

Scientists report first step in strategy for cell replacement therapy in Parkinson's disease

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Induced pluripotent stem cells (iPSC) are a promising avenue for cell replacement therapy in neurologic diseases. For example, mouse and human iPSCs have been used to generate dopaminergic (DA) neurons that improve symptoms in rat Parkinson's disease models. Reporting in the current issue of the *Journal of Parkinson's Disease*, a group of scientists from Japan evaluated the growth, differentiation, and function of human-derived iPSC-derived neural progenitor cells (NPCs) in a primate model, elucidating their therapeutic potential.

"We developed a series of methods to induce human iPSCs to become NPCs, using a feeder-free culture method, and grafted NPCs at different stages of differentiation into the brain of a monkey PD model," explains lead investigator Jun Takahashi, MD, PhD, of Kyoto University. "We developed a method to evaluate the growth and DA activity of the grafts using [magnetic resonance imaging](#) (MRI), [positron emission tomography](#) (PET), immunocytochemistry, and behavioral analyses, all of which will be useful in preclinical research."

Investigators grafted human iPSCs into the brains of [laboratory mice](#) and a monkey treated with MPTP, a neurotoxin that causes Parkinson's symptoms. They found that iPSCs incubated in feeder-free culture generated functional midbrain DA neurons. "In previous studies, midbrain DA neurons were induced from human iPSCs, but the method required coculture with stromal mouse feeder cells or Matrigel," noted Dr. Takahashi. "Our feeder-free method would be more suitable for clinical use."

Pre-treatment with growth factors was required to promote the maturation of functional DA neurons in vivo. MRI and PET imaging allowed real-time monitoring of in vivo cell proliferation and activity. The study demonstrates that dopamine synthesis, transport, and reuptake reflect DA activity in the grafted NPCs, an approach that can also be used in human patients.

"Our results contribute to the evaluation of the survival, differentiation, and function of human iPSC-derived neuronal cells in a primate PD model. Although we have to perform additional preclinical studies using more primate models before clinical application, we believe our findings contribute as the first step for developing a strategy for cell replacement therapy in Parkinson's disease," Dr. Takahashi concludes.

More information: The article is "Transplantation of Human Induced Pluripotent Stem Cell-Derived Midbrain Dopaminergic Neurons into the Brain of a Primate Model in Parkinson's Disease," by T. Kikuchi, A. Morizane, D. Doi, H. Onoe, T. Hayashi, T. Kawasaki, H. Saiki, S. Miyamoto, and J. Takahashi. *Journal of Parkinson's Disease*. 1(2011) 395-412. [DOI: 10.3233/JPD-2011-11070](https://doi.org/10.3233/JPD-2011-11070)

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