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Transforming Growth Factor-α Increases the Yield of Functional Dopaminergic Neurons from *in vitro* Differentiated Human Embryonic Stem Cells Induced by Basic Fibroblast Growth Factor

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Embryonic stem (ES) cells proliferate extensively in the un-differentiated state and have the potential to differentiate into a variety of cell types in response to various environmental cues. The generation of functional dopaminergic neurons from ES cells is promising for cell replacement therapy to treat Parkinson's disease. We compared the *in vitro* differentiation potential of pluripotent human embryonic stem (hES, MB03) cells induced with basic fibroblast growth factor (bFGF) or retinoic acid (RA). Both types of treatment resulted in similar neural cell differentiation patterns at the terminal differentiation stage, specifically, 75% neurons and 11% glial cells. Additionally, treatment of hES cells with brain derived neurotrophic factor (BDNF) or transforming growth factor (TGF)-α during the terminal differentiation stage led to signi-ficantly increased tyrosine hydroxylase (TH) expression, compared to control (P<0.05). In contrast, no effect was observed on the rate of mature or glutamic acid decarboxylase-positive neurons. Immunos-taining and HPLC analyses revealed the higher levels of TH (20.3%) and dopamine in bFGF and TGF-α treated hES cells than in RA or BDNF treated hES cells. The results indicate that TGF-α may be successfully used in the bFGF induction protocol to yield higher numbers of functional dopaminergic neurons from hES cells.

Key words) *hES cell, Dopaminergic neuron, b-FGF, Retinoic acid, BDNF, TGF-α*