3rd International Conference on

NEUROLOGY AND BRAIN DISORDERS

Li Zhang, J Brain Neurol 2019, Volume 3

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BIOGRAPHY

Li Zhang completed her PhD at UCLA and Postdoctoral studies at the MIT Department of Biology. She is the Cecil H and Ida Green Distinguished Chair in Systems Biology Science at the University of Texas at Dallas. Her laboratory has studied heme signaling and function for 20+ years and published many original research articles and a book entitled "HEME BIOLOGY: THE SECRET LIFE OF HEME IN REGULATING DIVERSE BIOLOGICAL PROCESSES" on this subject. Her laboratory has also helped unravel the functions of molecular chaperones, oxygen signaling and the actions of neurotoxicants. Her research interest is to elucidate the molecular events underlying altered heme iron homeostasis in AD pathogenesis and lung tumorigenesis.

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ALTERED HEME IRON HOMEOSTASIS IN ALZHEIMER'S DISEASE

Mitochondrial dysfunction and bioenergetic deficits have been identified as early and potentially causative events in Alzheimer's disease (AD) pathogenesis. Importantly, heme is a key factor in mitochondrial function and bioenergetics. Heme is a central metabolic and signaling molecule regulating diverse molecular and cellular processes relating to oxygen utilization and metabolism. Heme serves as a prosthetic group in proteins and enzymes involved in oxygen transport, utilization and storage such as globin's and cytochromes. Multiple subunits in mitochondrial respiration or oxidative phosphorylation (OXPHOS) complexes II-IV contain heme. Further, heme acts as a signaling molecule to coordinate the expression of genes encoding globins and cytochromes as well as the translocation and assembly of these protein/enzyme complexes. Heme binds to and directly regulates the activities of many proteins controlling processes ranging from tyrosine kinase signaling to microRNA processing. Thus, researchers assessed the importance of altered heme metabolism in AD pathogenesis. To investigate the role of altered heme metabolism in AD, they identified heme-related proteins whose expression is altered in AD patients and mouse models exhibiting amyloid pathology. They detected the levels of proteins involved in heme synthesis, uptake degradation and function during neuronal differentiation and characterized the effects of Aβ. They found that the expression levels of the rate-limiting heme synthetic enzyme ALAS1 and heme degradation enzyme HO-2 are selectively decreased in AD patients and mice. Aβ selectively reduces the levels of HO-2 and heme degradation, which are elevated to support neuronal functions in fully differentiated neuronal cells. Our data show that lowered heme metabolism, particularly the decreased levels of heme degradation and HO-2 are likely a very early event in AD pathogenesis.