PAG-3 AND *UNC-3* INTERACT TO DETERMINE NEURAL FATES IN THE VENTRAL CORD, AND THEIR MAMMALIAN COUNTERPARTS MAY SIMILARLY INTERACT DURING BLOOD CELL DEVELOPMENT

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To understand how programmed cell death is regulated during development, we are studying mechanisms that determine the pattern of programmed cell deaths in the ventral cord. In the midbody the six Pn.aap cells survive and differentiate to form VC motor neurons, while lineally-equivalent cells in the anterior and posterior die. Through two genetic screens we have found that *unc-3* and *pag-3* mutants have both extra cell corpses and extra VC motor neurons in the ventral cord. In *pag-3* mutants these phenotypes are a consequence of a P cell lineage defect wherein the Pn.aaa neuroblast reiterates the fate of its mother, Pn.aa, to generate extra Pn.aap cells, some of which live and some of which die. Analysis of the number of Pn.aap cells in *unc-3 pag-3* double mutants suggests that *unc-3* and *pag-3* may function together to determine the number of Pn.aap cells. This functional interaction is not obligatory in all cells as *unc-3 pag-3* mutants, but neither single mutant, are Mec, suggesting redundant functions, and *unc-3* functions without *pag-3* to prevent dauer-formation at 27°C. UNC-3 and PAG-3 are coexpressed in ventral cord motor neurons.

Our finding of similar phenotypes in the ventral cord of *pag-3* and *unc-3* mutants prompted us to ask whether mammalian homologues of *pag-3* and *unc-3*, the *Gfi-1* and *O/E* genes respectively, might also function together to promote particular cell fates. *Gfi-1* and *O/E-1* are known to be coexpressed in hematopoietic cells, and *O/E-1* is required for development of the B cell lineage in mice. *Gfi-1* may directly regulate apoptosis. The O/E-1 protein is known to physically interact with a C_2H_2 Zn-finger protein ROAZ, suggesting the possibility that PAG-3, which encodes a C_2H_2 Zn-finger protein, might interact directly with UNC-3 in the ventral cord to specify Pn.aaa neuroblast fate and/or to regulate terminal neuronal fates, including programmed cell death, and that a Gfi-1 protein might interact with an O/E protein in hematopoietic cells. We are currently testing these ideas.