Hermaphrodites carrying dominant mutations in the gene egl-41 (egl, egg-laying defective) lack the hermaphrodite-specific HSN neurons but have the male-specific CEM neurons and therefore are weakly masculinized (1, 2). Our analyses with a deficiency (nDf42) and a duplication (ctDp8) that span the egl-41 locus indicate that egl-41 is not haplo-insufficient and that the dominant mutations cause an altered function that is antagonized by wild-type activity. The existing egl-41 alleles (n1069, n1074, n1077, e2055, n3717) therefore most likely represent gain-of-function (gf) mutations causing altered function. It has previously been shown that egl-41(gf) mutations enhance the masculinizing effect of weak loss-of-function (lf) mutations in tra-2 (tra, transformer) and suppress the feminizing effect of a tra-2(mx) (mx, mixed character) allele (1, 3). In addition, a null mutation of fem-1 (fem, feminization) was found to be epistatic to egl-41(gf) mutations (3). Our analyses furthermore indicate that lf mutations of fem-2 and fem-3 are epistatic to egl-41(gf) mutations as well and that egl-41(gf) mutations are epistatic to a her-1lf (her, hermaphroditization) mutation. We suggest the gene defined by egl-41(gf) mutations is part of the genetic pathway that specifies sexual fate and acts between her-1 and the fem genes. To determine the lf phenotype of egl-41 and to facilitate the cloning of the gene by transformation rescue, we performed an F1 screen for dominant revertants of the phenotype caused by the egl-41(gf) mutation n1077. We screened 20,000 haploid genomes and identified one mutation, bc189, that is closely linked to the egl-41 locus. bc189 completely suppresses the egl-41(n1077gf) phenotype but causes no obvious additional abnormalities. We therefore cloned the gene by combining fine mapping, using SNPs, and our observation that the dominant phenotype of egl-41(n1077gf) is antagonized by wild-type activity. egl-41 proved to be identical to a gene previously characterized, sel-10 (sel, suppressor/enhancer of lin-12). sel-10 was identified as a negative regulator of lin-12/Notch (lin, lineage abnormal) signaling and encodes an F-box protein (4, 5). The egl-41(gf) mutations as well as bc189 are missense mutations in the sel-10 ORF (G566R and D482N, respectively). We will therefore now refer to egl-41 as sel-10.

sel-10(bc189 n1077) suppresses a partial lf mutation of lin-12, enhances a gf mutation of lin-12, and suppresses a lf mutation of sel-12 and therefore genetically behaves like the canonical lf allele of sel-10, ar41. Surprisingly, using the same criteria, sel-10(n1077gf) also behaves like a sel-10(II) mutation. Furthermore, preliminary data indicate that, just like sel-10(gf) mutations, bc189 n1077 as well as ar41 enhance the masculinizing effects of weak tra-2(II) mutations. These results suggest that sel-10 is normally involved in the determination of sexual fate and that sel-10(gf) mutations share certain characteristics with sel-10(II) mutations. Using biochemical and molecular approaches, we are currently seeking potential targets of the F-box protein SEL-10 in the sex determination pathway.