World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:14, No:06, 2020

Investigation of the Effects of Monoamine Oxidase Levels on the 20S Proteasome

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Abstract : The two main contributing factors to familial and idiopathic form of Parkinson's disease (PD) are oxidative stress and altered proteolysis. Monoamine oxidase-A (MAO-A) plays a significant role in redox homeostasis by producing reactive oxygen species (ROS) via deamination of for example, dopamine. The ROS generated induces chemical modification of proteins resulting in altered biological function. The ubiquitin-proteasome system, which consists of three different types or proteolytic activity, namely "chymotrypsin-like" activity (CLA), "trypsin-like" activity (TLA) and "post acidic-like" activity (PLA), is responsible for the degradation of ubiquitinated proteins. Defects in UPS are known to be strongly correlated to PD. Herein, the effect of ROS generated by MAO-A on proteasome activity and the effects of proteasome inhibition on MAO-A protein levels in WT, mock and MAO-A overexpressed (MAO-A+) SHSY5Y neuroblastoma cell lines were investigated. The data in this study report increased proteolytic activity when MAO-A protein levels are significantly increased, in particular CLA and PLA. Additionally, 20S proteasome inhibition induced a decrease in MAO-A levels in WT and mock cells in comparison to MAO-A+ cells in which 20S proteasome inhibition induced increased MAO-A levels to be further increased at 48 hours of inhibition. This study supports the fact that MAO-A could be a potential pharmaceutical target for neuronal protection as data suggests that endogenous MAO-A levels may be essential for modulating cell death and survival.

Keywords : monoamine oxidase, neurodegeneration, Parkinson's disease, proteasome
Conference Title : ICPN 2020 : International Conference on Psychopharmacology and Neuropharmacology
Conference Location : Toronto, Canada
Conference Dates : June 18-19, 2020