117. TWO MODIFIER SCREENS FOR NEW GENES INVOLVED IN PROGRAMMED CELL DEATH

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Most genes involved in the execution of programmed cell death (PCD) in *C. elegans* have been identified by screening for mutations that cause the survival of cells that normally die. The cloning of these genes has resulted in the identification of many of the key components that control PCD. To identify new genes that play a role in PCD, we are performing two modifier screens using a *lin-11::gfp* reporter that is expressed in Pn.aap cells. In the ventral cord of wild-type animals, six of the Pn.aap cells survive and express *lin-11*, while the six others undergo PCD. By contrast, in mutants defective for killing, such as strong loss-of-function mutations in *ced-3*, all 12 Pn.aap cells survive and express *lin-11*. The survival of Pn.aap cells can be easily monitored in strains carrying the *lin-11::gfp* reporter using a fluorescence-equipped dissecting microscope.

The first modifier screen, a *ced-4* suppression screen, is designed to identify genes that protect cells from undergoing PCD. We are screening for a reduction in the number of GFP-positive cells (*i.e*., an increase in PCD) in the ventral cords of animals bearing a partial loss-of-function mutation in *ced-4*. To date, approximately 40,500 mutagenized genomes have been screened for zygotic defects in cell survival: 5,000 were screened clonally and 35,500 non-clonally. Two strong suppressors have been obtained. The first suppressor, *n3418*, identified in the clonal screen, confers recessive suppression and sterility. We have mapped the mutation to a small region on chromosome III. The second suppressor, *n3696*, identified in the non-clonal screen, confers dominant suppression and is an intragenic mutation in *ced-4*.

The second modifier screen, a *ced-3* enhancer screen, is designed to identify genes that play a subtle role in the execution of PCD. Again using the *lin-11::gfp* reporter, we are screening for an increase in the number of GFP-positive cells (*i.e*., a decrease in PCD) in the ventral cords of animals bearing a partial loss-of-function mutation in *ced-3*. We have screened approximately 35,000 genomes non-clonally and isolated 212 enhancers. Of these, at least 13 are alleles of *ced-7*, 12 are alleles of *ced-3*, six are alleles of *ced-4*, and four are alleles of *ced-9*. Twenty-five of the remaining 170 isolates have obvious engulfment defects. On the basis of complementation tests and map position, we have identified at least four new cell-killing genes.