## Abstract View

# FUNCTIONAL EFFECTS OF ES CELL-DERIVED DOPAMINE NEURONS IN AN ANIMAL MODEL OF PARKINSON'S DISEASE

J.A.Rodriguez[1]; J.Q.Lu[2]; I.Velasco[1]; S.Rivera[4]; S.Zoghbi[2]; J.S.Liow[2]; J.Musachio[2]; J.Shah[3]; F. Chin[3]; H.Toyama[3]; J.Seidel[3]; M.Green[3]; M.Ichise[2]; V.Pike[2]; P.Thanos[4]; R.Innis[2]; R.D.Mc Kay[1*]

*1. Lab. of Mol. Biol. - NINDS, 2. Mol. Imaging Br. - NIMH, 3. Clin. Ctr., NIH, Bethesda, MD, USA*

*4. Med. Dept., Brookhaven Natl. Lab., Upton, NY, USA*

The goal of this study was to analyze in vivo and in vitro features of dopamine (DA) neurons generated from embryonic stem (ES) cells. Wild-type R1 ES cells were differentiated into DA neurons and stained for makers expressed in the midbrain region. Sprague-Dawley rats with unilateral 6-hydroxydopamine lesion were treated with either ES cell-derived DA neuron transplantation or sham procedures. Six and eight months later, PET scans were performed to measure DA transporters (DAT with [18F]FECNT and D2 receptors with [11C]raclopride. The behavior of the grafted and sham animals was evaluated with rotational tests. After the [11C]raclopride scan the animals were sacrificed and the expression of proteins characteristic of midbrain DA neurons was assessed in the grafted brains. The pattern of expression of these proteins was distinct from both normal DA neurons in vivo and from the ES-derived DA neurons differentiated in vitro. Grafted animals showed overcompensation in rotational tests, indicative of the survival of DA neurons. PET scanning with [18F]FECNT clearly visualized DAT in the transplanted striatum. The [11C]raclopride scan showed an increase in D2 receptor availability in the lesioned animals, an effect that was largely reversed by the grafted cells. The number of tyrosine hydroxylase (TH)+ neurons was proportional to [18F] FECNT signal and behavioral recovery. In vivo functional assessment of DA neurons is an important issue to develop robust cell therapy paradigms with clinical value. These results suggest that PET studies in animal models can be used to optimize the in vivo function of DA neurons routinely generated from ES cells.

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