

Primary cell culture from human striatal primordium. Contribution to research on neuronal plasticity

Erica Sarchielli, Mirca Marini, Stefano Ambrosini, Annamaria Morelli, Gabriella B. Vannelli

Department of Experimental and Clinical Medicine, Anatomy and Histology Section, University of Florence, Florence, Italy

Throughout fetal life, striatal neurons originated in the ganglionic eminence from a population of dividing stem cells. Little is known about the molecular mechanisms that regulate the activation, self-renewal and differentiation of striatal neuronal precursors. In order to identify the regulatory mechanisms controlling striatal cell neurogenesis and differentiation, we have recently isolated and propagated in vitro primary cell cultures from the human fetal striatal primordium (1). These cells express both neuronal and striatal properties, and are responsive to BDNF and FGF2. In this study, we found that human striatal precursor (HSP) cells are a mixed population mainly constituted of neuronal-restricted progenitors and striatal neurons (DARPP32-, GAD1-expressing cells) and neural/stem cells, which under specific in vitro differentiating conditions not only generate neurons, astrocytes and oligodendrocytes, but also possess the ability of osteogenic differentiation. We also observed that BDNF and FGF2 exert different effects on HSP depending on the differentiation state of these cells. In fact, both neurotrophins promote cell proliferation, migration and the expression of neural stem/progenitor markers in undifferentiated HSP cells, while they stimulate neuritogenesis in the neuronal differentiated component as demonstrated after specific neuronal induction. We have previously reported that striatal primordium from human fetus was able to grow into the brain of Huntington's disease (HD) patients and that this process was associated with metabolic change and some clinical benefit (2,3). Our results add new insight into the developmental processes of human fetal striatal grafts in HD and, in addition, have implications for cell based transplantation approaches in the CNS.

References

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Keywords

Huntington's disease, fetal graft, striatal neuroblasts, neurotrophins.