Online publication ahead of print, AJMHS Vol 63, 2023

Zinc Superoxide Dismutase and Amyotrophic Lateral Sclerosis: Deciphering the Role and Implications for Therapeutic Interventions

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Abstract

Amyotrophic lateral sclerosis (ALS) stands as a complex and devastating neurodegenerative disorder characterized by the progressive degeneration of motor neurons, ultimately leading to paralysis and respiratory failure. Despite extensive research, the intricate molecular underpinnings of ALS remain elusive, hampering therapeutic advancements. This narrative review delves into the intriguing link between copper-zinc superoxide dismutase (CuZnSOD) and ALS pathogenesis. CuZnSOD, a metalloenzyme essential for maintaining cellular redox balance by neutralizing superoxide radicals, becomes a paradoxical player in select ALS cases.

Early identification of SOD1 mutations paved the way for understanding familial ALS, shedding light on the intricate interplay between genetic factors and neurodegeneration. Mutant SOD1 proteins have been implicated in protein misfolding and aggregation within motor neurons, creating a toxic environment that triggers cellular stress and inflammation. Notably, the relationship between CuZnSOD and metal ions, particularly copper and zinc, adds complexity to ALS pathology. Proper folding and function of CuZnSOD hinge on these metal ions, and disruptions in metal homeostasis may induce SOD1 misfolding, accentuating protein aggregation and oxidative stress. Perturbations in

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copper and zinc levels have been observed in ALS motor neurons, hinting at a potential role in disease progression.

Through a synthesis of genetic and mechanistic insights, this review underscores the multifaceted connections between CuZnSOD, mutant SOD1, oxidative stress, and ALS pathogenesis. We navigate the nuanced landscape of ALS research, emphasizing the interdisciplinary collaboration required to unravel its complexities. By probing into the dynamic relationship between CuZnSOD, metal ions, and ALS, we aim to illuminate the molecular intricacies driving motor neuron degeneration and stimulate innovative therapeutic avenues. This narrative review serves as a compass, guiding researchers toward a comprehensive understanding of ALS and its complex interplay with CuZnSOD- mediated mechanisms.

Keywords: Zinc superoxide dismutase, ZnSOD, Amyotrophic lateral sclerosis, Therapeutic interventions, Genetic predisposition.