1-S17-4 Symposium17

Therapeutic strategy for Parkinson's disease: Targeting zinc-binding protein in astrocytes

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Parkinson's disease (PD) is a progressive neurodegenerative disease with motor symptoms, such as tremor, akinesia/bradykinesia, rigidity and postural instability due to a loss of nigrostriatal dopaminergic neurons, and non-motor symptoms, such as orthostatic hypotension and constipation. Although nosotropic treatments to improve the motor disability in PD are being assessed at present, the main challenge remains to develop of neuroprotective or disease-modifying treatments. Therefore, it is desirable to find approaches that can inhibit the progression of dopaminergic neurodegeneration. Astrocytes are known to play an important role in the maintenance of the neuronal environment and exert neuroprotective effects by production of antioxidants, release of neurotrophic factors, and uptake of potentially neurotoxic molecules. In the previous study, we demonstrated that astrocytes produced antioxidative molecules metallothionein (MT)-1/2 in response to oxidative stress, and protected dopaminergic neurons against oxidative stress. MTs are cysteine-rich and metal-binding proteins such as zinc, copper, and cadmium to function in zinc homeostasis and metal detoxification. In this symposium, we will outline a new therapeutic strategy of neuroprotection against dopaminergic neurodegeneration by targeting MTs in astrocytes.