An Australian Government Initiative

DEMENTIA RESEARCH

Inaugural Lecture

Launch of Dementia Collaborative Research Centre: Prevention, Early Intervention and Risk Reduction

Metals, oxidative stress and dementia: from biomarkers to prevention

By Professor Ashley I. Bush

Date: Monday 13 August 2007

Time: 10:00-10:45

Venue: The Finkel Lecture Theatre,
John Curtin School of Medical Research
Australian National University

Ashley I. Bush (MBBS, 1982; PhD, 1992 University of Melbourne, Australia) is the Director of the Oxidation Disorders Laboratory, at the Mental Health Research Institute of Victoria, Australia; Professor of Pathology, University of Melbourne; and adjunct faculty in psychiatry at Massachusetts General Hospital and Adjunct Professor of Neuroscience at Cornell University Medical Center. His laboratory uncovered the interaction of biometals (copper, zinc and iron) with beta-amyloid that contributes to both oxidation damage and amyloid accumulation in Alzheimer's disease. This has lead to the development of novel therapeutic compounds that are currently in clinical trials. He has received several awards including the Beeson Award, the Zenith Award from the Alzheimer Association, the Australian Research Council Federation Fellowship, and the Potamkin Prize from the American Academy of Neurology. He has authored over 165 publications.

SYNOPSIS: Alzheimer's disease (AD) affects about 10% of people over the age of 60 and is a growing burden to society. While there is some symptomatic treatments for AD, there are no drugs that attack the underlying cause of the disease. The hunt for curative drugs has been based on the central role for beta-amyloid (Abeta) in forming the main pathology of the disease, amyloid. We have discovered that amyloid accumulation in AD is driven by the abnormal interaction of Abeta with biological metals (zinc and copper) that are normal components of brain chemistry. Small molecules that block this reaction are being developed as the basis for potential new drugs for AD. One such drug developed in Melbourne was clioquinol, which is very effective at stopping AD-like brain damage in laboratory mice, and showed promise in a clinical trial in 2003. However, this drug has been vastly improved upon by a second-generation version called “PBT2”. This drug candidate reverses memory loss in mouse models of AD within days of treatment. PBT2 has been successfully tested for toxicology and phase 1 studies, and is currently being tested in AD patients in a phase 2 clinical trial that should be completed by the end of this year.

DCRC Dementia Collaborative Research Centres

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