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Improvement of Motor Behavior of Parkinson's Disease Animal Model by Nurr1 Transfected Human Embryonic Stem Cells

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The purpose of this study is to evaluate the efficacy of *in vitro* differentiated human embryonic stem (MB03) cells expressing Nurr1 in relief of symptomatic motor behavior of Parkinson's disease (PD) animal models. MB03 cell was genetically modified to express Nurr1 protein (Nr#24/MB03) and was induced to differentiate according to 2- /4+ protocol using retinoic acid and ascorbic acid. The differentiation-induced cells were selected for 10 to 20 days thereafter in N2 medium. Upon selection, cells expressing GFAP, TH, and NF200 were 38.7%, 11.0%, and 20.5%, respectively. In order to examine therapeutic effects of the differentiated cells in PD animal model, rats were unilaterally lesioned by administration of 6-hydroxydopamine HCl into medial forebrain region (AP - 4.4 mm, ML 1.2 mm, DV 7.8 mm with incision bar set at - 2.4 mm), as a reference to bregma and the surface of the skull. Confirmation of successful lesion by apomorphine-induced rotational behavior, differentiated cells were transplanted into the striatum (AP 1.0 mm, ML 3.5 mm, DV - 5.0 mm; AP 0.6 mm, ML 2.5 mm, DV -4.5 mm). Improvements of asymmetric motor behavior by the transplantation were examined every two weeks after the surgery. In two weeks, numbers of rotation by the experimental rats were -14.8±33.9% ($p<0.05$) of the number before transplantation, however, the ratio increased slightly to 13.6±56.3% in 8 weeks. In contrast, the ratio of sham-grafted animals ranged from 112.3±8.5% to 139.2±28.9% during the examination. This result suggests that *in vitro* differentiated Nr#24/MB03 cells survived at least for 8 weeks when grafted into brains of PD animal model, and that symptomatic motor behavior was improved.

Key words: ***Human embryonic stem cell, Parkinson's disease, Nurr1, Retinoic acid***