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In Vitro Differentiation-induced hES Cells Relieve Symptomatic Motor Behavior of PD Animal Model

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Human embryonic stem (hES) cells can be induced to differentiate into tyrosine hydroxylase expressing (TH+) cells that may serve as an alternative for cell replacement therapy for Parkinson's disease (PD). To examine *in vitro* differentiation of hES (MB03, registered in NIH) cells into TH+ cells, hES cells were induced to differentiate according to the 4-/4+ protocol using retinoic acid (RA), ascorbic acid (AA), and/or lithium chloride (LiCl) followed by culture in N2 medium for 14 days, during which time the differentiation occurs. Immunocytochemical stainings of the cells revealed that approximately 21.1% of cells treated with RA plus AA expressed TH protein that is higher than the ratio of TH+ cells seen in any other treatment groups (RA, RA+LiCl or RA+AA+LiCl). In order to see the differentiation pattern *in vivo* and the ability of *in vitro* differentiation-induced cells in easing symptomatic motor function of PD animal model, cells (2 x 10^5cells/2$\mu\ell$) undergone 4-/4+ protocol using RA plus AA without any further treatment were transplanted into unilateral striatum of MPTP-lesioned PD animal model (C57BL/6). Following the surgery, motor behavior of the animals was examined by measuring the retention time on an accelerating rotar-rod for next 10 weeks. No significant differences in retention time of the animals were noticed until 2 weeks post-graft; however, it increased markedly at 6 weeks and 10 weeks time point after the surgery. Immunohistochemical studies confirmed that a reasonable number of TH+ cells were found at the graft site as well as other remote sites, showing the migrating nature of embryonic stem cells. These results suggest that *in vitro* differentiated hES cells relieve symptomatic motor behavior of PD animal model and should be considered as a promising alternative for the treatment of PD.

Key words) ***hES cell (MB03), Tyrosine hydroxylase, Parkinson's disease, Transplantation, Behavior***