Application of Lanyu pigs as the animal model in Parkinson's disease

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Lanyu pigs are the local miniature pig in Taiwan and have been widely used in various biomedical studies. Here we introduced how to generate the Lanyu pig model of Parkinson's disease (PD) and utilize porcine induced pluripotent stem cells (piPSC) to recover their defective walking behaviors. The mature female Lanvu pigs were subjected to the PD induction with subcutaneously injecting 5 mg/kg of 1-methyl-4phenyl-1,2,3,6-tetrahydropyridine hydrochloride (MPTP) for 3 months. This treatment induced PD symptoms of the pigs with behavior scores of 5-6 points, revealing moderate to severe muscle rigidity, motility defects, and abnormal positions of the legs or head. Next, we designed a protocol to induce piPSC differentiation into D18 neuronal progenitors (D18 NPs), and they were transplanted into the striatum of Lanyu pig brains for 17 weeks to evaluate their therapeutic effects of PD. After 8 weeks of cell transplantation, the defective behavior was significantly ameliorated and fully recovered at the 14th week of cell transplantation. The number of dopaminergic neurons was also significantly improved at the end of the experiment although the number was still about 50% lower than that in the control group. Taken together, our findings suggest that 5 mg/kg of MPTP can induce moderate to severe PD syndromes, and piPSC- derived D18 NPs exhibit a potential for the treatment of PD in a Lanyu pig model.

Key words: Lanyu pigs, Parkinson's disease, porcine induced pluripotent stem cells, iPSC-based cell therapy