

From Cell-corpse Engulfment to Cell Migration in *C. elegans*

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Cytoskeleton rearrangement is important in various developmental processes in multi-cellular organisms, including cell migration and the engulfment of apoptotic cells. In Caenorhabditis elegans, the conserved GTPase signaling pathway mediated by CED-2/CrkII, CED-5/DOCK180 and CED-10/Rac is important for the engulfment of apoptotic cells and the migration of two specific gonadal cells, distal tip cells (DTCs). We have identified and characterized a new gene, ced-12, which functions in the conserved GTPase pathway.

CED-12 is similar to human ELMO and dCED-12, indicating the conservation of CED-12-like proteins among species. Ectopic-expression studies showed that ced-12 functions within engulfing cells and migrating DTCs during cell-corpse engulfment and DTC migration. Our results from bypass experiments suggest that ced-12 acts upstream of ced-10 in the genetic pathways that controls cell-corpse engulfment as well as DTC migration. We found that CED-12 and CED-5 interact in vitro and so did their human homologs ELMO and DOCK180. We propose that CED-12 functions with CED-5 to activate CED-10 in a GTPase signaling pathway that regulates the polarized extension of cell surfaces in engulfing cells and migrating cells. We suggest that CED-12-like molecules act in the conserved Rac GTPase signaling pathway to regulate cytoskeleton dynamics in mammals, as CED-12 does in C. elegans.

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