Department of Biochemistry and Molecular Biology

PhD Oration

Wednesday 5th of September
3:30-4:30pm
Bio21 Institute Auditorium
30 Flemington Road, Parkville

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Deciphering Cell Death Signalling Pathways in Neuronal Excitotoxicity by Proteomics Approach

Excitotoxicity, a major pathological cellular process directing neuronal death, is caused by over-stimulation of ionotropic glutamate receptor. The neuronal death pathways of glutamate-mediated excitotoxicity contribute to brain damage in several acute neurological disorders such as cerebral stroke, traumatic brain injury and other chronic neurodegenerative diseases. During excitotoxicity, the damaged neurons release excess amount of glutamate which in turn overstimulated the extrasynaptic NMDA receptors, a subtype of glutamate receptors. The NMDA receptors are highly permeable to Ca2+ ions and upon overstimulation, excessive Ca2+ ions enter into the cellular space and over activates different Ca2+ dependent enzymes such as nitric oxide synthase (nNOS). This disproportion also activates different proteases, lipases and other enzymes such as NADPH oxidase 2 (NOX2). nNOS and NOX2 exert their neurotoxic action by initiating oxidative stress whereas proteases such as calpains govern cell death signal by proteolysis of specific neuronal proteins. These whole phenomena cause imbalance in protein abundance, phosphorylation state and functionality. Therefore, we aim to identify the association of post translationally modified neuronal proteins, proteases and NMDA receptors in glutamate mediated excitotoxicity by proteomics method. The first part will focus on the crucial role of phosphorylation and global changes of neuronal proteins in glutamate induced excitotoxicity by global and phosphoproteomic approach. Then the second part of this project entail on the identification and quantitation of the neuronal proteins by N-terminomics that undergo proteolysis in glutamate mediated neuronal excitotoxicity. Especially the investigation focuses on deciphering the signalling events triggered by overstimulation of NMDA receptor by glutamate. The final goal of this project is to unveil potential driver signalling pathways involved in excitotoxic neuronal death.

ALL WELCOME. Please join us for Pizza to celebrate this PhD Oration!
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