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Negative Regulators of EGF-Signaling in *C. elegans*

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Vulval differentiation in *C. elegans* is mediated by an Epidermal growth factor(EGF)-EGF receptor(EGFR) signaling pathway. We have cloned *unc-101* and *sli-1*, negative regulators of vulval differentiation in *C. elegans*. *unc-101* encodes a homolog of AP47, the medium chain of the *trans*-Golgi clathrin-associated protein complex. Most of the *unc-101* alleles are deletions or nonsense mutations, suggesting that these alleles severely reduce the *unc-101* activity. We showed that the functions of AP47 are conserved between nematodes and mammals. *sli-1* encodes a protein similar to the mammalian proto-oncogene *c-cbl*.

unc-101 mutations can cause a greater than wild type vulval differentiation in combination with certain mutations in *sli-1*. A mutation in a new gene, *rok-1*, causes no defect by itself, but causes a greater than wild-type vulval differentiation in the presence of a *sli-1* mutation. The *unc-101; rok-1; sli-1* triple mutants display a greater extent of vulval differentiation than any double mutant combinations of *unc-101*, *rok-1* and *sli-1*. Therefore, *rok-1* locus defines another negative regulator of the vulval induction pathway.