

**Importance of MAP kinase pathways in neuronal and dopaminergic differentiation of mesencephalic neural progenitor cells**

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**Summary:** Fetal mesencephalic neural stem cells (NSC) derived from both human and rodent brain are reported to differentiate into mature and functional dopaminergic neurons. Interleukin (IL)-1 is the essential factor for induction of dopaminergic differentiation of mesencephalic NSCs in vitro leading to specific up-regulation of dopaminergic key fate-determining transcription factors, such as Nurr1 and Ptx3. The exact intracellular molecular events and possible cross-talk between different signaling pathways are largely unknown. The aim of the proposed study is therefore to characterize the intracellular IL-1 receptor type I pathways and possible cross talk between different pathways. In particular the influence of different members of the MAP kinase pathway (JUN kinase, p38-MAP kinase, ERK1/2) shall be illuminated. The understanding of the machinery of dopaminergic differentiation is the basic requirement for both the establishment of stable cell sources for cell replacement in Parkinson's disease (PD) and to influence (stimulate) endogenous regeneration in PD. The findings are for the development of regenerative therapy-strategies of PD, like for example progenitor-cell-based neurotransplantation, of outstanding importance.