Mark A. Smith, Ph.D.
Case Western Reserve University
Cleveland, Ohio

Xanthine Oxidase in Alzheimer's: Mechanistic and Therapeutic Opportunities

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Oxidative stress has been implicated as one possible cause of Alzheimer pathology. Unfortunately, treatments using antioxidant drugs to slow or halt the disease have had little success. These drugs are designed to remove free radicals from tissue, but they are often unable to keep up with the rate at which free radicals are produced.

Mark A. Smith, Ph.D. and colleagues are studying free radical production and antioxidant therapies in the brain. They have found that a major source of free radicals in the brain is an enzyme called xanthine oxidase. The researchers have also found preliminary evidence that persons taking allopurinol, a drug that inhibits xanthine oxidase, have a lower risk of developing Alzheimer's disease.

Dr. Smith and colleagues plan to perform in-depth studies of xanthine oxidase and its possible role in Alzheimer's disease. They will examine the activity of xanthine oxidase in the serum and cerebrospinal fluid of persons with Alzheimer's disease to determine if enzyme activity is related to disease onset. They will also study genetic variants of xanthine oxidase to determine if some variants are more closely associated with disease than others.

Using mice that have been genetically altered to exhibit Alzheimer-like disease characteristics, Dr, Smith's team will study whether allopurinol or other inhibitors of xanthine oxidase slow or prevent the onset or progression of disease. These studies will help to determine whether inhibitors of xanthine oxidase warrant further study as potential treatments to slow or halt the progression of Alzheimer's disease.