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Neuroprotective and neurorestorative strategies for Parkinson's disease

Parkinson Disease (PD) is a prevalent neurodegenerative disease affecting millions of predominantly elderly individuals worldwide. Despite intensive efforts devoted to drug discovery, the disease remains incurable. Compounding this problem is the current lack of a truly representative mammalian model of PD. Interestingly; the drosophila has emerged as a good system to model the salient features of the disease, including Dopaminergic (DA) neurodegeneration and associated locomotion defects. Taking advantage of this and also the utility of the drosophila as a tool for drug discovery, we have uncovered several neuroprotective compounds and associated targets. These include AMP Kinase (AMPK) activators that are relevant in human PD cases. Our results support the use of drosophila PD model as an intermediate *in vivo* host for phenotype-based drug screening. Because PD involves the degeneration of neurons in a rather circumscribed region in the brain, neuro-restorative therapy via cell replacement represents another strategy to treat the disease. Here, we have exploited the induced pluripotent stem cell (iPS) technology to derive transgene integration- and feeder-free iPS from cells lining the human umbilical cord, an immune-privileged organ that mediates interactions across the feto-maternal interface. Collectively designated as CLiPS (Cord Lining-derived iPS), we demonstrated that CLiPS-derived DA neuronal precursors transplanted into an immune-competent 6-hydroxydopamine mouse model of PD not only survived but also differentiated into mature DA neurons in the absence of pharmacological immunosuppression. Further, the engrafted mice showed functional motor recovery and restoration of dopamine level (illuminated via PET imaging). These results position CLiPS as a promising source of donor cells for allogeneic cell replacement therapy for PD (Supported by NMRC-TCR).

Biography

Kah-Leong Lim has completed his PhD from the Singapore Institute of Molecular and Cell Biology in 1999. He has completed his Postdoctoral training at the Department of Pathology in Harvard Medical School (2000-2001) and subsequently at the Department of Neurology in Johns Hopkins University School of Medicine (2001-2002), where he has worked on the topic of Parkinson's disease with Professor Ted Dawson. He is currently the Deputy Director of Research at the National Neuroscience Institute of Singapore and Director of Basic and Translational Research in the Singhealth Duke-NUS Neuroscience Academic Clinical Program.

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