Therapeutic Application of Human Induced Pluripotent Stem Cells for Neurodegenerative Diseases

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My laboratory has recently focused on the preparation, differentiation, and characterization of hiPSC or hESCs for the cell replacement therapy to cure the neurodegenerative diseases (Cooper et al., 2012, Song et al., 2019, Schweitzer et al., 2020, Kim et al., 2021). In the previous studies, our research team has studied for molecular characterization of multiple human iPSC lines that derived from different genetic forms of Parkinson's disease including PINK1 and LRRK2genes, and healthy control subjects. We measured several aspects of mitochondrial responses in the iPSC-derived neural cells including production of reactive oxygen species, mitochondrial respiration, proton leakage and intraneuronal movement of mitochondria. Cellular vulnerability associated with mitochondrial function in iPSC-derived neural cells from PD patients and at-risk individuals could be rescued with coenzyme Q10, rapamycin or the LRRK2 kinase inhibitor GW5074. Analysis of mitochondrial responses in iPSC-derived neural cells from PD patients carrying different mutations provides insights into convergence of cellular disease mechanisms between different familial forms of PD and highlights the importance of oxidative stress and mitochondrial dysfunction in PD. This study was one of earlier disease mechanism studies using human iPSC-derived neuronal cells. In addition, more recently, I have been involved in human iPSC-based cell therapy of Parkinson's disease. Although cell replacement therapy has been considered as the most potent therapeutic approaches in next generation, there are lots of huddles to make it possible. For cell therapy, healthy cells need to be prepared for proper kinds of differentiated cells, at the proper differentiation timing (stages), with proper environments including glial cells and/or trophic factors. We investigated how to differentiate human pluripotent stem cells to neural precursor cells, dopaminergic neurons, glutamatergic neurons, astrocytes, etc in 2D or 3D culture environments. In this regard, I and my collaborators recently developed noble spotting techniques to obtain higher quality population of dopaminergic neurons from human pluripotent cells with increased efficiency. We have also developed new differentiation techniques with only small molecules chemicals without expensive growth factors and cytokines, which will dramatically decrease the experimental cost for stem cell-based neuroscience research and therapy. These human iPSC or ESC induced cell will provide not only cell source for the cell replacement, but also very potent research tool for the neurodegenerative diseases as human model. In summary, we have studied pathological mechanism of neurodegenerative diseases and cell therapy using stem cells. Our multi-disciplinary research will provide invaluable platforms of stem cell-based neuroscience research tools and may lead to noble therapeutic development for neurodegenerative and neuropsychiatric disorders.