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Induced pluripotent cells for modelling of Parkinson's disease

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Parkinson’s disease (PD) is a neurodegenerative disease caused by a loss of dopaminergic neurons in the substantia nigra of the brain. There are two types of PD, namely, familial PD and sporadic PD. Sporadic PD is usually a late-onset disease, and it accounts for the majority of PD cases. There is no treatment for PD, and therefore, modelling of the disease is essential to understand the disease and to aid in finding a treatment for it. One of the first models was created by using modified lentiviruses for efficient reprogramming. The second model was made where the sporadic PD-induced pluripotent cells were differentiated to form dopaminergic neurons by retroviral delivery of octamer-binding transcription factor 4 (OCT4), Kruppel-like factor 4 (KLF4) and sex-determining region Y-box 2 (SOX2). The derived neurons showed increased expression of cleaved caspase 3, shortened neurite length and defective autophagosome clearance.   Another model was made where dopaminergic neurons were derived from LRRK2-mutant (leucine-rich repeat kinase-mutant). In this study, a link between DNA methylation and dysregulated gene expression was identified, a common occurrence in PD. It was also found that various epigenetic changes were the cause of DNA methylation. piRNA (piwi-interacting RNA) is a complex of piwi protein and RNA. Further, it is a large class of small non-coding RNA molecules expressed in animal cells that are involved in the epigenetic and post-transcriptional silencing of transposons.   A study found that there is a change in piRNA of dopaminergic neurons that are made from induced pluripotent cells, isolated from patients with PD. More research on piRNA in dopaminergic neurons could enable us to understand the disease in a better way. Therefore, this has proved the importance of models made from induced pluripotent cells and their potential to help in the identification of more such mechanisms in Parkinson’s disease.

Keywords: Parkinson's disease, Sporadic PD, Induced pluripotent cells, Dopaminergic neurons, DNA methylation, piRNA

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