A VISIBLE ALLELE OF THE MUSCLE GENE *sup-10 X* OF *C. ELEGANS*

IVA GREENWALD[1] AND H. ROBERT HORVITZ

Department of Biology, Massachusetts Institute of Technology, 56-633, Cambridge, Massachusetts 02139

Manuscript received August 30, 1985
Revised copy accepted November 21, 1985

ABSTRACT

In this paper, we extend our previous analyses of a set of genes in *Caenorhabditis elegans* that are involved in muscle structure and function: *unc-93 III*, *sup-9 II*, *sup-10 X* and *sup-11 I*. We describe an unusual, visible allele of *sup-10*, examine how this allele interacts genetically with mutations in other genes of this set and propose that the wild-type products of the *unc-93* and *sup-10* loci may be components of a protein complex. We also describe a new gene of this set, *sup-18 III*, and the interaction of *sup-18* alleles with mutations in the other genes.

WE have studied genetic interactions among four genes of *Caenorhabditis elegans* involved in muscle structure and function: *unc-93 III*, *sup-9 II*, *sup-10 X* and *sup-11 I* (GREENWALD and HORVITZ 1980, 1982). One of these genes, *unc-93*, was defined by the rare semidominant mutation *e1500*, which results in abnormal muscle structure and a characteristic "rubber-band" behavioral phenotype. (Rubber-band connotes a particular uncoordinated, egg-laying defective and long phenotype.) The other three genes were defined by extragenic suppressors of *e1500*: null alleles of *sup-9* and *sup-10* suppress the mutant phenotype of *unc-93(e1500)* (GREENWALD and HORVITZ 1980); rare neomorphic (altered function) alleles of *sup-11*, which has an embryonic lethal null phenotype, are dominant suppressors of *unc-93(e1500)* (GREENWALD and HORVITZ 1982). The abnormal muscle phenotype of *unc-93(e1500)* suggested that these genes function in muscle cells; direct evidence that at least *sup-10* functions in muscle cells has been provided by mosaic analysis (HERMAN 1984).

In our initial study of *unc-93*, we found that, although the rare alleles *e1500* and *n200* result in morphological and behavioral abnormalities, null alleles of *unc-93* do not result in a visible phenotype, *i.e.*, the null phenotype of *unc-93* is wild type (GREENWALD and HORVITZ 1980). We suggested that a possible explanation for this observation is that an alternative protein (such as that encoded by another member of a postulated *unc-93* gene family) or an alter-

[1] Current address: Laboratory of Molecular Biology, MRC Centre, Hills Road, Cambridge, CB2 2QH, England.

native pathway functions in *unc-93* null mutants, but that rare mutations, such as *e1500*, encode toxic products that cannot be bypassed by the postulated redundant activity. Spontaneous reversion to a wild-type phenotype, which is a striking feature of *unc-93(e1500)*, results from loss of gene activity at *unc-93* (or at the suppressor loci *sup-9* and *sup-10*) and appears to reflect the forward *C. elegans* spontaneous mutation rate. We also suggested that some members of other gene families might have similar genetic properties, *i.e.*, they may be defined by rare visible alleles that revert intragenically by loss-of-function mutations. Currently, more than ten genes with these properties have been defined in *C. elegans* (E. PARK, I. GREENWALD and R. HORVITZ, unpublished observations). At least one gene, *sup-7*, that has these properties is known to be a member of a tRNA gene family (WATERSTON 1981; WILLS *et al.* 1983); also, a member of the actin gene family, *act-1* (formerly called *unc-92*), may have some of these features (LANDEL *et al.* 1984).

In addition to suppressors that arise by loss-of-function mutations, we also identified one locus, *sup-11*, at which rare neomorphic alleles act as dominant suppressors of *unc-93(e1500)*. However, null alleles of *sup-11* do not have suppressor activity and are recessive embryonic lethal mutations (GREENWALD and HORVITZ 1982).

We report here the existence of a rare visible allele of *sup-10*, a gene originally defined by loss-of-function mutations that suppress *unc-93(e1500)*. We describe how this rare allele interacts genetically with mutations in *unc-93*, *sup-9* and *sup-11*. We also describe a new suppressor locus, *sup-18 III*, and how *sup-18* alleles interact with alleles of *unc-93* and *sup-10*.

MATERIALS AND METHODS

General methods: General methods for the handling, culturing and ethyl methanesulfonate (EMS) mutagenesis of *C. elegans* have been described (BRENNER 1974). All experiments were performed at 20° unless otherwise indicated.

Strains and genetic nomenclature: The mutations used in this study were as follows:

LG I: *sup-11(n403)*.

LG II: *sup-9(n180)*.

LG III: *unc-93(e1500)*, *unc-93(n200)*, *unc-93(e1500 n234)* [*n234* is an amber mutation in *unc-93*], *dpy-17(e164)*, *daf-4(e1364)*, *unc-36(e251)*, *unc-32(e189)*, *nDf16*.

LG X: *lin-15(n765)*, *sup-10(n183)* [reference allele of *sup-10*].

The mutations *dpy-17(e164)*, *unc-36(e251)* and *unc-32(e189)* were described by BRENNER (1974), *daf-4(e1364)* by RIDDLE (1977) and *lin-15(n765)* by FERGUSON and HORVITZ (1985). *nDf16* was isolated and characterized by V. AMBROS and M. FINNEY (personal communication).

Two spontaneous *sup-18* alleles, *n463* and *n528*, which arose as suppressors of *unc-93(e1500)*, have been used as reference alleles in this study.

Alleles generated during the course of this study are listed in Table 1.

This paper conforms to the standardized nomenclature for *C. elegans* genetics (HORVITZ *et al.* 1979).

Analysis of wild-type revertants of *sup-10(n983)* X: Revertants were crossed with *dpy-17* males. If reversion resulted from an autosomal recessive suppressor, cross progeny hermaphrodites would be wild type, but males would be of the Unc(*n983*) phenotype. Such revertants were crossed with males of two "tester" genotypes to see if they carried alleles of *sup-9* or *unc-93*, which we had defined previously (GREENWALD and HORVITZ 1980). (1) When revertant hermaphrodites were crossed with *sup-9*; *unc-*

TABLE 1

Alleles generated during the course of this study

Gene	Alleles	Mutagen	Parent genotype
sup-9 II	*n659, n668*	EMS	*unc-93 (e1500) sup-18 (n463)*
	n1009, n1012, n1016, n1020, n1023, n1025, n1026, n1028, n1037	EMS	*sup-10 (n983)*
sup-18 III	*n463, n527, n528*	Spontaneous	*unc-93 (e1500)*
	n628	EMS	*unc-93 (e1500)*
	n1010, n1014, n1015, n1022, n1029, n1030, n1031, n1033, n1035, n1036	EMS	*sup-10 (n983)*
unc-93 III	*n657, n660, n663, n666, n667*[a]	EMS	*unc-93 (e1500) sup-18 (n463)*
	n1011, n1018, n1019, n1021, n1024, n1027	EMS	*sup-10 (n983)*
sup-10 X	*n661, n664*	EMS	*unc-93 (e1500) sup-18 (n463)*
	n983	EMS	*N2*
	n1007, n1008, n1013, n1017, n1034[b]	EMS	*sup-10 (n983)*

[a] Because these alleles were generated in a *unc-93 (e1500)* background, the alleles are actually *unc-93 (e1500 n657)*, etc.

[b] Because these alleles were generated in a *sup-10 (n983)* background, the alleles are actually *sup-10 (n983 n1007)*, etc.

93(e1500) males, cross-progeny males were phenotypically wild type if the new suppressor mutation was an allele of *sup-9*; otherwise, they would have been Unc(*n983*). (2) Similarly, when revertant hermaphrodites were crossed with males of genotype *unc-93(e1500 n234)*, a null allele of *unc-93* that confers no visible phenotype, cross-progeny males were phenotypically wild type if the new suppressor mutation was an allele of *unc-93*; otherwise, they would have been Unc(*n983*).

Some wild-type revertants yielded the Unc(*n983*) progeny in both of the tester crosses and, therefore, did not appear to carry *sup-9* or *unc-93* alleles. Three of these suppressor mutations were mapped to LG III, suggesting that they might be related to *sup-18*, which, as described in the RESULTS section, was defined by partial suppressors of *unc-93(e1500)*. When such revertant hermaphrodites were crossed with *sup-18(n463)*/+ males, wild-type and Unc(*n983*) males were seen, indicating that these complete suppressors of *sup-10(n983)* were indeed alleles of *sup-18*.

***sup-18* map data:** Two-factor (data not shown) and three-factor crosses established that *sup-18* is a new locus on LG III. From the heterozygote *unc-93(e1500) sup-18(n528)/daf-4(e1364) unc-32(e189)*, 10 of 21 Unc-32 non-Daf hermaphrodites segregated *sup-18*. From the heterozygote *unc-93(e1500) sup-18(n528)/unc-36(e251) dpy-19(e1259)*, 5 of 5 Dpy non-Unc hermaphrodites segregated *sup-18*, suggesting that *sup-18* maps left of or very close to *unc-36*. Given the established order, *unc-93—daf-4—unc-36—dpy-19—unc-32* (SWANSON, EDGLEY and RIDDLE 1984), these data indicate that the likely map position of *sup-18* is between *daf-4* and *unc-36*.

Double-mutant combinations: Combinations of alleles were constructed by standard procedures (HERMAN and HORVITZ 1980), employing balancer mutations in *trans* when necessary to assist the construction. All constructions were checked by appropriate complementation tests.

RESULTS

Phenotype of *n983*: The *n983* mutation was isolated by CHAND DESAI of our laboratory in a screen for egg-laying defective mutants (*e.g.*, TRENT, TSUNG

and HORVITZ 1983). When viewed with the dissecting microscope, *n983* homozygous hermaphrodites appear uncoordinated, egg-laying defective (*i.e.*, eggs tend to hatch internally, although most hermaphrodites do release some eggs and larvae) and long and exhibit a characteristic rubber-band response to touch (*i.e.*, when stroked on the head, they contract and then relax). This phenotype is strikingly similar to that conferred by the semidominant mutations *e1500* and *n200*, which are alleles of *unc-93 III* (GREENWALD and HORVITZ 1980). However, *n983* is recessive and, as will be described below, maps to the *X* chromosome and is an allele of *sup-10 X*.

The *n983* mutation appears to be a rare allele of *sup-10 X*: Null alleles of *sup-10* [abbreviated as *sup-10(0)*] were previously obtained by reverting the rubber-band phenotype of *unc-93(e1500)* (GREENWALD and HORVITZ 1980). The *sup-10(0)* alleles completely suppress the mutant phenotype of *unc-93(e1500)* and *unc-93(n200)* and do not result in a visible phenotype in an *unc-93*(+) genetic background.

The *n983* mutation, like *sup-10*, is linked to *lin-15 X* (within 0.5%; data not shown). A complementation test indicated that *n983* is an allele of *sup-10*, *i.e.*, hermaphrodites of genotype *n983/sup-10(0)* are mutant (although somewhat less severely abnormal than homozygous *n983* hermaphrodites). In addition, as described in the next section, phenotypically wild-type revertants of *n983* were isolated. One class of revertant that was obtained comprises mutations that are tightly linked (within 0.2%; data not shown) to *n983*; these linked revertants, here represented as "*n983-rev*," appear to be null alleles of *sup-10* by two criteria. First, *n983-rev* mutations, like the *sup-10(0)* alleles, are recessive suppressors of the mutant phenotype of *unc-93(e1500)*, *i.e.*, wild-type segregants were obtained among the progeny of *unc-93(e1500); n983-rev/+* hermaphrodites. Second, the suppression by *n983-rev* of *unc-93(e1500)* is not complemented by *sup-10(0)*, *i.e.*, all segregants from *unc-93(e1500)/+; n983-rev/sup-10(0)* are wild type.

Interactions of *sup-10* mutations with mutations in other genes: In the next two sections, we describe the phenotypes of certain double mutants containing *sup-10(n983)*. We examined two groups of double mutants. First, we obtained wild-type revertants of *sup-10(n983)* and characterized the intragenic and extragenic suppressors thereby generated. All of these suppressors proved to be alleles of genes we had previously defined in our studies of *unc-93*. Second, certain double-mutant combinations were deliberately constructed, including combinations of rubber-band alleles of *unc-93* and *sup-10*. Table 2 summarizes the results of the next two sections.

Extragenic suppressors of *sup-10(n983)*: Thirty-two independent wild-type homozygous revertant strains were obtained after EMS mutagenesis. Reversion events occurred at an overall frequency of 3×10^{-3} per haploid genome (frequency = number of revertants/2 × number of F_1's; BRENNER 1974). This frequency is greater than that of 5×10^{-4} expected for mutations that eliminate gene function at a single locus (BRENNER 1974; GREENWALD and HORVITZ 1980, 1982) and suggested that more than one locus is involved. Revertants were characterized as described in MATERIALS AND METHODS. Five revertants

TABLE 2

Phenotypes of hermaphrodites of different genotypes

Genotype	Phenotype
unc-93 (e1500)	Rubber band[a]
unc-93 (n200)	Rubber band (weak)
sup-10 (n983)	Rubber band
unc-93 (0)	Wild type
sup-10 (0)	Wild type
unc-93 (e1500); sup-10 (0)	Wild type
unc-93 (0); sup-10 (n983)	Wild type
unc-93 (e1500); sup-10 (n983)	Motile, non-Egl[b]
unc-93 (0); sup-10 (0)	Wild type
sup-9 (0); unc-93 (e1500)	Wild type
sup-9 (0); sup-10 (n983)	Wild type
unc-93 (e1500); sup-18 (0)	Motile, non-Egl
sup-18 (0); sup-10 (n983)	Wild type
sup-11 (n403)/+; unc-93 (e1500)	Nearly wild type
sup-11 (n403)/+; sup-10 (n983)	Rubber band
sup-11 (n403); unc-93 (e1500)	Motile, scrawny
sup-11 (n403); sup-10 (n983)	Motile, scrawny

Data from GREENWALD and HORVITZ (1980, 1982) and this study.

[a] Rubber band connotes a particular uncoordinated, egg-laying defective and long phenotype.

[b] non-Egl = able to lay eggs.

appeared to be *sup-10* null alleles based on criteria described above. The remaining 27 revertants harbored autosomal recessive suppressors. One "suppressor" locus proved to be *unc-93*: six apparent null alleles of *unc-93* were found among the wild-type revertants of *sup-10(n983)*; in addition, we constructed a double mutant containing an *unc-93 amber* mutation and *sup-10(n983)*, and we showed that this double mutant is phenotypically wild type. We shall consider this observation further in the DISCUSSION.

Another suppressor locus defined in our previous work reappeared in this study: apparent null alleles of *sup-9 II* suppress *unc-93(e1500)* and *unc-93(n200)* (GREENWALD and HORVITZ 1980). Nine wild-type revertants of *sup-10(n983)* harbored *sup-9* alleles. These *sup-9* alleles also suppress *unc-93(e1500)*.

Ten wild-type revertants of *sup-10(n983)* harbored putative null alleles of *sup-18 III*. We describe this new locus below. We have also obtained *sup-18* alleles as partial revertants of *unc-93(e1500)*: such partial revertants have the Unc(*e1500*) rubber band behavior and motility defect as larvae, but as adults they show improved motility and lay eggs [*unc-93(e1500)* hermaphrodites never lay eggs]. The partial suppression of *unc-93(e1500)* by *sup-18* contrasts with the complete suppression of *sup-10(n983)* by *sup-18*.

***sup-11(n403)* suppression of *sup-10(n983)*:** The *sup-11* locus was defined by rare neomorphic alleles that act as dominant suppressors of *unc-93(e1500)* and *unc-93(n200)*. Such suppressor alleles arise at a frequency of less than 10^{-5}

TABLE 3

Brood sizes of *unc-93* and *sup-10* mutants

Genotype	Average brood	Egg-laying
Wild type	327[a]	Lays eggs
unc-93 (e1500)	26 ± 2.4	Never lays eggs or releases larvae; forms "bags"[b]
unc-93 (n200)	208 ± 22.6	Lays eggs[c]
sup-10 (n983)	101 ± 18.9	Release some eggs or larvae; forms "bags"
unc-93 (e1500); sup-10 (n983)	207 ± 22.3	Lays eggs
unc-93 (n200); sup-10 (n983)	72 ± 13.8	Release some eggs or larvae; forms "bags"

Total progeny of four hermaphrodites of each genotype were counted; average brood size and average deviation are indicated. An egg-laying defective hermaphrodite produces fewer progeny than does an egg-laying competent hermaphrodite. Brood size, at least in part, reflects egg-laying capability: muscle mutants, such as *unc-93 (e1500)*, tend to have low brood sizes. At least one component of this reduced brood size can be directly attributed to defective muscle function: by mosaic analysis, HERMAN (1984) showed that the inability of *unc-93 (e1500)* hermaphrodites to lay eggs results from sex-muscle dysfunction. Thus, we infer that suppression of the egg-laying defect of *e1500* in certain mutant backgrounds results from the restoration of more normal muscle function, which is manifested in the larger brood sizes of suppressed hermaphrodites.

[a] Data of HODGKIN (1983).

[b] "Bags of worms" are formed when larvae hatch internally and kill their mothers.

[c] Somewhat bloated.

after EMS mutagenesis and suppressor homozygotes have a "Scrawny" phenotype but are motile (GREENWALD and HORVITZ 1982). We constructed a double mutant containing *sup-10(n983)* and the reference allele *sup-11(n403)*. This double mutant is motile (*i.e.*, non-"rubber band") and scrawny; however, *sup-11(n403)/+; sup-10(n983)* hermaphrodites and males have the rubber-band phenotype. Thus, *sup-11(n403)* results in recessive suppression of *sup-10(n983)*, in contrast to its dominant suppression of *unc-93* rubber-band alleles.

Rubber-band double-mutant combinations: Double mutants containing rubber-band alleles of *unc-93* and *sup-10* were obtained among segregants from *unc-93 +/+ dpy-17; sup-10 +/+ lin-15* hermaphrodites. The *unc-93(e1500); sup-10(n983)* adult hermaphrodites are less mutant than are either single mutant: the double-mutant hermaphrodites lay eggs, are more motile, have a more normal body shape and have larger broods than do the single mutants (Table 3).

Animals of genotype *unc-93(e1500); sup-10(n983)* are much more uncoordinated as larvae than as adults. As larvae, the double-mutant hermaphrodites are similar in phenotype to the single mutants. This age-dependent phenotype is similar to that seen in *unc-93(e1500) sup-18(0)* hermaphrodites (see below). Both the abnormal movement and body shape of the *unc-93(e1500); sup-10(n983)* double mutant, like those of each single mutant, are less severe at 25° than at 20°.

The *unc-93(n200); sup-10(n983)* double mutant is similar to the *sup-10(n983)* single mutant (recall that *unc-93(n200)* is not greatly uncoordinated). The

brood size of the double mutant is reduced to an extent that is consistent with the independent (multiplicative) combined effect of the two single mutants.

The *sup-18* locus: The *sup-18 III* locus was defined by spontaneous and EMS-induced partial revertants of *unc-93(e1500)*. Hermaphrodites of genotype *unc-93(e1500) sup-18* are uncoordinated as larvae, but as adults they lay eggs and exhibit improved motility. Alleles of *sup-18* were not isolated in our original mutageneses, because revertants were generally recognized as motile larvae (GREENWALD and HORVITZ 1980). Alleles of *sup-18* have also been isolated among phenotypically wild-type revertants of *sup-10(n983)*, as described above. Map data for *sup-18* are given in MATERIALS AND METHODS.

The *sup-18* mutations described here are likely to be null alleles by two criteria. (1) Alleles of *sup-18* arise after EMS mutagenesis of *sup-10(n983)* at the frequency expected for a null mutation in an average gene (see above). In addition, many *sup-18* alleles have arisen spontaneously, which is consistent with the interpretation that they result from loss of gene activity (GREENWALD and HORVITZ 1980). (2) *nDf16*, a deficiency of *sup-18*, fails to complement *sup-18* for suppressor activity. Hermaphrodites of genotype *unc-93(e1500) sup-18(n528)/unc-93(e1500) nDf16* are uncoordinated as larvae, but as adults they are motile and lay eggs; in addition, *nDf16/+* does not suppress *unc-93(e1500)*. Thus, a deficiency of *sup-18* is equivalent to *sup-18(n528)* in complementation tests, suggesting that *sup-18* suppressor mutations represent loss of *sup-18* activity.

sup-18(n463), a spontaneous mutation that arose as a suppressor of *unc-93(e1500)*, was separated from the linked *unc-93(e1500)* mutation by recombination. The *sup-18(n463)* homozygote has no visible phenotype. A *sup-18* allele isolated as a suppressor of *unc-93(e1500)* suppresses *sup-10(n983)*, and a *sup-18* allele isolated as a suppressor of *sup-10(n983)* suppresses *unc-93(e1500)*.

Phenotypically wild-type revertants of the larval uncoordinated phenotype of *unc-93(1500) sup-18(n463)* were isolated by examining the F_1 and F_2 progeny of EMS-mutagenized hermaphrodites for motile larvae. Suppressor mutations thereby generated were analyzed by crosses similar to those described above for the *sup-10(n983)* revertants and were found to be apparent null alleles of *sup-9* (two alleles), *unc-93* (five alleles) and *sup-10* (two alleles) (Table 1).

DISCUSSION

A striking uncoordinated, egg-laying defective and long (rubber-band) phenotype can result from rare mutations at either of two loci: *unc-93 III* and *sup-10 X*. The null phenotype of each of these loci is wild type. Null alleles of *unc-93* or *sup-10* can be generated by intragenic reversion of the visible alleles *unc-93(e1500)*, *unc-93(n200)* and *sup-10(n983)*; reversion results from loss-of-function mutations, which eliminate a mutant phenotype likely to result from altered gene activity. Null alleles of *unc-93* suppress the rubber-band allele of *sup-10*, and null alleles of *sup-10* suppress the rubber-band alleles of *unc-93*. In addition, apparent null alleles of *sup-9 II* suppress the rubber-band alleles of *unc-93* and *sup-10*, and apparent null alleles of *sup-18 III* partially suppress

the rubber-band phenotype of *unc-93(e1500)* and completely suppress the rubber-band phenotype of *sup-10(n983)*. As with *unc-93* and *sup-10*, both *sup-9* and *sup-18* appear to have wild-type null phenotypes.

We previously discussed three classes of explanation for how null mutations at extragenic suppressor loci, such as *sup-10*, might suppress rubber-band alleles of *unc-93* (GREENWALD and HORVITZ 1980): (1) elimination of a positive regulator of *unc-93* gene expression, (2) elimination of a negative regulator of an alternative pathway or product and (3) elimination of a product that interacts with the mutant gene product to generate a toxic effect. The existence of a rubber-band allele of *sup-10*, and the suppression of mutant alleles at either *unc-93* or *sup-10* by null alleles at the other locus, makes the third model seem most attractive: the mutant phenotypes of *unc-93(e1500)* and *unc-93(n200)* result from the interaction of their altered products with the *sup-10*(+) product, and the mutant phenotype of *sup-10(n983)* results from the interaction of its altered product with that encoded by *unc-93*(+); elimination of either wild-type product prevents the formation of the toxic substance (possibly a protein complex).

We should like to extend this argument further to suggest that the wild-type products of *unc-93* and *sup-10* interact. We favor this hypothesis because of the existence of rubber-band alleles at both loci. Although it is conceivable that a rare rubber-band allele of *unc-93* could result in an altered product that has acquired a novel ability to interact with the *sup-10*(+) product, or that a rare rubber-band allele of *sup-10* generates a product with a novel ability to interact with the *unc-93*(+) product, it seems unlikely that rubber-band mutations at both loci could result unless the *unc-93*(+) and *sup-10*(+) products interact.

In this context, it is interesting to note that the double mutant *unc-93(e1500); sup-10(n983)* has a phenotype that is less severe than either single mutant. It is conceivable that the mutual suppression reflects a corrective interaction between the mutant proteins, *i.e.*, proper function is restored to a protein complex. However, it is possible that suppression results from the failure of the mutant proteins to interact, since the toxic effect is generated by an interaction of particular *unc-93* and *sup-10* products; an alleviation of the mutant phenotype might result even if wild-type function is not restored, because complete elimination of function does not confer a visible phenotype.

The basis for the suppression of rubber-band alleles by *sup-9* and *sup-18* mutations remains unknown and may be via any of the three mechanisms described above. However, suppression by *sup-11* must result from a different mechanism, because *sup-11* suppressor alleles, such as *sup-11(n403)*, are rare "neomorphic" alterations of an essential gene. *sup-11(n403)* acts as a dominant suppressor of both *unc-93* rubber-band alleles and as a recessive suppressor of *sup-10(n983)*. This apparent gene- and allele-nonspecificity is consistent with the interpretation that *sup-11* suppressor alleles bypass the defect caused by the rubber-band mutations (GREENWALD and HORVITZ 1982).

Our analysis of these five genes is part of a general attempt by several laboratories to utilize *C. elegans* for the study of muscle structure and function.

Many genes involved in muscle structure have been identified genetically (*e.g.*, WATERSTON, THOMSON and BRENNER 1980; ZENGEL and EPSTEIN 1980), including genes that encode four identified protein components of the somatic musculature (EPSTEIN, WATERSTON and BRENNER 1974; WATERSTON, EPSTEIN and BRENNER 1974; LANDEL *et al.*, 1984; D. MOERMAN, G. BENIAN, R. BARSTEAD, L. SCHRIEFFER and R. WATERSTON, personal communication). Given the recent development of relatively straightforward approaches to the molecular cloning of *C. elegans* genes (EIDE and ANDERSON 1985 and personal communication; D. MOERMAN, G. BENIAN and R. WATERSTON, personal communication; I. GREENWALD, unpublished observations; G. RUVKUN, V. AMBROS and R. HORVITZ, unpublished observations), continued genetic and molecular genetic analysis of muscle genes should contribute significantly to our understanding of muscle structure, assembly and function. In addition, gene systems such as the one described here, with their well-characterized genetic interactions, should continue to provide useful tools for a variety of genetic manipulations (*e.g.*, HERMAN 1984).

We should like to thank CHAND DESAI for isolating *sup-10(n983)* and JONATHAN HODGKIN for comments on this manuscript. This work was supported by the following grants: United States Public Health Service research grants GM24663 and GM24943, Research Career Development Award HD00369 to H.R.H. and Predoctoral Training grant GM07287.

LITERATURE CITED

BRENNER, S., 1974 The genetics of *Caenorhabditis elegans*. Genetics **77:** 71–94.

EIDE, D. and P. ANDERSON, 1985 Transposition of Tc*1* in the nematode *Caenorhabditis elegans*. Proc. Natl. Acad. Sci. USA **82:** 1756–1760.

EPSTEIN, H. F., R. H. WATERSTON and S. BRENNER, 1974 A mutant affecting the heavy chain of myosin in *Caenorhabditis elegans*. J. Mol. Biol. **90:** 291–300.

FERGUSON, E. L. and H. R. HORVITZ, 1985 Identification and characterization of 22 genes that affect the vulval cell lineages of the nematode *Caenorhabditis elegans*. Genetics **110:** 17–72.

GREENWALD, I. S. and H. R. HORVITZ, 1980 *unc-93(e1500)*: a behavioral mutant that defines a gene with a wild-type null phenotype. Genetics **96:** 147–164.

GREENWALD, I. S. and H. R. HORVITZ, 1982 Dominant suppressors of a muscle mutant define an essential gene of *Caenorhabditis elegans*. Genetics **101:** 211–225.

HERMAN, R. K., 1984 Analysis of genetic mosaics of the nematode *Caenorhabditis elegans*. Genetics **108:** 165–180.

HERMAN, R. K. and H. R. HORVITZ, 1980 Genetic analysis of *Caenorhabditis elegans*. In: *Nematodes as Biological Models*, Vol. 1, Edited by B. M. ZUCKERMAN. Academic Press, New York.

HODGKIN, J., 1983 *X*-chromosome dosage and gene expression in *Caenorhabditis elegans*: two unusual dumpy genes. Mol. Gen. Genet. **192:** 452–458.

HORVITZ, H. R., S. BRENNER, J. HODGKIN and R. HERMAN, 1979 A uniform genetic nomenclature of the nematode *Caenorhabditis elegans*. Mol. Gen. Genet. **175:** 129–133.

LANDEL, C., M. KRAUSE, R. WATERSTON and D. HIRSH, 1984 DNA rearrangements of the actin gene cluster in *Caenorhabditis elegans* accompany reversion of three muscle mutants. J. Mol. Biol. **100:** 497–514.

RIDDLE, D. L., 1977 A genetic pathway for daver larva formation in *Caenorhabditis elegans*. Stadler Genet. Symp. **9:** 101–120.

SWANSON, M. M., M. L. EDGLEY and D. L. RIDDLE, 1984 The nematode *Caenorhabditis elegans* pp. 286–299. In: *Genetic Maps*, edited by S. J. O'BRIEN. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York.

TRENT, C., N. TSUNG and H. R. HORVITZ, 1983 Egg-laying defective mutants of the nematode *Caenorhabditis elegans*. Genetics **104:** 619–647.

WATERSTON, R. H., 1981 A second informational suppressor, *sup-7*, in *Caenorhabditis elegans*. Genetics **97:** 307–325.

WATERSTON, R. H., H. F. EPSTEIN and S. BRENNER, 1974 Paramyosin of *Caenorhabditis elegans*. J. Mol. Biol. **90:** 285–290.

WATERSTON, R. H., J. N. THOMSON and S. BRENNER, 1980 Mutants with altered muscle structure in *Caenorhabditis elegans*. Dev. Biol. **77:** 271–302.

WILLS, N., R. F. GESTELAND, J. KARN, L. BARNETT, S. BOLTEN and R. H. WATERSTON, 1983 The genes *sup-7 X* and *sup-5 III* of *C. elegans* suppress amber nonsense mutations via altered transfer RNA. Cell **33:** 575–583.

ZENGEL, J. and H. EPSTEIN, 1980 Identification of genetic elements associated with muscle structure in the nematode *Caenorhabditis elegans*. Cell Motil. **1:** 73–97.

Communicating editor: R. K. HERMAN