Human neural progenitor cells generated from induced pluripotent stem cells can survive, migrate, and integrate in the rodent spinal cord.

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Public Summary:
We have previously shown that human neural progenitor cells (NPCs) transplanted into the brain, spinal cord or retina in animal models of disease can survive, migrate, and provide beneficial effects. NPCs can be isolated from different regions of the fetal human brain for expansion in culture and differentiation into neurons and astrocytes. However, human fetal tissue has problematic issues including limited sources and ethical concerns that create a pressing need for alternative sources. Here we describe a new and limitless source of NPCs derived from human induced pluripotent stem cells (iPSCs), which originate from reprogrammed adult somatic cells. iPSCs offer limitless cellular expansion and banking, differentiation into almost any cellular lineage, and an unprecedented opportunity for autologous transplantation. Here, we report a new protocol for the transformation of adherent iPSCs into free-floating NPC spheres (EZ spheres) that are easy to maintain and expand indefinitely using the chopping method. These EZ spheres could be differentiated towards NPC spheres with a spinal cord phenotype. Suspension cultures of NPCs derived from human iPSCs or fetal tissue have similar characteristics, though they were not similar when grown as adherent cells. In addition, iPSC-derived NPCs survived grafting into the spinal cord of athymic nude rats with no signs of overgrowth and with a very similar profile to human fetal-derived NPCs. These results suggest that human iPSC-derived NPCs behave like fetal-derived NPCs and could thus be a novel and valuable alternative for cellular regenerative therapies of neurological diseases.

Scientific Abstract:
Transplantation of human neural progenitor cells (NPCs) into the brain or spinal cord to replace lost cells, modulate the injury environment or create a permissive milieu to protect and regenerate host neurons is a promising therapeutic strategy for neurological diseases. Deriving NPCs from human fetal tissue is feasible, though problematic issues include limited sources and ethical concerns. Here we describe a new and abundant source of NPCs derived from human induced pluripotent stem cells (iPSCs). A novel chopping technique was used to transform adherent iPSCs into free-floating spheres that were easy to maintain and were expandable (EZ spheres) (Ebert et al., 2013). These EZ spheres could be differentiated towards NPC spheres with a spinal cord phenotype using a combination of all-trans retinoic acid (ATRA) and epidermal growth factor (EGF) and fibroblast growth factor-2 (FGF-2) mitogens. Suspension cultures of NPCs derived from human iPSCs or fetal tissue have similar characteristics, though they were not similar when grown as adherent cells. In addition, iPSC-derived NPCs (iNPCs) survived grafting into the spinal cord of athymic nude rats with no signs of overgrowth and with a very similar profile to human fetal-derived NPCs (fNPCs). These results suggest that human iNPCs behave like fNPCs and could thus be a valuable alternative for cellular regenerative therapies of neurological diseases. J. Comp. Neurol., 2014. (c) 2014 Wiley Periodicals, Inc.

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