REGULATION OF THE NK-2 HOMEOBOX 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, stomatagastric 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(spl^{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.