1999 International Worm Meeting abstract 114

The Cell-corpse Engulfment Gene *ced-1* Encodes A Transmembrane Receptor That May Act To Recognize Dying Cells

Z Zhou, B Horvitz

HHMI, Dept. Biology, MIT

The engulfment of cells by their neighbors is an evolutionarily conserved process that serves to remove unwanted or potentially harmful cells. The molecules that mediate this fundamental process are only now beginning to be elucidated. In *C. elegans*, mutations in seven genes that define two partially redundant pathways cause cell corpses to persist abnormally. *ced-2*, *5*, *10*, and *12* are part of a Crk/DOCK180/Rac signaling pathway proposed to mediate cytoskeletal reorganization (see abstract by Reddien and Horvitz). *ced-6* encodes an adaptor-like protein and *ced-7* encodes an ABC transporter. We propose that these two genes act in one of the pathways together with *ced-1* to control cell-corpse recognition and to initiate phagocytosis.

We have cloned *ced-1* and found that it encodes a transmembrane receptor-like protein. CED-1 is localized on the surface of many cells in embryos and early larvae. Induced expression of *ced-1* can rescue the engulfment defects of *ced-1* mutants hours after the corpses have formed, suggesting that the activity of CED-1 in engulfing cells, rather than in corpses, is responsible for its engulfment function. We hypothesize that CED-1 acts as a receptor that recognizes corpses. Currently we are attempting to identify the ligand(s) for CED-1, which may be corpse-specific cell surface molecules, and proteins that interact with the cytoplasmic domain of CED-1, which may be downstream signaling molecules.

We have also performed a large scale genetic screen for new engulfment mutants. Using a *sem-4* mutant background, we examined F2 bags of worms for F3 embryos with persistent corpses. We isolated 68 potential engulfment mutants. These mutants define distinct phenotypic categories, including viable mutants with strong or weak engulfment defects; viable mutants that have persistent abnormal-looking corpse-like bodies; and mutants that are both engulfment-defective and embryonic lethal. We hope the further characterization of these mutants will both help us understand the known engulfment genes and identify additional genes involved in this process.