The TRPM2 channel nexus from oxidative damage to Alzheimers pathologies: an emerging novel intervention target for age-related dementia

ABSTRACT

Alzheimer's disease (AD), an age-related neurodegenerative condition, is the most common cause of dementia among the elder people, but currently there is no treatment. A number of putative pathogenic events, particularly amyloid β peptide (Aβ) accumulation, are believed to be early triggers that initiate AD. However, thus far targeting Aβ generation/aggregation as the mainstay strategy of drug development has not led to effective AD-modifying therapeutics. Oxidative damage is a conspicuous feature of AD, but this remains poorly defined phenomenon and mechanistically ill understood. The TRPM2 channel has emerged as a potentially ubiquitous molecular mechanism mediating oxidative damage and thus plays a vital role in the pathogenesis and progression of diverse neurodegenerative diseases. This article will review the emerging evidence from recent studies and propose a novel 'hypothesis' that multiple TRPM2-mediated cellular and molecular mechanisms cascade Aβ and/or oxidative damage to AD pathologies. The 'hypothesis' based on these new findings discusses the prospect of considering the TRPM2 channel as a novel therapeutic target for intervening AD and age-related dementia.

Keyword: Alzheimer’s disease; Neurodegeneration; Neuroinflammation; Neurovascular dysfunction; Oxidative damage; TRPM2 channel