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II.

06/17/2008 - Adult Human Dental Pulp Stem Cells Differentiate Towards Functionally Active Neurons Under Appropriate Environmental Cues

Stem Cells: First published online May 22, 2008

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Human adult dental pulp stem cells (DPSC) reside within the perivascular niche of dental pulp and are thought to originate from migrating cranial neural crest (CNC) cells. During embryonic development, CNC cells differentiate into a wide variety of cell types including neurons of the peripheral nervous system. Previously, we have demonstrated that DPSC derived from adult human third molar teeth differentiate into cell types reminiscent of CNC embryonic ontology. We hypothesized that DPSC exposed to the appropriate environmental cues would differentiate into functionally active neurons. The data demonstrated that ex vivo expanded human adult DPSC responded to neuronal inductive conditions both in vitro and in vivo. Human adult DPSC, but not human foreskin fibroblasts (HFF) acquired a neuronal morphology, and expressed neuronal specific markers at both the gene and protein levels. Culture expanded DPSC also exhibited the capacity to produce a sodium current consistent with functional neuronal cells when exposed to neuronal inductive media. Furthermore, the response of human DPSC and HFF to endogenous neuronal environmental cues was determined in vivo using an avian xeno-transplantation assay. DPSC expressed neuronal markers and acquired a neuronal morphology following transplantation into the mesencephalon of embryonic day two chicken embryo, while HFF maintained a thin spindle fibroblastic morphology. We propose that adult human DPSC provide a readily accessible source of exogenous stem/precursor cells which have the potential for use in cell therapeutic paradigms to treat neurological disease.

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Adult tissues contain highly proliferative, clonogenic cells that meet criteria of multipotent stem cells and are potential sources for autologous reparative and reconstructive medicine. We demonstrated that human dental pulp contains self renewing human dental pulp stem cells (hDPSCs) capable of differentiating into mesenchymal-derived odontoblasts, osteoblasts, adipocytes, chondrocytes and striated muscle, and interestingly, also into non-mesenchymal melanocytes. Furthermore, we showed that hDPSC cultures include cells with the label-retaining and sphere-forming abilities, traits attributed to multipotent stem cells, and provide evidence that these might be multipotent neural crest stem cells.