glutamate receptor (NMDAR). Although several blockers of NMDARs were developed, their success in bringing about neuroprotection at the clinical level has so far been limited. This calls for a review of the current strategy and development of alternative approaches.

NMDAR has several subtypes arising from different combinations of subunits. These subtypes differ among themselves in their pharmacological and electrophysiological properties and also in their spatiotemporal distribution. It is necessary that these subtypes be targeted selectively for effective drug therapy. Most of the currently used drugs lack subtype specificity. Greater emphasis on development of subtype-specific drugs is a potential new strategy for better success in neuroprotection by NMDAR antagonists.

The lack of sufficient number of drugs, particularly those targeting NMDAR subtypes, could have been a consequence of the difficulties faced by the drug discovery process. Screening for drugs critically depends on the assay used for NMDAR activity. Drug screening against NMDAR uses electrophysiology or calcium imaging as activity assays. These methods are real time in nature and, hence, are technically demanding as well as expensive. We have developed a novel endpoint assay for calcium channels that is simple to use and is less expensive with the potential to aid high throughput screening efforts. In a limited screening for NMDAR inhibitors using this assay, we have identified several small molecules with NMDAR inhibitory potency. We have also identified a plant extract that inhibits a subtype of NMDAR. The extract also showed neuroprotective activity against excitotoxicity in primary cortical neurons in culture and *in vivo*.

We have also analyzed biochemical changes in the brain during excitotoxicity toward identifying downstream steps that could be drug targets. Many of the biochemical changes induced by excitotoxicity were prevented upon neuroprotective treatment by the NMDAR inhibitory plant extract that we identified. The facilitation provided by the new calcium channel assay methodology, the realization of the importance of subtype targeting, and the identification of new downstream steps as druggable targets are new approaches toward developing strategies for neuroprotection.

S10

Banking the Brain and Blood: Lifestyle Factors, Nutrigenomics, and Nutraceuticals Leading to Healthy Brain Aging

K. Ranil D. De Silva

Interdisciplinary Center for Innovation in Biotechnology & Neuroscience, Faculty of Medical Sciences, University of Sri Jayewardenepura (USJP), Sri Lanka

Address for correspondence: Prof. K. Ranil D. De Silva, Interdisciplinary Center for Innovation in Biotechnology & Neuroscience, Faculty of Medical Sciences, University of Sri Jayewardenepura (USJP), Sri Lanka.

E-mail: ranil@sjp.ac.lk

Studying environmental, cultural, lifestyle, and genetic factors, such as gene-diet interaction (nutrigenomics) leading to healthy brain aging and longevity, is crucial for identifying differential responses in clinical settings, as well as neurobiologic biomarkers that may be associated with neurological diseases. The human brain bank and Deoxyribonucleic acid (DNA) repository established in Sri Lanka is one of the largest biobanks in the Indian subcontinent that could facilitate as a cornerstone in translational neuroscience.

Primarily, we examined the possible protective role of Sri Lankan diet on healthy brain aging, and it was studied utilizing the following: the established *Human Brain Tissue* ($n = 76$) and *DNA/Gene Bank* of patients and controls with stroke, as well as neurodegenerative and neuromuscular disease, from one of the largest biobanks in the South Asian region (over 2500). Anatomicopathological studies were performed in cerebral arteries of 447 adult and 34 fetal postmortem brains and gene expression studies in six cerebral arteries. Age-related cytoskeletal pathologies were studied in 76 aging and diseased human brains using histopathological/immunohistochemical techniques for tau and β-amyloid biomarkers, and vascular genetic variants such as apolipoprotein E, angiotensin-converting enzyme, methylene tetrahydrofolate reductase (MTHFR C677T), and factor V Leiden (FVL G1691A).

We performed the first-ever comparison between Sri Lanka (Colombo, $n = 50$) and India (Bangalore, $n = 42$) on age-related cytoskeletal pathologies in aging autopsy brains, thus indicating the true extent of dementia burden in this part of the world. Furthermore, an *in-vitro* hypoxic model using human brain epithelial cells was studied with treatment of Ceylon green tea extract before inducing hypoxia.

The author will discuss the prevention of cumulative risk and formulate interventions in preventative neuroprotective measures through natural products, nutrigenomics, and lifestyle factors for optimization of better brain health. Furthermore, ongoing research by the author based on natural products would lay a stepping-stone for developing neuroprotective nutraceuticals based on unique regional natural products.

S11

Traffic Jams in Neurons

Sandhya Koushika

Department of Biological Sciences, Tata Institute of Fundamental Research (TIFR), Mumbai, Maharashtra, India

Address for correspondence: Dr. Sandhya Koushika, Department of Biological Sciences, Tata Institute of Fundamental Research (TIFR), Mumbai, Maharashtra, India.