Neuro-Avatar: A reverse translational model of an ongoing cell therapy clinical trial for Parkinson's disease

Andrew Welleford [1] • Nader El Seblani, MD [1] • Craig van Horne, MD, PhD [2] •

Jorge Quintero, PhD [1] • Francois Pomerleau, MS [1] • Greg Gerhardt, PhD [1]

[1]Neuroscience, University of Kentucky • [2]Neurosurgery, University of Kentucky

Abstracts will be considered for both poster and platform presentations

Movement disorders

Currently two clinical trials (NCT01833364 and NCT02369003) are underway which feature the implantation of autologous peripheral nerve grafts to the brain (targeted to the Substantia Nigra, Nucleus Basalis of Meynert, or Putamen) in combination with Deep Brain Stimulation (DBS) for the treatment of patients with Parkinson's disease. This nerve tissue is harvested from the sural nerve, a cutaneous sensory nerve located in the lateral ankle, of patients undergoing DBS surgery. The nerve receives a conditioning injury 14 days before grafting, and samples are collected from the pre-conditioned and post-conditioned nerve. As of 9/3/18, 60 patients have received DBS plus the graft procedure.
RNA sequencing of these nerve samples shows transcriptome changes consistent with the expected pro-regenerative changes of transdifferentiated repair phenotype Schwann cells. However, the neurobiology of the graft within the brain, the regenerative activity of the pre vs post-lesioned nerve, and the survival of grafted tissue have not been examined.
In order to address these questions, this study aimed to develop an animal model of the grafting procedure using the same human tissue grafted into patients with Parkinson's disease. Athymic nude (Hsd:RH-Foxn1rnu) rats were stereotaxically implanted with segments of human peripheral nerve (pre-conditioned or post-conditioned) into the dorsal striatum. Each animal received a unilateral graft with a contralateral sham insertion. Two weeks or six months post-implant the brains of these animals were processed for histopathological analyses. Assessment of graft cell survival, graft morphology, and host tissue response will be reported. In summary, this study completes the translational science cycle by using clinical trial findings and samples to answer basic science questions that will in turn guide future clinical trial design.