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Clues toward understanding EGF/ Wnt signal integration in the specification of P12 fate: analysis of the *egl-5* promoter

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The *C. elegans Hox* gene *egl-5* is most similar, based on sequence analysis, to *Abdominal-B.* Consistent with its assignment into this paralog group, *egl-5* is expressed in the posterior region of the worm. Immuno-staining results have shown that in the hermaphrodite, *egl-5* is expressed in the hermaphrodite specific neuron, body wall muscle, posterior lateral microtubule neuron, PVC interneuron, M, V6, the rectal epithelial cells K, F, B, U and the P12 neuroectoblast cell.

The two most posterior P cells are P11 and P12. The anterior products of their first division are both neuroblasts. P11.p fuses with the epidermal syncytium and P12.p divides again during late L1. The anterior division products, the epidermal cells P12.pa and P11.p are distinguishable by their distinct nuclear morphologies and positions.

Earlier ablation experiments have shown that before interdigitating at the ventral midline during early L1, either of the two most posterior P cells can adopt the P12 fate. Previous genetic analysis indicates that P12 fate specification requires the synergistic action of the EGF and the Wnt signaling pathways. Reduction - or loss of function mutations in components of the EGF or the Wnt pathway result in partially penetrant P12 to P11 or P11 to P12 transformations. Double mutants of EGF and Wnt pathway components significantly enhance the frequency of transformation. P12 is not specified in an *egl-5(lf)* mutant and overexpression of *egl-5* can rescue the loss of P12 specification phenotype of *let-23* mutants.

In order to understand how information from the EGF and Wnt pathway are integrated at a *cis*-regulatory level, we have undertaken an analysis of the *egl-5* promoter to determine elements required for *egl-5* expression in P12. Do the two pathways converge on the *egl-5* promoter or upstream of it? We have identified an approximately 1.3 kb. fragment of *egl-5* promoter sufficient to drive expression of a

heterologous promoter in the cells K, F, B, U, body wall muscle and P12. We are further dissecting this region in an attempt to identify P12 specific elements. Additionally, we hope to utilize this P12 enhancer as a tool to identify additional players involved in *egl-5* activation in P12.