PARKINSON DISEASE

Protein-based stem cells generate healthy dopamine neurons

Stem cells have shown promise for the treatment of Parkinson disease (PD), but the safety and efficacy of transplanted cells induced by different methods has been variable. Now, Yong-Hee Rhee and colleagues have compared the safety of several types of human induced pluripotent stem cells (hiPSCs), and found that those derived via protein-based techniques were able to generate healthy dopamine neurons and rescue motor deficits in a rat model of PD.

PD results from a progressive loss of nigrostriatal dopamine neurons, and transplant therapy is an attractive treatment strategy. Fetal-tissue transplants have shown some success, but their availability is limited. hiPSCs are a promising alternative for personalized therapy; many cells can be generated and the chances of immunorejection are low. Several reprogramming methods can generate hiPSCs, the most common of which are lentiviral and retroviral methods, but these can generate mutations and lead to chromosomal aberrations. The authors previously derived hiPSCs through the use of proteins rather than viruses, and in the current study they aimed to systematically compare the safety of cells generated by protein-based and virus-based methods.

The researchers examined eight hiPSC lines that had been generated by delivery of viral vectors or arginine-tagged reprogramming proteins. The virus-generated cells had abnormal properties and showed early senescence and cell death, whereas the protein-based hiPSCs differentiated and functioned normally. The hiPSC lines all efficiently generated functioning midbrain-type neurons that exhibited gene-expression, physiological and electrophysiological properties similar to authentic dopamine neurons.

Rhee *et al.* then aimed to determine whether these hiPSCs could be used to treat PD-like symptoms. They transplanted neural precursor cells from protein-based hiPSCs into a rat model of PD. The transplanted tissue survived well and was able to rescue motor deficits in the model animals.

These findings suggest that protein-based hiPSCs are a safer, viable alternative to virus-induced cells, and that they could potentially be used for transplantation and treatment in patients with PD.

Kwang-Soo Kim, one of the researchers, comments that “the efficiency of protein-based iPSC generation needs to be improved to widely use this technology for personalized medicine.” Future studies will

TuJ1 is a marker for neurons, HuC/D is a marker for human neuronal cells and TH (tyrosine hydroxylase) is a marker for dopamine neurons. This image demonstrates that protein-based hiPSCs generated mature human dopamine neurons. Image provided by Prof. Kwang-Soo Kim.

examine whether protein-based hiPSCs can resolve issues of immunogenicity that have been encountered in other studies. The researchers are continuing their work with rodent models of PD and aim to develop the potential applications of hiPSCs.

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