PB-25

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 an efficacy of *in vitro* differentiated human embryonic stem (hES, MB03) cells expressing Nurr1 in relief of symptomatic motor behavior of Parkinson's disease (PD) animal models. MB03 was genetically modified to express Nurr1 protein 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, or NF200 were 38.8%, 11%, 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 (6-OHDA) into medial forebrain region (MFB, 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, ML 3.5, DV -5.0; AP 0.6, ML 2.5, DV -4.5). 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 $-14.8\pm33.9\%$ ($p<0.05$) of the number before transplantation, however, the ratio increased slightly to $13.6\pm56.3\%$ in six weeks. In contrast, the ratio of sham-grafted animals ranged from 112.3+8.5% to 139.2+28.9% during the examination. Immunohistochemical studies further confirmed the presence, survival, migration, and expression of TH of the transplanted huamn cells.

key words) *hES cell, Nurr1, Parkinson's disease, Transplantation*