ZUCKERKANDL’S ORGAN IMPROVES LONG-TERM SURVIVAL AND FUNCTION OF NEURAL STEM CELL DERIVED DOPAMINERGIC NEURONS IN PARKINSONIAN RATS

R.K. Chaturvedi

Developmental Toxicology Division, Indian Institute of Toxicology Research, Lucknow, India

Transplantation of neural stem cells (NSC) derived dopamine (DA) neurons has emerged as an alternative approach to fetal neural cell transplantation in Parkinson’s disease (PD). Survival of these neurons following transplantation is limited due to limited striatal reinnervation, limited host-graft interaction, and lack of continuous neurotrophic factors supply. In the present study, an attempt has been made to increase survival and function of NSC derived DA neurons, by co-grafting with Zuckerkandl’s organ (a paraneural organ that expresses neurotrophic factors); to provide continuous NTF support and developmental cues to transplanted DA neurons in the rat model of PD. 24 weeks post transplantation, a significant number of surviving functional NSC derived DA neurons were observed in the co-transplanted group as evident by an increase in the number of tyrosine hydroxylase immunoreactive (TH-IR) neurons, TH-IR fiber density, TH-mRNA expression and TH-protein level at the transplantation site (striatum). Significant behavioral and neurochemical recovery (DA-D2 receptor binding and DA and DOPAC levels) were observed in the NSC+ZKO co-transplanted group as compared to the NSC or ZKO alone transplanted group. In vivo results were substantiated by in vitro studies, suggesting ZKO increases the NSC derived DA neuronal survival, differentiation, DA release and neurite outgrowth and protection against 6-OHDA toxicity in co-culture condition. The present study suggests that long-term and continuous NTF support provided by ZKO to the transplanted NSC derived DA neurons, helped in their better survival, axonal arborization and integration with host cells, leading to long-term functional restoration in the rat model of PD.