The Sp1 Family Transcription Factor SPTF-3 Promotes M4 Sister Cell Death through *egl-1* Expression in the M4 Sister Cell

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In *C. elegans*, 131 somatic cells undergo programmed cell death during wild-type hermaphrodite development. While genes that cause programmed cell death have been well studied, less is known about how a particular cell is specified to survive or to die by programmed cell death. To identify pathways involved in the cell-type specific specification of programmed cell death, we screened for mutants defective in the programmed cell death of the sister of the pharyngeal M4 motor neuron. The M4 neuron is generated during embryonic development and survives to regulate muscle contraction in the pharynx, while the M4 sister undergoes programmed cell death.

By a genetic screen and a subsequent candidate-gene approach, we have identified seven genes required for M4 sister cell death: *ceh-32*, *ceh-34*, *eya-1*, *sptf-3, gcn-1, abcf-3* and *pig-1*. Here we describe our studies of the Sp1 family transcription factor SPTF-3, which promotes M4 sister cell death through *egl-1* expression in the M4 sister cell. From our genetic screen, we recovered *n4850*, an allele of *sptf-3* that causes a defect in the death of the M4 sister cell but not of other cells, including the I1 sister cells, the NSM sister cells or the VC homologs of the ventral nerve cord. This result indicates that *sptf-3* is specifically involved in M4 sister cell death rather than in all programmed cell deaths. *sptf-3* encodes an Sp1 family transcription factor that contains three zinc finger domains. The *sptf-3(tm607Δ)* deletion lacking two of the zinc finger domains causes a defect not only in M4 sister cell death but also in pharyngeal morphology, leading *sptf-3(tm607Δ)* animals to die by the early L1 stage. A translational *sptf-3::gfp* transgene is expressed during embryogenesis in most cells, including those of the pharynx. These results suggest that *sptf-3* is required for both pharyngeal development and the regulation of M4 sister cell death.

We found that *sptf-3* is required for expression of the pro-apoptotic BH3-only gene *egl-1* in the M4 sister cell. While *egl-1* is known to function in the M4 sister cell, our mosaic analysis indicates that the *sptf-3* function is required at or later than the stage of the great-great-grandmother cell of the M4 sister cell. One possibility is that SPTF-3 likely regulates *egl-1* expression indirectly through other genes. We previously reported that the *C. elegans* Six family homeodomain proteins CEH-32 and CEH-34 directly activate *egl-1* expression in the M4 sister cell. *ceh-32(ok343Δ)* and *sptf-3(tm607Δ)* animals share a "pharynx unattached" (Pun) phenotype, suggesting that *sptf-3* and *ceh-32* regulate pharyngeal development in the same pathway. We are currently testing whether SPTF-3 promotes *egl-1* expression through *ceh-32* expression in the M4 sister cell.

Poster
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