2001 International Worm Meeting abstract 661

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# Making the Matrix: MEC-1, a Multifunctional Extracellular Protein

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In electron micrographs, the *C. elegans* touch receptor neurons have two distinguishing characteristics: a bundle of 15-protofilament microtubules and extensive extracellular matrix. In the current molecular model for touch sensitivity both of these feature are thought to provide tethering points for the mechanosensory channel. *mec-1* is needed for the elaboration of the extracellular matrix. The *mec-1* gene was first identified by mutations that cause touch insensitivity. In the initial characterization of *mec-1* mutants (**Chalfie** and Sulston, 1981), loss of *mec-1* was found to affect the touch cells in two ways: it caused the loss of most of the extracellular matrix and it prevented the attachment of touch cell processes near the cuticle and the engulfment of lateral touch cell processes by the surrounding hypodermis that normally occurs during development. These observations suggested that the attachment of the touch cells was important for their function. Since *him-4* mutations prevent the attachment and engulfment without affecting touch sensitivity (Vogel and Hedgecock, 2001), attachment, per se, is not essential for touch sensitivity. We have now cloned *mec-1* and find that the touch sensitivity and attachment functions map to different portions of the molecule.

*mec-1* encodes a 1999 amino acid polypeptide with an N-terminal signal sequence followed by a Kunitz-type domain, two EGF domains, 14 additional Kunitz-type domains, and a C-terminus of 160 amino acids. Nine of the Kunitz domains form a large cluster just prior to the C-terminus. The Kunitz and EGF domains are likely to be protein interaction domains. The only other protein with both of these domains is MEC-9, another extracellular protein needed for touch sensitivity, although a substantial class of *C. elegans* proteins have Kunitz domains interspersed with other extracellular matrix motifs. A *mec-1::gfp* fusion is expressed in the touch cells, several other lateral neurons, and the intestinal muscles.

We have characterized eleven *mec-1* alleles: eight are nonsense mutations or mutations at splice junctions that would lead to premature termination, two are missense mutations affecting cysteines in the last Kunitz domain, and one is a Tc1 insertion 100 or so amino acids from the C terminus (and after the EGF and Kunitz domains). The last three mutations and two of the nonsense mutations causing termination in the next to last Kunitz domain result in touch insensitive animals whose touch cells are normally engulfed. By looking at the phenotype caused by other nonsense mutations in a *smg-5* background, which presumably allows for normal production of truncated proteins, we have found two additional nonsense mutations that permit normal engulfment of the touch cell processes. These mutations suggest that engulfment requires the N-terminal region through the sixth Kunitz domains, but not the large C-terminal cluster of Kunitz domains. Thus, the MEC-1 protein has a C-terminal region that is essential for mechanosensory function but not for attachment and engulfment of the touch cell processes.