

HISTAMINE: A POSSIBLE NEUROMODULATOR IN *C. ELEGANS*

Melissa Hunter-Ensor, Bob Horvitz

HHMI, Dept. Biology, MIT, Cambridge, MA 02139

Many invertebrates use neuromodulators such as histamine to achieve behavioral flexibility. Histidine decarboxylase is a biosynthetic enzyme that synthesizes histamine from the amino acid histidine. We have identified a gene that encodes a putative L-aromatic amino acid decarboxylase (*adc-1*) similar to human and *Drosophila melanogaster* histidine decarboxylases. To identify *adc-1* expressing cells we generated several P_{*adc-1*}::*gfp* transcriptional fusions. We observed GFP expression in the AIA interneurons and the HSN neurons, as well as in a neuron within the ventral ganglion. Using antibodies against histamine, we identified histamine-like immunoreactivity in adult *C. elegans*. This histamine-staining appears to colocalize with the anti-GFP staining of P_{*adc-1*}::*gfp* expressing worms. We will generate antibodies against bacterially-expressed ADC-1 fusion proteins to aid in our identification of *adc-1* expressing cells.

Because ADC-1 is similar to dopa decarboxylase, a biosynthetic enzyme required for serotonin and dopamine synthesis, we tested whether *adc-1* mutants are defective in dopamine or serotonin biosynthesis. Immunocytochemistry with an anti-serotonin antibody demonstrated that *adc-1* worms synthesize serotonin. Dopamine levels, which we assayed using the method of formaldehyde-induced fluorescence, also appeared normal in *adc-1* animals.

To analyze the function of *adc-1* we obtained three independent deletion mutations in the *C. elegans adc-1* gene. These deletions, which were generously provided by M. Dong and M.R. Koelle, perturb coordination between the head and body during backward movement. Specifically, while wild-type worms move backwards in a smooth sinusoidal wave, *adc-1* mutants wag their noses back and forth during reversals. We plan to define the neural circuit involved in this behavior and to determine if histamine is synthesized by ADC-1.