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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