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**Glial cell line-derived neurotrophic factor-secreting human neural progenitors show long-term survival, maturation into astrocytes, and no tumor formation following transplantation into the spinal cord of immunocompromised rats.**

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**Public Summary:**

The human fetal brain contains neural progenitor cells (NPCs) that can be isolated and grown in culture. NPCs can be used for cellular gene therapy by genetically modifying them to release a therapeutic drug, for instance growth factors. In this study, human NPCs were genetically engineered to secrete glial cell line-derived neurotrophic factor (GDNF), a powerful growth factor that has been shown to have a beneficial effects on neurological diseases. These GDNF-secreting NPCs were expanded to produce a research-grade product using the same protocols developed for large-scale, clinical-grade production campaigns. In this study, we showed that the hNPCs survived long-term (229 days) following transplantation into the spinal cord of rats and continued to secrete GDNF. The cells had an overall decrease in proliferation after transplantation, preventing tumor formation. A subpopulation of NPCs matured overtime to become astrocytes, one type of cell in the brain that has been shown to play an important role in neurodegenerative diseases like amyotrophic lateral sclerosis. Together these data show that genetically engineered NPCs are safe for transplantation and could be useful as a source of cells for long-term delivery of both GDNF and astrocytes to the damaged central nervous system.

**Scientific Abstract:**

Human neural progenitor cells (hNPCs) derived from the fetal cortex can be expanded in vitro and genetically modified through lentiviral transduction to secrete growth factors shown to have a neurotrophic effect in animal models of neurological disease. hNPCs survive and mature following transplantation into the central nervous system of large and small animals including the rat model of amyotrophic lateral sclerosis. Here we report that hNPCs engineered to express glial cell line-derived neurotrophic factor (GDNF) survive long-term (7.5 months) following transplantation into the spinal cord of athymic nude rats and continue to secrete GDNF. Cell proliferation declined while the number of astrocytes increased, suggesting final maturation of the cells over time in vivo. Together these data show that GDNF-producing hNPCs may be useful as a source of cells for long-term delivery of both astrocytes and GDNF to the damaged central nervous system. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 License, where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially. <http://creativecommons.org/licenses/by-nc-nd/3.0>.

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