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The TRA-1 sex-determination protein regulates sexually dimorphic programmed cell death by transcriptionally repressing the *egl-1* cell-death activator gene

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The cell-death activator gene *egl-1* (*egl*, *eg*g-*l*aying defective) acts as a negative regulator of the cell-death inhibitor gene *ced-9* and is the most upstream acting component of the central pathway required for programmed cell death in the *C. elegans* soma. *egl-1* encodes a BH3-containing protein, which has been proposed to activate cell death by binding to and thereby negatively regulating the Bcl-2-like CED-9 protein (1).

A loss-of-function mutation in *egl-1* blocks most if not all somatic cell deaths that occur during development. This mutation is a five bp deletion in the coding region of *egl-1* and results in the formation of a truncated EGL-1 protein (1). Dominant gain-of-function mutations in the *egl-1* gene, by contrast, result in ectopic cell death: *egl-1*(gf) mutations cause the activation of the cell-death pathway in the HSNs (HSN, *h*ermaphrodite-*s*pecific *n*euron) not only in males but also in hermaphrodites, in which the HSNs normally survive (2).

The *egl-1*(gf) mutations are single-base changes within a putative binding site for TRA-1 (TRA, transformer), the terminal and global regulator of somatic sex (3). This site is located 5.6 kb downstream of the *egl-1* transcription unit. TRA-1 binds to this site *in vitro*, and this binding is disrupted by the introduction of the *egl-1*(gf) mutations. We propose that TRA-1 acts as a repressor of *egl-1* transcription in the HSNs to ensure the survival of these neurons in hermaphrodites. This hypothesis is supported by our finding that the *tra-1* gene determines the cell-death fate of the HSNs in an *egl-1*-dependent manner.

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3. Zarkower, D. and Hodgkin, J. (1992). Cell *70*, 237-269.