

Glial cell line-derived neurotrophic factor

Glial cell line-derived neurotrophic factor (GDNF) is a protein that, in humans, is encoded by the GDNF gene.

GDNF is a small protein that potently promotes the survival of many types of neurons.

It signals through GFR α receptors, particularly GFR α 1. It is also responsible for the determination of spermatogonia into primary spermatocytes, i.e. it is received by RET proto-oncogene (RET) and by forming gradient with SCF it divides the spermatogonia into two cells. As the result there is retention of spermatogonia and formation of spermatocyte.

Dysfunctional **astrocytes** may contribute to **Amyotrophic lateral sclerosis** and **glial cell line-derived neurotrophic factor** (GDNF) can be protective. Baloh et al. showed that human **neural progenitor cells** transduced with GDNF (CNS10-NPC-GDNF) differentiated to astrocytes protected spinal motor neurons and were safe in animal models. CNS10-NPC-GDNF were transplanted unilaterally into the lumbar **spinal cord** of 18 ALS participants in a phase 1/2a study (NCT02943850). The primary endpoint of safety at 1 year was met, with no negative effect of the transplant on motor function in the treated leg compared with the untreated leg. Tissue analysis of 13 participants who died of disease progression showed **graft** survival and GDNF production. Benign **neuromas** near delivery sites were common **incidental findings** at post-mortem. This study shows that one administration of engineered neural progenitors can provide new support cells and GDNF delivery to the ALS patient spinal cord for up to 42 months post-transplantation ¹⁾.

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Baloh RH, Johnson JP, Avalos P, Allred P, Svendsen S, Gowing G, Roxas K, Wu A, Donahue B, Osborne S, Lawless G, Shelley B, Wheeler K, Prina C, Fine D, Kendra-Romito T, Stokes H, Manoukian V, Muthukumaran A, Garcia L, Bañuelos MG, Godoy M, Bresee C, Yu H, Drazin D, Ross L, Naruse R, Babu H, Macklin EA, Vo A, Elsayegh A, Tourtellotte W, Maya M, Burford M, Diaz F, Patil CG, Lewis RA, Svendsen CN. Transplantation of human neural progenitor cells secreting GDNF into the spinal cord of patients with ALS: a phase 1/2a trial. Nat Med. 2022 Sep 5. doi: 10.1038/s41591-022-01956-3. Epub ahead of print. PMID: 36064599.

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