

REGULATION OF THE NK-2 HOMEODOMAIN GENE IN THE DEVELOPING NERVOUS SYSTEM. Mellerick, D., Nakayama, K., Nakayama, N., Kim, Y., Webber, K., Lad, R., and Nirenberg, M.; Laboratory of Biochemical Genetics, National Heart, Lung, and Blood Institute, NIH, Bethesda, Maryland.

Nuclei in the ventral half of the *Drosophila* ventrolateral neurogenic anlage and in the procephalic region initially express NK-2 in late stage 4/early stage 5 embryos. These nuclei give rise to subsets of NK-2 positive neuroectodermal cells, neuroblasts, ganglion mother cells (GMC), and neurons in the subesophageal ganglion, ventral nerve cord, stomatogastric nervous system and some cephalic ganglia. NK-2 mRNA also is expressed in the anterior and posterior midgut primordia. Later in development, NK-2 is detected in the PNS. Initially, NK-2 is expressed in a fairly uniform horizontal stripe, about 7 nuclei in width, on each side of the embryo that extends from 0 to 90% EL. During gastrulation, the horizontal stripe of NK-2 positive cells is subdivided into 12 vertical stripes due to decreases in NK-2 mRNA in some cells. As development proceeds NK-2 expression decreases in additional cells resulting in the formation of 2 clusters of NK-2 positive neuroectodermal cells per hemisegment adjacent to the mesectoderm in stage 9 or 10 embryos. Predominantly medial neuroblasts segregate from these clusters and continue to express NK-2 in GMC and neuronal progeny.

Genes that affect NK-2 expression were identified by *in situ* hybridization in various mutant backgrounds. In *snail* mutants, the developmental fate of mesodermal precursor cells was changed to cells that expressed the NK-2 gene, while in *twist/snail* double mutants, cells that develop as mesoderm ~~and~~ mesectoderm in wild type embryos expressed NK-2, as well as ventral neuroectodermal cells. In *single-minded* mutants, which lack mesectodermal cells, NK-2 expressing neuroectodermal cells, neuroblasts, and their progeny were detected at the ventral midline. A similar pattern of NK-2 expression was detected in *E(sp1^D)m8* mutants. These results suggest that NK-2 is activated in the ventral 45% of the embryo, presumably by dorsal, but is not expressed in mesoderm due to repression by *snail*, or in mesectoderm due to repression by *single-minded* and *m8* protein.

snail is expressed in neuroblasts, which should repress activation of the NK-2 gene by dorsal. The 5'-flanking region of the NK-2 gene contains many binding sites for NK-2 protein, which suggests that NK-2 protein may be required to maintain NK-2 gene expression (Wang et al, these abstracts). Putative sites for dorsal, *snail*, and *m8* overlap, or are adjacent to, many NK-2 protein binding sites. These results suggest that the NK-2 gene receives and integrates information from the ventral-dorsal and anterior-posterior gradients of gene regulators to generate an alternating pattern of clusters of neuroectodermal cells that are precursors of different types of neuroblasts.