

The *BarH* Class Homeodomain Gene *ceh-30* is Directly Regulated by TRA-1 to Specify the Sexually Dimorphic Survival of the CEM Neurons

Hillel Schwartz and Bob Horvitz

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

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 identify genes that act in cell-death specification, we performed a screen for hermaphrodites in which the male-specific CEM neurons, which die during normal hermaphrodite development but survive in males, fail to die. The reporter *pkd-2::gfp* (kindly provided by Maureen Barr and Paul Sternberg) expresses in the CEMs of males and in the CEMs of hermaphrodites defective in programmed cell death. Using *pkd-2::gfp* as a marker for CEM survival, we screened 60,000 mutagenized haploid genomes and recovered at least 145 independent mutations that cause CEM survival, including at least 50 alleles of known cell-death genes and 63 mutations that cause sexual transformation.

Three mutations from this screen, *n3713*, *n3714*, and *n3720*, semidominantly cause CEM survival in hermaphrodites but cause no other obvious defects in programmed cell death or sex determination. CEM survival caused by these mutations is not affected by loss of the *fem* genes, the most downstream genes required for masculinization, indicating that this gene may act downstream of sex determination. The *n3714* phenotype of CEM survival is not affected by a duplication covering the locus, indicating *n3714* causes increased wild-type function or altered function.

In a screen for suppressors of *n3714*, we found one mutation, *n4111*, that is tightly linked to *n3714* and dominantly suppresses the dominant CEM survival phenotype of *n3714*. In contrast to *n3714* hermaphrodites, which inappropriately have surviving CEMs, *n4111 n3714* males inappropriately lack CEMs. The CEMs of *n4111 n3714* males are restored by mutations that prevent programmed cell death but not by a null mutation in *tra-1*, a gene required for feminization and the most downstream gene in the sex-determination pathway. Other deaths and sexually dimorphic characteristics are not affected by *n4111 n3714*.

n4111 is a nonsense mutation in the *BarH* class homeodomain gene *ceh-30*. *n3713*, *n3714*, and *n3720* are mutations in an evolutionarily conserved TRA-1 binding site in an intron of *ceh-30*. We propose that *ceh-30* is specifically required for CEM survival in males and that in hermaphrodites *ceh-30* is prevented from protecting the CEMs by direct transcriptional repression by TRA-1. It remains to be determined how *ceh-30* protects the CEMs and to what extent this cell-type specific anti-apoptotic function of *ceh-30* is shared by *BarH* class homeodomain genes in other organisms.