Inhibition of Touch Cell Fate by egl-44 and egl-46

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In wild-type C. elegans six cells develop as receptors for gentle touch. In egl-44 and egl-46 mutants (which were first identified because of defects in the HSN neurons; Desai et al., 1988, Nature 336: 638), however, the FLP neurons also possess touch receptor-like features and express touch receptor genes (Mitani et al., 1993, Development 119: 773). Because these genes appear to repress the expression of touch cell fate, we have cloned them and characterized their action on touch cell-specific genes. egl-44 encodes a TEF (transcription enhancer factor)-like protein, and like TEF proteins, EGL-44 contains a TEA/ATTS DNA-binding domain and a putative transcriptional regulation domain. A gfp::egl-44 rescuing fusion is expressed in nuclei of neurons (including the FLP and HSN cells), hypodermis and intestine, but not in touch cells. egl-46 encodes a zinc-finger protein that with two Drosophila proteins and two proteins from humans and mice defines a novel zinc-finger subfamily. A gfp::egl-46 rescuing fusion is expressed predominantly and transiently (except for in a few cells) in nuclei of neurons, including FLP, HSN, and the touch cells. The late and transient expression of gfp::egl-46 in the Q lineages and the previously identified lineage defects in egl-46 mutants, suggest that the gene may control the production and differentiation of terminal cells in this lineage. In contrast to its expression in many other cells, egl-46 is continually expressed in the FLP neurons; this expression is dependent on egl-44.

To test whether coexpression of egl-44 and egl-46 prevented the expression of touch cell characteristics, we ectopically expressed egl-44 and egl-46 in the touch cells. This expression resulted in touch insensitivity and the loss of mec-7, mec-4, and mec-18 expression. In addition, as with the FLP cells, coexpression of egl-44 and gfp::egl-46 led to the continued expression of the florescent protein. These defects were not seen when egl-44 was expressed in the touch cells of egl-46 mutant animals. These results suggest that expression of both genes are needed to repress touch cell fate in the FLP cells.

EGL-44 and EGL-46 are likely to repress the expression of touch cell function genes by binding to their promoters and preventing the binding of the MEC-3::UNC-86 complex. EGL-44 and EGL-46 bind to each other in in vitro S-Tag pull down experiments. In addition, the binding of EGL-44 to specific sites in the mec-4 and mec-7 promoters is enhanced by the presence of EGL-46. These binding sites are near those of UNC-86 and MEC-3, and the binding of these latter proteins is prevented by the presence of EGL-44 and EGL-46. We are currently examining the roles of different domains of EGL-44 and EGL-46 in this binding to understand further the action of these genes in the combinatorial control of touch cell fate.