BOSE INSTITUTE COLLOQUIUM

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Main Auditorium, Unified Academic Campus
Bose Institute

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Title and Abstract :

"Astro"logy and Autism: New insights from recordings in human brain cells

Pre-clinical studies of fragile X syndrome (FXS) have focused on neurons, with the role of glia remaining largely underexplored. We examined the astrocytic regulation of aberrant firing of FXS neurons derived from human pluripotent stem cells. Human FXS cortical neurons, co-cultured with human FXS astrocytes, fired frequent short-duration spontaneous bursts of action potentials compared with less frequent, longer duration bursts of control neurons co-cultured with control astrocytes. Intriguingly, bursts fired by FXS neurons co-cultured with control astrocytes are indistinguishable from control neurons. Conversely, control neurons exhibit aberrant firing in the presence of FXS astrocytes. Thus, the astrocyte genotype determines the neuronal firing phenotype. Strikingly, astrocytic-conditioned medium, and not the physical presence of astrocytes, is capable of determining the firing phenotype. The mechanistic basis of this effect indicates that the astroglial-derived protein, S100b, restores normal firing by reversing the suppression of a persistent sodium current in FXS neurons. Our results identify an important cell non-autonomous contribution of human astrocytes in correcting aberrant electrical activity in human FXS neurons, thereby suggesting a framework for exploring new therapeutic strategies aimed at human neuron-glia interactions.