

SCHEDULE OF EVENTS

8:00a.m.

Registration & Continental Breakfast

Alumni Gallery, Room 1-65, W.T. Young Library

8:30a.m.

Welcome

Dr. Eli Capilouto, President

Dr. Robert DiPaola, Provost

Dr. Lisa Cassis, Vice President for Research

Dr. Ana Franco-Watkins, Dean, College of A&S

Prof. Mark Lovell, Chair, Department of Chemistry

Prof. D. Allan Butterfield, Organizer

AA Auditorium, Room 1-62, W.T. Young Library

9:00a.m.

Prof. Barry Halliwell

National University of Singapore

AA Auditorium, Room 1-62, W.T. Young Library

"Is Ergothioneine a Protective Factor Against Neurodegeneration and a Promoter of Healthy Ageing?"

Increased damage by oxygen radicals and other "reactive oxygen species" appears to play a key role in the development of neurodegenerative diseases, especially dementias, and diets rich in antioxidants (high intake of fruits and vegetables) seem neuroprotective (as well as being protective against many other diseases). However, attempts to treat / prevent such diseases by giving high doses of antioxidants such as vitamins E and C and carotenoids have, overall, been unsuccessful. Reasons for this will be discussed.

A major focus of our work at the moment is a unique diet-derived thiol/thione with antioxidant properties, namely ergothioneine (ET). Low blood levels of ET appear to be a risk factor for the development of neurodegenerative and cardiovascular diseases, frailty, eye disease, pre-eclampsia, and age-related diseases generally. We have identified "risk levels" of plasma ET concentrations in human subjects, levels below which are associated with increased disease risk. In animal studies, ET has exhibited the ability to modulate inflammation, scavenge certain ROS, protect against acute respiratory distress syndrome, decrease brain damage in models of Parkinson and Alzheimer diseases, prevent

endothelial dysfunction, protect against ischemia-reperfusion injury, counteract iron dysregulation, hinder lung and liver fibrosis, and mitigate damage to the gastrointestinal tract, and testis. ET may also influence the gut microbiome. There is evidence that ET is specifically accumulated at sites of tissue injury, so we have called it an "adaptive antioxidant" that may not interfere with the normal physiological roles of ROS. But does low ET predispose to age-related diseases or is it a spurious correlation? We will present animal studies that suggest the former, but only double-blind placebo-controlled human clinical trials will provide the final answer.

Caveats in the use of ergothioneine include its potential to generate trimethylamine-N-oxide by the action of ergothionease enzymes in gut bacteria and its ability to be taken up by many bacteria, a few of which might be pathogenic (e.g. *H. pylori*, *M. tuberculosis*). These caveats will be discussed in detail.

10:15am

Prof. Marzia Perluigi

Sapienza University of Rome

AA Auditorium, Room 1-62, W.T. Young Library

"Redox Imbalance and Metabolic Defects in the Brain of Down Syndrome Individuals: a Synergistic Path to Alzheimer's Neurodegeneration"

Down Syndrome (DS is the most common genetic disorder due to the abnormal triplication of chromosome 21 resulting in a variety of pathological conditions of DS subjects. Among these, individuals affected by DS show with ageing the accumulation of oxidative damage associated with defects of the proteostasis network. DS is currently considered a human genetic model of early onset Alzheimer disease (AD). The talk will discuss the role of trisomic genes which, directly and indirectly, contribute to the occurrence of an aberrant redox-phenotype and how it contributes to the dysfunction of several cellular functions. Among these, we hypothesize that redox dysregulation is closely linked to metabolic defects, including reduced glucose metabolism, energy production and aberrant insulin signaling.

11:30a.m.

Lunch & Break

1:30p.m.

Prof. Mark Mattson

Johns Hopkins University

AA Auditorium, Room 1-62, W.T. Young Library

"Sculptor and Destroyer"

Of the approximately 100 billion neurons and 100 trillion synapses in the human brain more than 90 percent deploy glutamate as their neurotransmitter. Glutamate is the brain's excitatory neurotransmitter and other neurotransmitters exert their effects on behaviors by subtly modifying the activity of glutamatergic neurons. Glutamate 'sculpts' neuronal networks. It plays major roles in the establishment of neuronal networks during brain development and in their adaptive modification throughout life. Glutamate is the learning and memory neurotransmitter. Glutamatergic neurotransmission plays a preeminent role in brain energy metabolism and is responsible for the neural network activity levels seen in functional MRI images of the brain. But glutamate has a dark side - it can destroy neuronal circuits. Hyperexcitability of glutamatergic neurons contributes to neuronal degeneration in epilepsy, stroke, and traumatic brain injuries. Excitotoxicity is also involved, albeit more insidiously, in the demise of neurons in Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and Huntington's disease. Moreover, dysregulation of glutamatergic neuronal networks is implicated in psychiatric disorders including schizophrenia, anxiety disorders, depression, and autism.

3:00p.m.

Poster Session

Jacobs Science Building, Atrium

4:15p.m.

Presentation of Poster Awards

Jacobs Science Building, Atrium

4:30p.m.

Close of the 48th Naff Symposium

Jacobs Science Building, Atrium

48th Annual Naff Symposium



Oxidative Stress in Neurodegeneration: Focus on Alzheimer Disease

April 21, 2023
W.T. Young Library

 College of Arts
and Sciences

Department of Chemistry



Oxidative Stress in Neurodegeneration: Focus on Alzheimer Disease

April 21, 2023

GUEST SPEAKERS



Prof. BARRY HALLIWELL

National University of Singapore

Biography

Barry Halliwell, D. Phil (Oxford), D. Sc. (London). Chairman, BMRC Advisory Council (BMAC), Agency for Science, Technology & Research (A*STAR). Distinguished Professor, Department of Biochemistry, National University of Singapore (NUS). Senior Advisor, Academic Appointments and Research Excellence, Office of the Senior Deputy President and Provost, NUS. Program Leader, Neurobiology Research Programme, Life Sciences Institute. Email: bchbh@nus.edu.sg Websites: <https://medicine.nus.edu.sg/bch/faculty/barry-halliwell/> and <https://www.lsi.nus.edu.sg/corp/neurobiology/programme-leader/>

Professor Halliwell graduated from Oxford University with BA (first class honors) and D.Phil degrees. He holds a Doctor of Science degree from the University of London. He was a faculty member with King's College London (1974-2000) and held a prestigious Lister Institute Research fellowship. He was a Visiting Research Professor of Internal Medicine and Biochemistry at the University of California Davis (1995-1999). He now holds several key positions in Singapore, as indicated above.

Professor Halliwell is recognized for his seminal work on the role of free radicals and antioxidants in biological systems, being one of the world's most highly cited researchers with a Hirsch-Index of 168 (Based on Scopus, Jan 2023). His Oxford University Press book with John Gutteridge, *Free Radicals in Biology and Medicine*, now in its fifth edition (2015), is regarded worldwide as an authoritative text. He was honored as a Citation Laureate (2021) for pioneering research in free-radical chemistry including the role of free radicals and antioxidants in human disease. The distinction is awarded by Clarivate to researchers whose work is deemed to be of "Nobel Class" as they are among the most influential, even transformative, in their fields. He was one of 16 scientists (only three in Chemistry) listed in the 2021 Hall of Citation Laureates.



Prof. MARZIA PERLUIGI

Sapienza University of Rome

Biography

Marzia Perluigi, PharmD, Ph.D., Head of Laboratory of Redox Biochemistry in Neuroscience (LRBN). Professional appointments: Professor of Biochemistry, Department of Biochemical Sciences "A. Rossi Fanelli" - Medical School Sapienza University of Rome. Fields of Expertise: Biochemistry and cell biology.

The major research interest is the study of the role of oxidative stress in Down Syndrome (DS) and Alzheimer Disease (AD). Projects involve both the analysis of post-mortem brains, biological fluids, and cellular and animal models of the diseases. In particular, current projects focus on defects of energy metabolism, failure of protein quality control (UPS and autophagy), impairment of mitochondrial activity, both in DS and AD. Further, preclinical studies are ongoing to test the neuroprotective effects of selected compounds able to prevent/slow the onset of dementia.

Prof. MARK MATTSON

Johns Hopkins University

Biography

Mark Mattson is the former Chief of the Laboratory of Neurosciences at the National Institute on Aging and is now on the faculty of Neuroscience at Johns Hopkins University School of Medicine. His research has advanced an understanding of the cellular signaling mechanisms that control the formation and plasticity of neuronal networks in the brain, and cellular and molecular mechanisms of brain aging and neurodegenerative disorders. His research has also elucidated how the brain responds adaptively to challenges such as fasting and exercise, and he has used that information to develop novel interventions to promote optimal brain function throughout life. Dr. Mattson is among the most highly cited neuroscientists in the world with more than 900 publications and 200,000 citations. He was elected a Fellow of the American Association for the Advancement of Science and has received many awards including the Metropolitan Life Foundation Medical Research Award and the Alzheimer's Association Zenith Award.

Mattson is the author of the book "The Intermittent Fasting Revolution: The Science of Optimizing Health and Enhancing Performance."



2023 NAFF Committee Members:

Prof. D. Allan Butterfield (Chemistry) [Chair]

Prof. Marcelo Guzman (Chemistry)

Prof. Daret St. Clair (Toxicology/Cancer Biology)

For more information, contact Prof. D. Allan Butterfield at david.butterfield@uky.edu