-2::gfp* (kindly provided by Maureen Barr and Paul Sternberg) expresses in the CEMs of males and in the CEMs of *ced-3(n717)* hermaphrodites, which are defective in essentially all programmed cell death. By using the *pkd-2::gfp* reporter as a marker for CEM survival, we were able to screen efficiently for survival of a single cell using a dissecting microscope equipped with fluorescence optics.

A screen of 60,000 mutagenized haploid genomes yielded at least 146 independent mutations that cause survival of the CEMs, including 40 alleles of known cell-death genes and at least 60 mutations that cause sexual transformation. Seven mutations, which define two genes, cause CEM survival but do not cause other obvious sexual transformation or a nonspecific defect in programmed cell death. Both genes act epistatically to null mutations in *fem-2* and *fem-3*, indicating that these genes likely act downstream of the sex determination pathway to control the activation of programmed cell death in the CEM neurons. Fine mapping and rescue experiments are currently in progress.