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Mini-Review

Oligodendrocyte development in the spinal cord and telencephalon: common themes and new perspectives

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factor-A gene (encoding one of the known ligands for PDGFRα) (Fruttiger et al., 1999). Taken together, this evidence indicates that PDGFRα$^+$ cells are the major — maybe the only — source of oligodendrocytes in the spinal cord. Recently, several new markers for the oligodendrocyte lineage have been identified. These are the basic helix-loop-helix proteins *Olig1* and *Olig2* (Lu et al., 2000; Zhou et al., 2000) and the high mobility group protein *Sox10* (Kuhlbrodt et al., 1998). Since they are thought to identify the earliest stages of the oligodendrocyte lineage, these markers might provide new insights into oligodendrocyte specification. In this review, we focus on the origin and early development of oligodendrocyte progenitor cells at two different levels of the neuraxis — the telencephalon and spinal cord — and discuss the impact that the new markers may have on our current understanding of oligodendrocyte development.

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2.1. Oligodendrocyte progenitors in both spinal cord and telencephalon have a ventral origin and populate dorsal parts of the neural tube by migration and proliferation

Since oligodendrocytes are evenly distributed throughout the adult CNS, it would be reasonable to suppose that they are produced from all regions of the neuroepithelium. However, there are now several lines of evidence that, in both spinal cord and telencephalon, oligodendrocytes originate from ventral subsets of neuroepithelial precursors.

One line of evidence comes from cell culture experiments. When E14 rat spinal cords are divided into dorsal and ventral halves and the cells from each half are cultured separately, oligodendrocytes develop only in ventral cultures (Warf et al., 1991; Hall et al., 1996). Similarly, cells cultured from the E15 rat ventral telencephalon (striatum) have a much greater oligodendrogenic capacity than those from dorsal telencephalon (cerebral cortex) after short-term culture (Birling and Price, 1998; Tekki-Kessaris et al., 2001) or transplantation into the retina (Kalman and Tuba, 1998). At later stages (E17–18) cells cultured from either the dorsal spinal cord or cerebral cortex readily give rise to numerous oligodendrocytes. Similar experiments have been perfomed with cells from avian spinal cord and forebrain (Orentas and Miller, 1996; Poncet et al., 1996; Pringle et al., 1996, 1998) (N. Tekki-Kessaris, unpublished observations). One interpretation of these results is that, in both forebrain and spinal cord, oligodendrocyte progenitors originate from ventral neuroepithelium and subsequently migrate into dorsal regions. Experiments in vivo with chick-quail chimeras confirm this conclusion (Pringle et al., 1998; Olivier et al., 2000).

Another line of evidence that oligodendrocytes in the spinal cord and forebrain have a ventral origin comes from lineage marker studies in situ. In the spinal cord, PDGFRα$^+$ oligodendrocyte progenitor cells first ap-

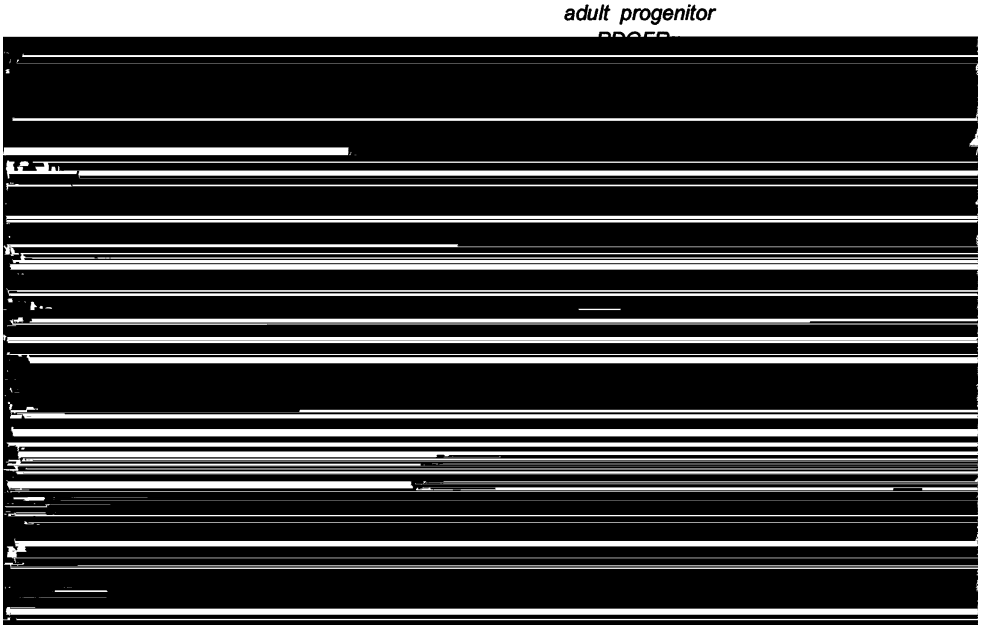

Fig. 1. Illustration of the various stages of oligodendrogenesis. Oligodendrocyte progenitors are specified in the neuroepithelium. Bipolar progenitors subsequently migrate away and proliferate. The majority of progenitors progress through a late progenitor and premyelinating oligodendrocyte stage before maturing into myelinating oligodendrocytes, whereas others persist in the adult CNS as a population of slowly dividing adult progenitor cells. Lineage markers, some of which are stage specific, are shown below.

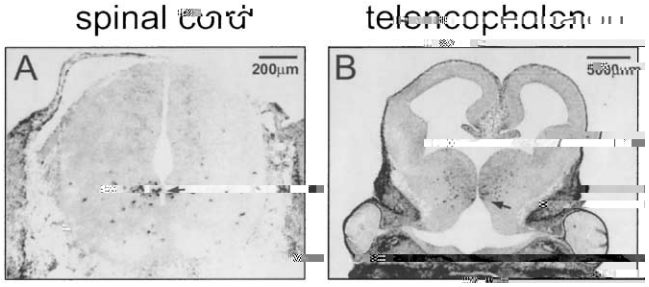

Fig. 2. (A) Transverse section through an E12.5 rat spinal cord; and (B) coronal section through an E12.5 mouse telencephalon showing expression of PDGFRα. In the spinal cord, PDGFRα$^+$ oligodendrocyte progenitors first arise in a ventral region of the neuroepithelium (arrow) and subsequently proliferate and migrate to populate the entire cord. In an analogous manner in the telencephalon PDGFRα$^+$ cells first arise in a ventral region at the boundary between the anterior hypothalamus and the MGE (arrow) and subsequently proliferate and migrate throughout the telencephalon including the cortex.

tors have a ventral origin in the forebrain, just as they do in the spinal cord.

After the initial appearance of PDGFRα$^+$ cells in the ventral spinal cord and telencephalon, these cells soon increase in number and begin to disperse, first through the ventral and then the dorsal spinal cord and telencephalon (Pringle and Richardson, 1993; Tekki-Kessaris et al., 2001) (see Fig. 3). These findings are mirrored in studies using other markers for oligodendrocyte progenitors, such as antibodies against NG2 proteoglycan (Levine and Stallcup, 1987; Stallcup and Beasely, 1987; Nishiyama et al., 1996; Dawson et al., 2000). It is clear from studies in which oligodendrocyte progenitors were labelled at source with DiI in vivo, that they are able to migrate distances of the order of several millimetres during development (Ono et al., 1997). The timing of appearance of PDGFRα$^+$ cells in the dorsal spinal cord and cerebral cortex corresponds to the marked increase in oligodendrogenic capacity of cells from the dorsal spinal cord and cerebral cortex (Warf et al., 1991; Birling and Price, 1998; Kalman and Tuba, 1998; Tekki-Kessaris et al., 2001) (see above). The implication of these findings is that oligodendrocyte progenitors populate the dorsal spinal cord and cerebral cortex by migration from their origins in the ventral spinal cord and anterior hypothalamus, respectively.

The experiments described above do not by them-

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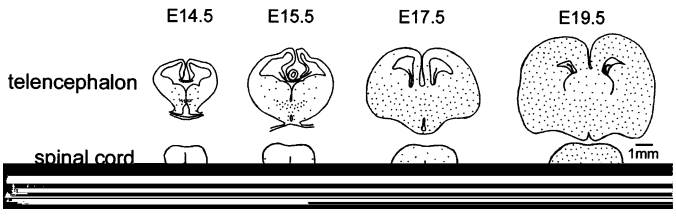

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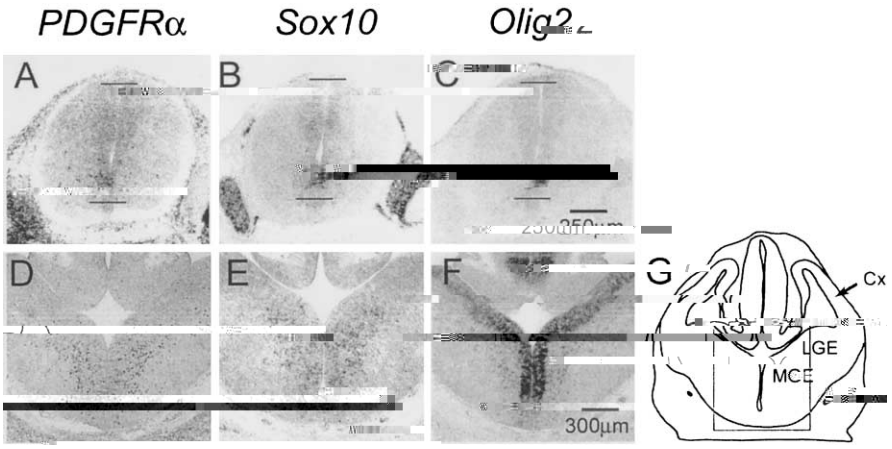
PDGFRα
Sox10
Olig2
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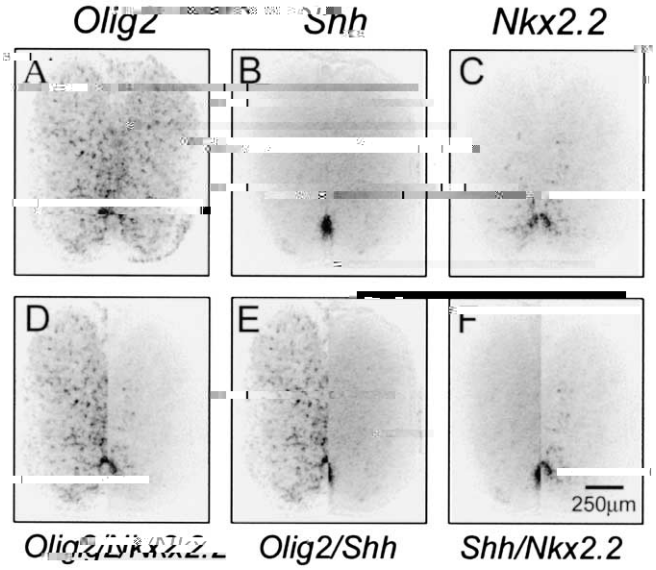
Olig2
Shh
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A
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F
250μm
Olig2/Nkx2.2
Olig2/Shh
Shh/Nkx2.2

determined and it remains possible that they are not oligodendrocyte progenitors but some other type of late-developing cell, for example astrocytes. In the telencephalon too, expression of *Olig2* persists in the ven-

Ono, K., Bansal, R., Payne, J., Rutishauser, U., Miller, R.H., 1995. Early development and dispersal of oligodendrocyte precursors in the embryonic chick spinal cord. Development 121, 1743–1754.

Ono, K., Yasui, Y., Rutishauser, U., Miller, R.H., 1997. Focal ventricular origin and migration of oligodendrocyte precursors into the chick optic nerve. Neuron 19, 283–292.

Orentas, D.M., Miller, R.H., 1996. The origin of spinal cord oligodendrocytes is dependent on local influences from the notochord. Dev. Biol. 177, 43–53.

Orentas, D.M., Hayes, J.E., Dyer, K.L., Miller, R.H., 1999. Sonic hedgehog signalling is required during the appearance of spinal cord oligodendrocyte precursors. Development 126, 2419–2429.

Perez-Villegas, E., Olivier, C., Spassky, N., Poncet, C., Cochard, P., Zalc, B., Thomas, J.-L., Martinez, S., 1999. Early specification of