Nanofibrous Scaffolds for Transplantation of Human Dopaminergic Neurons

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USA

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Nanofibrous Scaffolds for Transplantation of Human Dopaminergic Neurons

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1

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nanofiber, dopaminergic neuron, scaffold, Transplantation, Parkinson Disease

Research Abstract

? DESCRIPTION (provided by applicant): This project aims to design innovative scaffolds that will integratively address two critical barriers for treating neurodegenerative diseases: (a) Cell Sourcing: support the maturation, specification, and function of reprogrammed human stem cell-derived neurons in vitro and (b) Subtype-specific Neuronal Transplantation: enable efficacious transplantation to treat neurodegenerative diseases in vivo. The central hypothesis is that 3D engineered microscale niches (EMNs) based on nanofibrous hydrogel scaffolds can support the

induction and maturation of subtype specific neurons in vitro prior to transplantation and promote the survival and enhanced functional interaction with host tissue following transplantation. A specific application of interest to this project is the treatment of neurodegenerative diseases like Parkinson’s disease (PD). To achieve our goal, two specific aims are proposed. The first aim is concerned with designing maturation-guiding EMNs of induced pluripotent stem cell (iPSC)-derived reprogrammed dopaminergic (DA) neurons. The 3-D EMNs will be based on transcription factor-transduced iPSCs cultured within nanofibrous hydrogels fabricated from self-assembling minimally immunogenic peptides. To guide the maturation and specification of the DA neurons, the EMNs will be functionalized with subtype specific cues. We will determine the emergent subpopulations of transplanted cells and examine changes in innervated host tissue through whole genome sequencing. The second aim will be focused on transplanting self-actuating EMNs of DA and excitatory neurons into the striatum of a mouse PD model. We hypothesize that a self-functioning E-DA mini neural circuitry within a microscaffold environment will provide sufficient excitatory drive to promote enhanced functional interaction of DA neurons with host tissue in vivo. We will transplant the self-actuating EMNs of E and DA neurons into the striatum of mice lacking DA innervations. We will evaluate the ability of self-actuating EMNs of E and DA neurons to improve functional deficits in the Parkinson’s disease symptoms, and again examine maturation outcomes of transplanted cells and innervated host tissues. The overall outcomes from this study will help to address the critical barriers such as the functioning and survival of transplanted tissue in the field of cell-replacement therapies for neurodegenerative diseases.

Further information available at:

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