

CELL SOURCE AND ENVIRONMENTAL SIGNALS REGULATE THE SPECIFICATION OF NEURAL STEM CELLS TO THE OLIGODENDROCYTE LINEAGE

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During development the major classes of neural cells, neurons, astrocytes and oligodendrocytes develop from neural stem cells. Immature cells of the oligodendrocyte lineage express antigens identified by antibodies to GD3 and mAbA2B5. These cells, while termed oligodendrocyte precursor cells (OPCs) are not restricted to an oligodendrocyte fate, however later in development they acquire expression of antigens recognized by mAb O4 and become restricted to the oligodendrocyte lineage. Differentiation of the OPCs is accompanied by expression of the marker of mature oligodendrocytes, galactocerebroside. To determine whether the initial source of NSCs alerted their propensity to generate oligodendrocytes and to define the cues that facilitate the commitment of NSCs to the oligodendrocyte lineage three murine neural stem cell lines from Stem Cell Sciences (UK) Ltd. were tested. Two of the cell lines, mNS-46 and NS-5 were neural stem cell lines derived from embryonic stem cells. By contrast, Cor 1-NS was a neural stem cell line derived from the frontal cortex of embryonic mouse.

A battery of potential OPC inducing signals including combinations of EGF, bFGF, PDGF-AA, NT-3, BMP-4, SHH, and N2 supplement(containing T3 and T4) were tested, however under the conditions utilized were not effective at increasing the proportion of O4+ cells in the cultures. By contrast, a published protocol on the tripotential differentiation capability of adherent neural stem cells resulted in a significant increase in the proportion of NS-5 cells that differentiated into O4+ cells.¹ We used the medium RHB-A[®] from Stem Cell Sciences (UK) Ltd. for our experiments and after 8 days of treatment, cultures from two of the cell lines contained between 25% and 40% O4+ cells while the third cell line had less than 1% O4+ cells. The two cell lines that differentiated with high proportion of O4+ cells were the neural stem cell lines derived from embryonic stem cells and by contrast, the third line was the neural stem cell line derived from the frontal cortex.

These data suggest that the origin or derivation of neural stem cells may influence their capacity to generate cells committed to the oligodendrocyte lineage and that environmental cues combined with intrinsic cues regulate neural cell fate selection.

¹Glaser T, Pollard SM, Smith A, Brüstle O (2007) Tripotential Differentiation of Adherently Expandable Neural Stem (NS) Cells. PLoS ONE 2(3):e298. doi:10.1371/journal.pone.0000298