Differentiation of neural stem cells into oligodendrocytes

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Cell transplantation has been suggested as a therapy to replace lost oligodendrocytes and to induce remyelination in MS. Recently, candidate sources for such cell grafts have become available: neural stem cells. Neural stem cells (NSC) are multipotent stem cells characterised by their potential for self-renewal and the ability to differentiate into neurons, astrocytes and oligodendrocytes. Controlled in vitro differentiation of NSC's into oligodendrocytes, however, is still a major challenge. Our research goal is to develop a differentiation procedure for NSC's yielding a pure population of oligodendrocyte precursor cells (OPC's) that can be tested for their remyelinating efficiency in animal models for MS.
NSC's were isolated from mice embryonic brain (E14), multiplied in medium containing bFGF and EGF and subsequently transferred to a culture medium without mitogenic agents allowing differentiation. To stimulate the preferential differentiation into OPC's, NSC's were transfected with genes that encode for transcription factors (Olig1, Olig2, Nkx2.2) known to initiate the generation of oligodendrocytes during embryogenesis. The genes were transfected with a nonviral transfection system, Nucleofector (Amaxa). To examine the induction of OPC differentiation by the forced expression of these transcription factors, the transfected NSC's were cultured during a period of 8 days. OPC's and other differentiated neural cells were identified by immunohistochemistry using antibodies directed against marker proteins for OPC's (O_4, A2B5, H8) for mature oligodendrocytes (GALC, MBP), for astrocytes (GFAP) and for neurons (MAP2).
First results showed that the singular transfection of the Olig1 gene can initiate the differentiation of OPC's but is insufficient to induce their differentiation into fully maturated oligodendrocytes. Presumably co-transfection with other "oligodendrogenic" transcription factors are required for full differentiation and maturation in vitro. In our presentation we will report on the efficiency of OPC differentiation induction after transfection with (a combination of) Olig2, Nkx2.2 and Olig1 genes.

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