TIFR Centre for Interdisciplinary Sciences
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Seminar

Decoding the Neural proteome in health and disease using (N)CATs

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Protein synthesis is one of the most critical processes in an organism's life, since proteins are the main executors of cellular function. In the brain there is a critical need for 'on-demand' protein synthesis in fast but spatially-restricted manner and this forms the foundation of several different types of memory encoding processes. Protein synthesis is therefore considered an inescapable requisite to proper brain functioning. Conversely dysregulated protein synthesis and expression is being linked to an increasing number of neurological diseases. Translation of mRNA to yield proteins is controlled by an elaborate control mechanism that is primarily downstream of signaling cascades that involve phosphorylating enzymes (or Kinases) called the mechanistic target of rapamycin complex 1 (mTORC1) and extra-cellular signal regulated kinase (ERK1/2). Both converge on p70 ribosomal S6 Kinase 1 (S6K1), yet another kinase, which then modulates the activity of downstream molecules that directly influence ribosome processing, initiation and elongation steps of translation. I will showcase how modulating S6K1, using genetic manipulation in mice and novel small molecule inhibitors, helped ameliorate disease-associated phenotypes in Fragile X Syndrome, a leading cause of inherited autism and intellectual disability.

In addition, I will discuss a method to overcome the informational gap that exists currently in neuroscience using non-canonical amino acid tagging (NCAT). Traditionally, most signaling and cell biology for neural systems is done in cultured cells, versus most circuit-based electrical properties are studied intact brain slices preparations. There are many cellular differences between a culture in a dish to a brain slice and this limits the extrapolation between the two experimental systems. To address this gap, I co-developed a tool that adopts existing proteomic techniques to work in intact brain tissue in response to a physiological stimulant like Brain Derived Neurotrophic Factor (BDNF) and in disease condition of Fragile X model mice. The method has allowed us to uncover novel schemes by which complex tissue respond to stimuli and regulate protein expression. Finally I will discuss how NCATs can be used to help devise reliable biomarkers for neuropsychiatric diseases.

Wednesday, Jul 27th 2016

4:00 PM (Tea/Coffee at 3:45 PM)

Seminar Hall, TCIS