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C. elegans rac GENES CONTROL AXON GUIDANCE, CELL MIGRATION, AND CELL-CORPSE ENGULFMENT

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Rac GTPases control cell polarity via regulation of the actin cytoskeleton. The pathways and developmental events controlled by Rac genes remain largely unresolved. There are three *C. elegans rac* genes, *ced-10*, *mig-2*, and *rac-2*. *ced-10* is necessary for the engulfment of cell corpses generated by programmed cell death, *mig-2* has a role in Q-cell migration, and *rac-2* has no previously ascribed function. *C. elegans* Rac regulatory proteins have been identified: CED-10 is regulated by CED-2 CrkII and CED-5 DOCK180 for phagocytosis, and UNC-73 Trio is a guanine nucleotide exchange factor that can act on Rac GTPases. To determine the developmental roles of and the pathways that control the three *C. elegans rac* genes, we examined axon guidance, cell migration, and engulfment in animals deficient for the function of one or more of the *rac* genes and/or Rac regulatory genes.

We found that *ced-10*, *mig-2*, and *rac-2* function redundantly to control axon guidance, as determined using ultrastructural studies and cell type-specific GFP reporters. Perturbing the function of one *rac* gene led to no defects in axon guidance, whereas perturbing the functions of any two *rac* genes did. All three *rac* genes appear to interact with *unc-73* for axon guidance. *ced-10; mig-2* double mutants showed severe defects in axon guidance, but *ced-2; mig-2* and *ced-5; mig-2* double mutants did not. Thus, *ced-10* acts independently from *ced-2* and *ced-5* for axon guidance, indicating that Racs can be regulated by different proteins for the control of different developmental events. *ced-10*, *mig-2*, and *rac-2* act redundantly, and together with *unc-73*, to control CAN cell migration; by contrast, *ced-10* and *mig-2* but not *rac-2* are each necessary for distal tip cell migration, indicating that the *rac* genes are redundant in some cell types and individually required in others. *ced-10* is the primary *rac* gene controlling the engulfment of cell deaths, with *mig-2* and *rac-2* having subtle roles only detected in genetically-sensitized backgrounds. *unc-73* had no detectable role in engulfment.

Our findings indicate that Rac signaling pathways are key integrators of cell polarity cues for multiple developmental processes and that distinct regulatory proteins modulate Rac activation and function in different developmental processes.