A screen for mutations that affect the localization of CED-4

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In the programmed cell death pathway, ced-4 is a key activator of the C. elegans caspase ced-3. Genetically, ced-4 is upstream of ced-3 and is necessary for normal programmed cell death to occur. egl-1 and ced-9 act upstream of ced-4 in the genetic pathway and are involved in activating and inhibiting ced-4 activity, respectively.

Previous work has shown that the localization of ced-4 seems intimately tied to its activity. In cells that are not undergoing programmed cell death, CED-4 is localized to mitochondrial membrane surfaces. When these cells are induced to die by overexpressing egl-1 or by ced-9 loss-of-function, CED-4 is localized to the perinuclear membrane. CED-4 localization appears to correlate with the life-or-death decision of a cell, but how and why the localization occurs is unknown.

When overexpressed, a CED-4::GFP fusion protein appears to localize to the mitochondria and perinuclear region of cells that are not undergoing programmed cell death. To identify factors important for the localization of CED-4, we will screen for mutants in which this CED-4::GFP fusion protein fails to localize to the perinucleus of viable cells.

1 Hersh, B., Chen, F., Conradt, B., Zhou, Z., and Horvitz, HR (1999) 12th International C. elegans Meeting