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The Development of Differential mabQ113-Immunoreactivity in the Rat Habenular Complex

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PLIOPLYS, A. V. AND R. HAWKES. *The development of differential mabQ113-immunoreactivity in the rat habenular complex.* BRAIN RES BULL **18**(1) 19–24, 1987.—Monoclonal antibody mabQ113 selectively labels a subset of Purkinje cells which are arranged in parasagittal bands throughout the vermis and hemispheres of the rat cerebellar cortex. No other cerebellar cell types are immunoreactive. By contrast, in the remainder of the brain the mabQ113 epitope is located primarily in glial cells. In general, the glial immunoreactivity is not differentially distributed. An exception is that mabQ113 densely and uniformly stains the lateral habenula (LHb) but gives no labelling of the medial habenula (MHb). During cerebellar development, the mabQ113 epitope is expressed in three stages. Before postnatal day 7 (P7) all Purkinje cells are negative. Secondly, all Purkinje cells become mabQ113+ between P7 and P12. The parasagittal bands are created between P12 and P30 by selective suppression of epitope expression. To explore whether epitope suppression is also responsible for differential staining patterns in other brain regions the ontogenic development of mabQ113 immunoreactivity has been mapped in the habenular complex. Neither the MHb nor the LHb express the mabQ113 epitope prenatally. P1 is the first age at which the LHb is stained. During the next few days the intensity of staining within the LHb steadily increases until the adult pattern is attained at P6. At no time is there expression of the mabQ113 antigen in the MHb. This also confirms that the two classes of habenular astrocytes, mabQ113−/GFAP+ and mabQ113+/GFAP+, are intrinsically different throughout postnatal life.

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AS a crossroads of limbic and striatal interconnections the habenular nuclei play a role in numerous aspects of brain function (reviewed in [38]). Although grouped together, the medial (MHb) and lateral (LHb) habenular nuclei have widespread, largely independent afferent and efferent connections (for the rat see [6, 7, 11, 12, 19, 20, 25, 34, 39]). Numerous biochemical differences between LHb and MHb have also been reported, involving components of the GABAergic [9, 10, 40] and cholinergic [13, 22, 23, 29, 32] pathways as well as several other neurotransmitters [2, 10, 20, 24] and neuropeptides [1, 5, 8, 21, 28, 34, 36, 37]. Recently, a monoclonal antibody, mabQ113, has been found to differentiate sharply between LHb and MHb. The mabQ113 epitope is of especial interest because in the cerebellum it is confined to a subset of Purkinje cells, about 30% of the total, which are clustered into a set of parasagittal bands separated by similar bands of mabQ113-Purkinje cells [15–18, 30]. No other cells in the cerebellum are immunoreactive. By contrast, when mabQ113 immunoreactivity was mapped in the rest of the rat CNS the distribution of reaction product was quite different. In all regions studied, the epitope was found in both neurons and glia, but principally in glial cells, and there was no evidence of a striped or patchy distribution [31]. One region in which the epitope was distributed non-uniformly was the habenular complex. MabQ113 densely and uniformly stained the LHb but did not stain the MHb. The reaction product was associated with the neuropil and electron microscope immunocytochemistry revealed that most staining was astrocytic, although some reaction product was also seen in adjacent neuronal profiles. Therefore, there seems to be a fundamental difference between the expression of the epitope in the cerebellum and the rest of the brain.

In the cerebellum the pattern of development of parasagittal mabQ113+ bands of Purkinje cells is complex. The mabQ113 immunoreactivity appears for the first time at postnatal day 7 (P7) in the Purkinje cells of the posterior lobe vermis. By P12, the immunoreactivity has spread to include Purkinje cells throughout the cerebellar cortex. However, at P12 there is no differentiation between mabQ113+ and mabQ113− bands of cells: all the Purkinje cells are mabQ113+. The parasagittal bands are created between P12 and P30 by the selective suppression of epitope expression in those Purkinje cells destined to become mabQ113− [16]. In view of this pattern of development in the cerebellar cortex,

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