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Simultaneous activation of Nrf2 and elevation of antioxidant compounds for reducing oxidative stress and chronic inflammation in human Alzheimer's disease

Biochemical and genetic defects that initiate and promote Alzheimer's Disease (AD) include: (a) Increased oxidative stress, (b) chronic inflammation (c) mitochondrial dysfunction, (d) A β 1-42 peptides generated from the amyloid precursor protein (APP), (e) proteasome inhibition, and (f) mutations in APP, presenilin-1 and presenilin-2 genes. Increased oxidative stress precedes other defects. Oxidative damage induces chronic inflammation. Therefore, reducing these defects simultaneously may decrease the development and progression of AD. Studies using individual antioxidants produced consistent benefits in animal models, but not in human AD. Individual antioxidant is oxidized in a high oxidative environment of AD, and acts as a pro-oxidant, and it cannot simultaneously elevate antioxidant enzymes and antioxidant compounds. This paper proposes that simultaneous elevation of the levels of antioxidant enzymes and antioxidant compounds may be necessary for optimally reducing oxidative stress and chronic inflammation in human AD. Supplementation enhances antioxidant compounds; but an elevation of the levels of antioxidant enzymes requires activation of Nrf2 (nuclear transcriptional factor-2). During acute oxidative stress, an activation of Nrf2 requires ROS; however, this mechanism impaired during chronic oxidative stress. Antioxidants activate Nrf2 without ROS stimulation. MicroRNAs that are evolutionary conserved small single-stranded RNAs formed from the non-coding region of DNA, regulate activation of Nrf2. The up-regulated microRNAs cause neurodegeneration by multiple mechanisms including decreasing Nrf2 levels. Antioxidant-induced up-regulated microRNAs activates Nrf2 by reducing Keap1 levels. Author has proposed a mixture of micronutrients that would simultaneously and optimally reduce oxidative stress and chronic inflammation by activating Nrf2 and enhancing the levels of antioxidants in AD.

Biography

Kedar N Prasad obtained PhD in Radiation Biology from the University of Iowa and a Post-doctoral Training at the Brookhaven National Laboratory. He was a Professor at the University of Colorado, and has published over 250 papers in prestigious peer-reviewed journals and wrote 25 reference books on radiobiology, nutrition in neurodegenerative disease and cancer. In 1982, he was invited by the Nobel Prize Committee to nominate a candidate for the Nobel Prize in Medicine. He is the former President of the International Society for Nutrition and Cancer and Chief Scientific Officer of the Premier Micronutrient Corporation. Currently, he is an independent Consultant.

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