

The Sigma-1 Receptor: Pathophysiological Roles and Therapeutic Potential in Neurodegenerative Diseases

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Abstract

The sigma-1 receptor, a chaperone protein mainly localized in the endoplasmic reticulum (ER), regulates cellular calcium homeostasis, stress responses, and neuronal activity. Recent accumulating evidence has indicated that genetic mutations of the sigma-1 receptor are related to neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS) and distal hereditary motor neuropathy. Preclinical studies have also shown that the activation of the sigma-1 receptor has a beneficial effect on neurodegenerative diseases, such as ALS and Alzheimer's disease, as well as ischemic diseases in the brain and the heart. In this review, we focus on cellular calcium handling by the sigma-1 receptor, and discuss the recent advances in the mechanisms by which the sigma-1 receptor is related to ALS and its role as a potential target in the treatment of neuronal disorders.

Key words: Sigma-1 receptor, Cellular calcium handling, Neurodegenerative disease, Ischemic injury