Focused Ultrasound Enhancement of an Intranasal Gene Therapy for Parkinson's Disease

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Opportunity

We have developed an intranasal gene therapy approach with the potential to stop Parkinson’s disease (PD) progression, and possibly reverse its symptoms. Our lab found a way to harvest the potential of glial cell line-derived neurotrophic factor (GDNF) as a treatment for PD. GDNF is a protein that activates survival and growth-promoting pathways in dopamine neurons, which die in PD, and restores the surviving neurons to function. However, GDNF does not cross the blood-brain barrier (BBB), so its use would require surgical injection into the brain. We use intranasal delivery of DNA nanoparticles (NPs) encoding GDNF as a way to both bypass the BBB and generate continuous production of GDNF within the brain. After intranasal administration of these DNA NPs, developed by Copernicus Therapeutics, Inc., GDNF levels peak at 1 week and persist over at least 6 months. We also showed that intranasal DNA NPs primarily transfect pericytes, cells lying along the outside of blood vessels throughout the brain.

Our current studies are determining whether it is possible to use focused ultrasound (FUS) to enrich or target delivery of intranasally administered DNA NPs to brain regions affected in PD. FUS causes temporary and localized disruption of the BBB, allowing enhanced delivery of therapeutic agents to desired regions in brain. We found that FUS increased GDNF in the sonicated right hemisphere and resulted in deeper penetration and more cell types producing GDNF than in non-sonicated areas. FUS + intranasal GDNF DNA NPs offer an exciting new treatment approach for early-stage PD.

Approach

3-part approach:

1. Gene therapy (DNA plasmid nanoparticles)
2. Intranasal delivery (to bypass the BBB and avoid systemic exposure)
3. Focused Ultrasound (to enhance delivery to target areas)

Impact

Value Proposition:

The unique feature about my research is that it combines three approaches (gene therapy, intranasal delivery, and focused ultrasound) to provide a long-term, completely noninvasive means of targeting therapeutics to brain.

This addresses the problem of: delivering a gene therapy to the brain for treatment of CNS disorders, such as Parkinson’s disease, without resorting to invasive surgical techniques and avoiding peripheral side effects.

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