

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

Keum Sil Lee, Hyun Ah Shin, Hwang Yoon Cho, Eun Young Kim, Young Jae Lee, Kyu Chang Wang¹, Yong Sik Kim², Hoon Taek Lee³, Kil Saeng Chung³, SePill Park, Jin Ho Lim⁴
Maria Infertility Hospital Medical Institute/Maria Biotech, ¹Seoul National University, Dept. of Neurosurgery, ²Seoul National University, Dept of Pharmacology, ³Konkuk University, ⁴Maria Infertility Hospital

Embryonic stem (ES) cells proliferate extensively in the undifferentiated 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 significantly 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. Immunostaining 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*