LINKS FOR WEB GENE THERAPY

OMIM: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>
 Parkinson disease: <http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=168600>

Huntington disease: <http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=143100>

Clive Svendsen's laboratory: <http://www.waisman.wisc.edu/scrp/svendsen.html>

Proof of delivery

Treating any disorder of the brain poses a special challenge owing to the difficulty of getting drugs across the blood–brain barrier. New work shows that implanting the brains of animal models with genetically engineered neural progenitor cells (NPC) reduces some symptoms of **Parkinson disease**, and might benefit other neurodegenerative diseases.

Parkinson disease affects 1.5 million people in the United States and is caused by the irreversible loss of dopamine-producing neurons, which coordinate muscle movement and balance. We know that some molecules — such as glial-cell-line-derived neurotrophic factor, or GDNF — can promote the regeneration of lost neurons, but delivering these agents to the brain by using viruses as carriers, or by injecting the molecule straight into the brain, could pose a risk to health or be inefficient. The group, led by Soshana Behrstock and Clive Svendsen, has hit on the different strategy of modifying cells to express GDNF. The engineered cells — human NPCs that were derived from fetal brains — were then transferred into the area of the brain in which GDNF was needed in parkinsonian rats and ageing rhesus monkeys.

Remarkably, the protein produced by the cells remained active for up to 3 months and was transported to the substantia nigra, the brain region that degenerates in Parkinson disease. In addition, the cells migrated across the affected region and led to increased fibre sprouting and survival of the host neurons.

Given that the effects of GDNF are not specific to the cells that are damaged in Parkinson disease it is

likely that these same cells can be used to treat other disorders, such as **Huntington disease** and amyotrophic lateral sclerosis (ALS). Whether this therapy can be attempted in humans will depend on devising a way to control the expression of GDNF in the engineered cells — in particular, to shut it off. The authors accomplished protein regulation in culture, but shut-off in animals proved more difficult and is being addressed in new experiments. Nevertheless, this work provides convincing evidence that stem cells are a valid route for targeting drugs to less accessible tissues such as the brain in a safe and efficient way.

Tanita Casci

ORIGINAL RESEARCH PAPER

Behrstock, S. et al. Human neural progenitors deliver glial cell line-derived neurotrophic factor to parkinsonian rodents and aged primates. *Gene Ther.* 15 December 2005 (doi:10.1038/sj.gt.3302679)

FURTHER READING Jakel, R. J. Using human neural stem cells to model neurological disease. *Nature Rev. Genet.* 5, 136–144 (2004) | Svendsen, C. N. & Langston, J. W. Stem cells for Parkinson disease and ALS: replacement or protection? *Nature Med.* 10, 224–225 (2004)

WEB SITE

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