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

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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 acting in cell-death specification, we screened for hermaphrodites with surviving CEM neurons, cells that die during normal hermaphrodite development but survive in males. The reporter *pkd-2::gfp* expresses in the CEMs of males and the CEMs of hermaphrodites defective in programmed cell death. We screened 60,000 mutagenized haploid genomes and recovered at least 145 independent mutations that cause CEM survival, including at least 48 alleles of known cell-death genes and 65 mutations that cause sexual transformation.

Three allelic 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. Dosage experiments indicate *n3714* causes increased wild-type function or altered function.

In a screen for suppressors of *n3714*, we found one loss-of-function mutation in the same gene, *n4111*. 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*, which is required for all feminization. Other cell deaths and sexually dimorphic characteristics are not affected by *n4111 n3714*.

n4111 is a nonsense mutation in the *BarH* class homeodomain gene *ceh-30*. The *ceh-30* gain-of-function mutations *n3713*, *n3714*, and *n3720* alter an evolutionarily conserved TRA-1 binding site. We propose that *ceh-30* is specifically required for CEM survival in males and that in hermaphrodites direct transcriptional repression by TRA-1 prevents *ceh-30* from protecting the CEMs. 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.

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