

The Effect of Traditional Chinese Medicine Compounds in Regulating Dendritic Cells Underlying Parkinson' Disease

Parkinson's Disease (PD) is the most common neurodegenerative movement disorder affecting the elderly. Currently, there is no cure for PD and patients rely on drugs to slow down disease progression. The hallmark of PD is the abnormal accumulation of aggregated α -synuclein protein in Lewy bodies that causes the loss of dopaminergic neurons in the midbrain. Consequently, activation of immune responses may result in neuroinflammation and neuronal cell death and to the development of PD. Although immune-related brain cells such as microglia and astrocytes are well studied, the role of dendritic cell (DC) that circulate from the periphery is less well characterised. Infiltrating DC may acquire misfolded or aggregated α -synuclein as antigen and activate peripheral inflammatory T cell subsets (i.e. Th17) that then infiltrate into the brain while overcoming the immunosuppressive IL-10+Treg cells, leading to neuroinflammation. Therefore, suppressing the activities of DCs may be a therapeutic strategy for treating PD. In this study, two traditional Chinese medicine compounds (TCMs), C1 and Celastrol, were chosen to evaluate their effects on DCs, including cytokines, maturation and T cell stimulation. Our data showed that Celastrol (but not C1) suppressed α -synuclein-pulsed DC cytokine expression of IL-1 β , IL-6, IL-23 and TNF- α while upregulated the immunosuppressive IL-10. Furthermore, co-culture experiments between α -synuclein-treated DC and CD4+ T cells resulted in the increased proportion of IL-17-secreting Th17 cells and IL-10+/Foxp3+ Treg cells. However, both C1 and Celastrol reversed this effect, which may be due to the decreased maturation of α -synuclein-treated DC based on MHC-II and CD86 expression analysis. While C1 and Celastrol can activate TFEB and autophagy, their function in regulating DC immune pathways provided a link between the two. In summary, our data provides insight to the novel immune mechanisms by DC and T cells that may underlie and contribute to PD that could be counteracted through the potentially anti-PD TCMs.

Keywords : Dendritic cell, alpha-synuclein, T cell subsets, Parkinson's disease

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