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pag-3 may specify both neuroblast cell fate and terminal fates during development of the ventral cord

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Pathways controlling the programmed deaths of specific cells in *C. elegans* are likely to be evolutionarily conserved, and human homologues of genes in these pathways are candidate disease genes. We recovered two alleles of the gene *pag-3* as mutations that result in increased numbers of cell corpses in the ventral cord (see abstract by Cameron, Tsung, and Horvitz). *pag-3* is a 336 amino acid Zn-finger protein with extensive identity to the mammalian proto-oncogene *Gfi-1*. We have shown that in *pag-3* animals the Pn.aaa neuroblast reiterates the fate of its mother, Pn.aa, generating supernumerary Pn.aap cells. These cells can undergo programmed cell death, resulting in an increased number of cell corpses in the ventral cord. These findings establish a role for *pag-3* in determining neuronal cell fate by regulating cell lineage.

pag-3 may also function to regulate terminal aspects of neuronal differentiation. To begin to test this idea we used an affinity-purified antiserum to define the expression pattern of PAG-3 and, in particular, to determine whether it is present during terminal differentiation. We found that PAG-3 protein is present in the touch neurons, the BDU neurons, and many neurons in the head and tail of embryos and adults. In the ventral cord, protein is first detected in the Pn.aa neuroblast, consistent with the lineage findings that descendants of this cell are abnormal. PAG-3 protein remains present through the birth of the mature VA, VB, and VC motor neurons derived from the Pn.aa neuroblast, then rapidly disappears from all but six cells in the mature ventral cord. Expression persists in adults in VA11 and VA12 as well as in four cells of the retrovesicular ganglion. PAG-3 expression during terminal differentiation of ventral cord neurons and its persistence through adulthood in specific subsets of ventral cord neurons suggest that *pag-3* may regulate both neuroblast lineage and specific aspects of neuronal differentiation.