

A noninvasive avenue for Parkinson's disease gene therapy

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Researchers at Northeastern University in Boston have developed a gene therapy approach that may one day stop Parkinson's disease (PD) in its tracks, preventing disease progression and reversing its symptoms. The novelty of the approach lies in the nasal route of administration and nanoparticles containing a gene capable of rescuing dying neurons in the brain. Parkinson's is a devastating neurodegenerative disorder caused by the death of dopamine neurons in a key motor area of the brain, the substantia nigra (SN). Loss of these neurons leads to the characteristic tremor and slowed movements of PD, which get increasingly worse with time. Currently, more than 1% of the population over age 60 has PD and approximately 60,000 Americans are newly diagnosed every year. The available drugs on the market for PD mimic or replace the lost dopamine but do not get to the heart of the problem, which is the progressive loss of the dopamine neurons.

The focus of Dr. Barbara Waszczak's lab at Northeastern University in Boston is to find a way to harvest the potential of glial cell line-derived neurotrophic factor (GDNF) as a treatment for PD. GDNF is a protein known to nourish dopamine neurons by activating survival and growth-promoting pathways inside the cells. Not surprisingly, GDNF is able to protect dopamine neurons from injury and restore the function of damaged and dying neurons in many animal models of PD. However, the action of GDNF is limited by its inability to cross the blood-brain barrier (BBB), thus requiring direct surgical injection into the brain. To circumvent this problem, Waszczak's lab is investigating intranasal delivery as a way to bypass the BBB. Their previous work showed that

intranasal delivery of GDNF protects dopamine neurons from damage by the [neurotoxin](#), 6-hydroxydopamine (6-OHDA), a standard [rat model](#) of PD.

Taking this work a step further, Brendan Harmon, working in Waszczak's lab, has adapted the intranasal approach so that cells in the brain can continuously produce GDNF. His work utilized [nanoparticles](#), developed by Copernicus Therapeutics, Inc., which are able to transfect brain cells with an expression plasmid carrying the gene for GDNF (pGDNF). When given intranasally to rats, these pGDNF nanoparticles increase GDNF production throughout the brain for long periods, avoiding the need for frequent re-dosing. Now, in new research presented on April 20 at 12:30 pm during Experimental Biology 2013 in Boston, MA, Harmon reports that intranasal administration of Copernicus' pGDNF nanoparticles results in GDNF expression sufficient to protect SN dopamine neurons in the 6-OHDA model of PD.

Waszczak and Harmon believe that intranasal delivery of Copernicus' nanoparticles may provide an effective and non-invasive means of GDNF gene therapy for PD, and an avenue for transporting other gene therapy vectors to the brain. This work, which was funded in part by the Michael J. Fox Foundation for Parkinson's Research and Northeastern University, has the potential to greatly expand treatment options for PD and many other central nervous system disorders.

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