**SPTF-3 SP1 and PIG-1 MELK function in distinct pathways to promote M4 neuron cell-type specific programmed cell death**

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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 cell-type specific programmed cell death, we screened for mutations that cause a defect in the 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 dies by programmed cell death.

Using genetic screens, we identified seven genes required for M4 sister cell death: *ceh-32*, *ceh-34*, *eya-1*, *sptf-3, pig-1, gcn-1* and *abcf-3*. Here we describe our studies of the SP1 family transcription factor SPTF-3 and the AMPA-related protein kinase PIG-1. Reduction of *sptf-3* function decreases expression of the pro-apoptotic BH3-only gene *egl-1* in the M4 sister and does not enhance a defect in M4 sister cell death in *ced-9* null mutants. By contrast, a loss of *pig-1* function does not affect *egl-1* expression in the M4 sister and enhances a defect in M4 sister cell death in *ced-9* null mutants. Also, *sptf-3; pig-1* double mutants have a stronger defect in M4 sister cell death than do either of the single mutants. These results indicate that *sptf-3* acts through the canonical cell-death execution pathway, while *pig-1* acts in a distinct pathway in the regulation of M4 sister cell death.

We previously reported that the *C. elegans* Six family homeodomain protein CEH-34 and the Eyes absent homolog EYA-1 promote the death of the M4 sister through the transcriptional activation of *egl-1* (Hirose et al., PNAS 107, 15479-15484, 2010). An *sptf-3* deletion does not affect *ceh-34* or *eya-1* expression in the M4 sister. This result suggests that *sptf-3* acts in a distinct pathway from that of *ceh-34* and *eya-1* to promote *egl-1* expression in the M4 sister.

Our findings indicate that M4 sister cell death is regulated by at least three different pathways, in which 1) *ceh-34* and *eya-1* promote *egl-1* expression, 2) *sptf-3* promotes *egl-1* expression via a pathway distinct from that of *ceh-34* and *eya-1*, and 3) *pig-1* functions independently of the canonical cell-death execution pathway.

Poster
Primary Session topic: Cell Death/ Apoptosis
Secondary session topic: Cell Fate/ Cell fate specification
No. characters (counting spaces): 2504