Genetic Mechanisms of Early Neurogenesis in *Drosophila melanogaster*

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**Abstract**

The neurogenic ectoderm of *Drosophila melanogaster* consists of the ventral neuroectoderm and the procephalic neuroectoderm. It is hypothesized that epidermal and central neural progenitor cells separate from each other in three steps: conference on the neuroectodermal cells the capability of producing neural or epidermal progenies, separation of the two classes of progenitor cells, and specification of particular types of neuroblasts and epidermoblasts. Separation of neuroblasts and epidermoblasts is controlled by proneural and neurogenic genes. *Delta* and *Notch* serve as mediators of direct protein-protein interactions. E(SPL)-C inhibits neurogenesis, creating epidermal cells. The achaete-scute complex (AS-C) controls the commitment of nonoverlapping populations of neuroblasts and leads the development of neuroectodermal cells as neuroblasts.

**Index Entries:** *Drosophila melanogaster; Delta; Notch; E(SPL)-C; AS-C.*

**Introduction**

In insects, the cells of the central nervous system (CNS) are generated by the proliferation of progenitor cells called neuroblasts, which develop from a special neurogenic region of the ectoderm. In *Drosophila melanogaster*, the neurogenic ectoderm consists of two parts, the ventral neuroectoderm, from which the ventral cord and the subesophageal ganglion will develop, and the procephalic neuroectoderm, from which the brain hemispheres emerge. Both regions give rise to neural progenitor cells; however, whereas the cells of the ventral neuroectoderm have to decide between developing either as neuroblasts or as epidermoblasts (progenitor cells of the epidermis), there is no clear picture as to how the procephalic neuroectoderm is organized and how neuroblasts develop from this region (Hartenstein and Campos-Ortega, 1984; Technau and Campos-Ortega, 1985; Jürgens et al., 1986; Stüttem and Campos-Ortega, 1991). Accordingly, this review will deal with the ventral neuroectoderm only.

In insects, the sensory organs develop from special cells called sensory organ mother cells, which originate within the epidermis in a pro-
cess analogous to that of the segregation of the neuroblasts. A hypothesis has been formulated to account for the development of the sensory organ mother cells in the epidermis of *Drosophila* (Ghysen and Dambly-Chaudière, 1989; ref. to Ghysen et al., 1993 for a recent review). Appropriately modified, this hypothesis can also be applied to the separation of neuroblasts and epidermoblasts in the neuroectoderm. The hypothesis proposes a sequence of three steps to explain how epidermal and central neural progenitor cells separate from each other. In the first step, all cells of the neuroectoderm acquire the capability to develop as neuroblasts, whereby contiguous groups of about four to five cells, so-called proneural clusters, are each enabled to give rise to a particular type of neuroblast. In the second step, one cell in each group is singled out by intervening neuralizing signals and segregates into the space between ectoderm and mesoderm to develop as a particular type of neuroblast. In the third step, the neuroblast sends signals to the surrounding cells preventing them from following a neural fate and permitting them to assume an epidermal fate. Therefore, three operations are included in this scheme; one confers on the neuroectodermal cells the capability to produce neural or epidermal progenies, another permits the separation of the two classes of progenitor cells, and the third specifies particular types of neuroblasts and epidermoblasts.

**Genetics of Early Neurogenesis**

The correct separation of neuroblasts and epidermoblasts is controlled by two groups of genes, the neurogenic and the proneural genes, the products of which form a complex genetic network (Table 1). Poulson (1937) called Notch a “neurogenic” gene following the convention in *Drosophila* genetics of naming a gene according to the phenotype of the mutation that leads to its discovery. Accordingly, other genes that cause the same embryonic phenotype as Notch have also been called neurogenic (Lehmann et al., 1981, 1983; Jiménez and Campos-Ortega, 1982). However, the functions of neurogenic genes promote epidermal development. Contrarily, “proneural” are genes whose functions promote neural development (Ghysen and Dambly-Chaudière, 1989, 1990; Romani et al., 1989). With respect to CNS development, the members of the achaete-scute complex (AS-C) and ventral nervous system condensation defective (vnd), and probably other as yet unidentified genes (Jiménez and Campos-Ortega, 1979, 1987, 1990; White, 1980; White et al., 1983) are proneural genes.

Evidence from various kinds of genetic analyses indicates that the neurogenic loci are linked in a chain of epistatic relationships, in which the E(spl)-C is the last link (Vässin et al., 1985; de la Concha et al., 1988; Shepard et al., 1989; Brand and Campos-Ortega, 1990). Hence, the function of each of these genes is dependent on that of another member of the group and, consequently, the function of the entire chain is perturbed if any of the links is missing. Loss-of-function of any of the neurogenic genes causes most ectodermal cells to develop as neuroblasts. Neuralization of the ectoderm of neurogenic mutants follows the pattern of neuroblast segregation in the wild-type and proceeds in pulses (Campos-Ortega and Haenlin, 1992). In the mutants, all the neuroectoderm cells from which neuroblasts normally segregate at each pulse take on neural fate until, in mid-stage 11, all cells in the neuroectoderm have adopted neural fate. Regions from which larval sensory organs develop also exhibit a high proportion of neural cells (Hartenstein and Campos-Ortega, 1986; Ghysen and Dambly-Chaudière, 1990; Goriely et al., 1991). Therefore, the wild-type functions of the neurogenic genes are formally required to suppress neural development of a large fraction of ectodermal cells and allow them to develop as epidermoblasts. The basis for this is a signal chain, the links of which are encoded by the neurogenic genes.

Embryos homozygous for loss-of-function mutations in the proneural genes exhibit a highly hypoplastic CNS and severe defects in the PNS (Jiménez and Campos-Ortega, 1979,