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RTICC

INTERNATIONAL GUEST SEMINAR

10th July
11:00-12:00



**4th Floor seminar Room, The Ruth and
Bruce Rappaport Faculty of Medicine**

“Proteasome Regulation: From Basic Mechanism to Neuro-protective Therapy”

Age-related neurodegenerative diseases, such as Alzheimer's Disease and Parkinson's Disease, pose major unmet health needs since neither cures nor treatments that address the root cause of these diseases currently exist. These diseases are associated with the accumulation of protein aggregates that are thought to impair cell function and eventually lead to neuronal degeneration. All our cells have potent clearance mechanisms to degrade unwanted and potentially dangerous proteins. The PI31 protein mediates fast transport of proteasomes, the nano-machines responsible for regulated protein degradation, between the neuronal cell body and synapses. Inactivation of PI31 impairs local protein degradation at synapses and initiates a cascade of events that eventually cause the formation of protein aggregates and neuronal degeneration. Strikingly, mutations that reduce the activity of PI31 have been found in human patients and cause a very severe, early onset form of Parkinson's Disease. These patients present a clear path for bringing PI31-based gene therapy to the clinic. If successful, this will make it possible to explore the neuro-protective role of PI31 in more common neurodegenerative diseases and normal brain aging.