Novel link between calcium, transferrin trafficking, and iron homeostasis

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Video Byte

Keywords: CAMKK2, CAMK4, calcium, transferrin, transferrin-receptor, trafficking, iron, iron homeostasis, glycolysis, respiration, cerebellum, liver, Cell Communication and Signa

Posted Date: October 29th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-100321/v1>

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Abstract

Alzheimer's disease is the sixth leading cause of death and one of the most prevalent forms of dementia, affecting over 50 million people worldwide. Unfortunately, the molecular signaling pathways underlying neurodegeneration in Alzheimer's disease are not clearly understood. A recent study identified a link between two physiological phenomena that are affected in Alzheimer's disease: disrupted calcium signaling, which is associated with memory loss and cognitive dysfunction; and increased iron accumulation, which results in neurotoxicity in the brain. Using genetically modified human cell lines and mice, the researchers studied the mechanistic connections between calcium signaling and iron transport. They found that calcium (Ca^{2+}) signaling through CAMKK2 and CAMK4 proteins had direct effects on transferrin protein-mediated iron transport. Transferrin, a serum iron transporter protein, was abnormally trafficked in mice lacking CAMK4, resulting in tissue-specific altered iron homeostasis, and in cell lines, lack of CAMKK2/CAMK4 affected calcium signaling during TF-mediated iron trafficking. Future studies will determine whether these pathways are associated with the pathogenesis of Alzheimer's disease, but this study is the first report of a mechanistic connection between neuronal calcium signaling and iron homeostasis in the brain, offering new therapeutic targets for the fight against Alzheimer's disease.