# THE CELL-CORPSE ENGULFMENT PROTEIN CED-1 IS A TRANSMEMBRANE RECEPTOR THAT RECOGNIZES CELL CORPSES

## Zheng Zhou, Bob Horvitz

HHMI, Dept. Biology, MIT, Cambridge, MA 02139

Engulfment of apoptotic cells by their neighbors is an evolutionarily conserved process that removes apoptotic cells before they release harmful contents. 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 CrkII/DOCK180/Rac signaling pathway proposed to mediate cytoskeletal reorganization. On the basis of genetic interactions, *ced-6* and *ced-7* appear to act together with *ced-1* to control cell-corpse recognition and to initiate phagocytosis. *ced-6* encodes an adaptor-like protein, and *ced-7* encodes an ABC transporter.

We have cloned *ced-1* and found that it encodes a transmembrane protein similar to human SREC (Scavenger Receptor from Endothelial Cells) in its extracellular domain and that contains candidate binding motifs for adaptor proteins in its intracellular domain. Scavenger receptors bind a variety of substrates, including lipoproteins and phospholipids, and some members such as SR-A and CD36 are thought to mediate the recognition of apoptotic cells by phagocytes. Our molecular studies indicate that *ced-1* is expressed and functions in engulfing, but not in dying, cells. More specifically, we found that CED-1 is localized to the surface of engulfing cells and clusters in the region of the plasma membrane adjacent to cell corpses. Our results suggest that CED-1 is a receptor that recognizes cell corpses and mediates their engulfment. We postulate that SREC, the *in vivo* function of which is unknown, and other CED-1-related proteins in mammals may be involved in the phagocytosis of apoptotic cells.

In addition to our study of *ced-1*, we have performed a large-scale genetic screen for new engulfment mutants. We isolated 68 potential engulfment mutants. These mutants define distinct phenotypic categories, some of which have not been described before. For example, six mutants display engulfment defects in embryos that fail to develop to hatching. We have cloned one gene identified from this screen. We hope the further characterization of these mutants will both help us understand the known engulfment genes as well as identify additional genes involved in this process.