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Effect of Parthenogenetic Mouse Embryonic Stem Cell (PmES) in the Mouse Model of Huntington's Disease

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Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder characterized by motor, cognitive, and psychiatric symptoms, accompanied by marked cell death in the striatum and cortex. Stereotaxic injection of quinolinic acid (QA) into striatum results in a degeneration of GABAergic neurons and exhibits abnormal motor behaviors typical of the illness. The objective of this study was carried out to obtain basic information about whether parthenogenetic mouse embryonic stem (PmES) cells are suitable for cell replacement therapy of HD. To establish PmES cell lines, hybrid F1 (C57BL/6xCBA/N) mouse oocytes were treated with 7% ethanol for 5 min and cytochalasin-B for 4 hr to initiate spontaneous cleavage. Thus established PmES cells were induced to differentiate using bFGF (20ng/ml) followed by selection of neuronal precursor cells for 8 days in N2 medium. After selection, cells were expanded at the presence of bFGF (20 ng/ml) for another 6 days, then a final differentiation step in N2 medium for 7 days. To establish recipient animal models of HD, young adult mice (7 weeks age ICR mice) were lesioned unilaterally with a stereotaxic injection of QA (60 nM) into the striatum and the rotational behavior of the animals was tested using apomorphine (0.1mg/kg, IP) 7 days after the induction of lesion. Animals rotating more than 120 turns per hour were selected and the differentiated PmES cells (1×10^4 cells/ul) were implanted into striatum. Four weeks after the graft, immunohistochemical studies revealed the presence of cells reactive to anti-NeuN antibody. However, only a slight improvement of motor behavior was observed. By Nissl staining, cell mass resembling tumor was found at the graft site and near cortex which may explain the slight behavioral improvement. Detailed experiment on cell viability, differentiation and migration explanted in vivo is currently being studied.

Key words) ***Huntington's disease, Parthenogenetic stem cell, Quinolinic acid***