NUS National University of Singapore | Life Sciences Institute

Neurobiology/Ageing Programme Seminar Series

D. Allan Butterfield, Ph.D.

The Alumni Association Endowed Professor of Biological Chemistry;
Director, Center of Membrane Sciences;
Director, Free Radical Biology in Cancer Shared Resource Facility, Markey Cancer Center;
Faculty Associate, Spinal Cord and Brain Injury Research Center;
Faculty, Sanders-Brown Center on Aging; and
Fellow, Society of Free Radical Biology and Medicine
University of Kentucky
Lexington, KY 40506-0055 USA

"PRECLINICAL AD TO MILD COGNITIVE IMPAIRMENT TO ALZHEIMER DISEASE: OXIDATIVE STRESS MEASURES AND PROTEOMICS PROVIDE INSIGHTS INTO MECHANISMS AND BIOMARKERS OF AD PROGRESSION"

Alzheimer disease (AD) is a major public health crisis facing the world due to the increased average age of developed countries. Our laboratory and others demonstrated that amyloid b-peptide, in the form of small oligomers, caused elevated indices of oxidative stress in *in vitro* and *in vivo* models of AD. Similarly, our lab was among the first to show elevated protein and lipid oxidation in brain of subjects with AD, and arguably its earliest form, mild cognitive impairment (MCI). Using redox proteomics methods pioneered in our laboratory oxidatively modified (and most often dysfunctional) proteins in brain of AD and MCI subjects have been identified. These proteomics-identified dysfunctional proteins are consistent with the pathology and clinical presentations of both disorders, and identify specific proteins that may play a role in progression of this dementing disorder. In preclinical AD (PCAD), patients score normally on mini-mental state examinations and have normal activities of daily living. However, upon autopsy PCAD subjects demonstrate significant AD pathology. Though no oxidative stress was demonstrable in brain of PCAD subjects, proteomics comparison to amnestic MCI brain revealed enolase as likely involved in memory loss associated with MCI. Recently, we have used similar methods to demonstrate oxidative stress in mitochondria isolated from peripheral lymphocytes from AD and MCI individuals that correlate inversely with performance on cognitive assessment paradigms, opening the possibility of a surrogate biomarker for the pathogenesis and progression of AD. Lastly, this seminar will summarize recent studies with atrovastatin in a preclinical model of AD, the aged beagle dog, that provide novel insights into potential mechanisms by which this agent could lead to decreased risk of developing AD in a manner independent of cholesterol lowering. Support: Grants from the National Institutes of Health.

Date: 16 May 2013 (Thursday) // Time: 12.00pm // Venue: Centre for Life Sciences Seminar Room 2

Host: A/P Lim Kah Leong, Chairman (Programme's Steering Committee)