Reelin alleviates pathological α-Synuclein aggregation and cell senescence in an *in vitro* model of Parkinson's Disease

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Statement of the Problem: Parkinson's disease (PD) is a neurodegenerative disorder caused by the gradual deterioration of midbrain dopaminergic (DA) neurons in the substantia nigra pars compacta. Changes in DA cells lead to tremor and rigidity, and induce a slow decline of the extrapyramidal motor system. Despite this, treatments for PD and its underlying pathogenesis remain understudied. Mesenchymal stem cells (MSCs) are multipotent cells that can differentiate into neuron-like cells, and they have been studied as part of potential therapy for PD. We questioned what the differences would be in molecular and cellular levels between the control and PD patient MSCs, and how to increase the survival rate of MSCs. Since PD is an age-related neurodegenerative disease associated with systemic problems, including inflammation, MSCs isolated from the abdominal adipose tissue were used in our cell model for PD to conduct gene expression profiling (GEP) investigation in this study.

Methods: Human adipose derived mesenchymal stem cells (MSCs) were obtained from a female volunteer, age of 68 as a control. An age matched female patient with PD, aged 68 years, who was not receiving any pharmacological treatment, was included in this study. For genome pathway analysis, DAVID software and KEGG pathways were selected. By DAVID software, our study found which pathways were down-regulated in PD cell.

Findings: Our results provide important data pertinent to research of the mechanisms underlying PD and potential treatment targets by transcriptome analysis in PD.

Conclusion: In this study, the GEP of MSCs on both PD cells and control group was analyzed. RELN was among ECM-receptor related genes whose expression is down-regulated in PD and hr-Reelin prevented PFF-induced α-Syn aggregation. A better understanding of Reelin functions and regulation in PD will be necessary to improve the prospects for successful treatment of PD.

Biography

Eunju Cho has her expertise in discovering potential therapeutic candidates to improve behavioral symptoms and to prevent exacerbating neuropathological features of Parkinson's disease (PD). She investigated the underlying mechanism of transient receptor potential vanilloid 1 (TRPV1) mediated therapeutic effects related to astrocyte responses in 1-methyl-4-phenylpyridinium (MPP+)-induced PD animal model during her M.S. thesis and she confirmed human relevance of altered Reelin gene and protein levels with neurodegenerative disease in PD patient-derived adipose stem cells during her Ph.D. course. Now she elucidated therapeutic effects and underlying mechanisms of Reelin with environmental enrichment in both cell model (Preformed fibrils) and transgenic mouse ((Prnp-SNCA*A53T)83Vle/J) model of PD. Based on her research, she has journal publications and two patents pending in South Korea regarding the Reelin protein in PD.

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