Discovery of ARE-Keap1-Nrf2 signaling pathway modulators as potential neuroprotectants

Failure of the intracellular antioxidant systems to keep check of oxidative stress caused by overproduction of reactive oxygen species (ROS) has severe effects on biomolecules such as lipids, proteins and DNA. Oxidative stress has been one of the main pathogenic hallmarks in neurodegenerative diseases (NDD). In particular, oxidative insults impose detrimental damages on neurons.

The deleterious consequences of oxidative stress are presumably lessened by an elevated capacity of the intracellular antioxidant systems to cope with the increased production of ROS. In recent years, research efforts to harness the intrinsic ability of a cell's antioxidative and detoxifying properties to counteract oxidative stress in NDD are prevalent. In particular, small molecules that can increase the expression and activity of a panel of phase II detoxifying and antioxidant enzymes through induction of the ARE-Keap1-Nrf2 signaling pathway have been actively exploited as a feasible pharmacological means to alleviate onset and progression of NDD.

In this seminar, we will discuss the role of the ARE-Keap1-Nrf2 signaling pathway in NDD. Furthermore, we will discuss about the small molecules currently under investigation in the laboratory that display potential to induce the ARE-Keap1-Nrf2 signaling pathway.

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