TIFR Centre for Interdisciplinary Sciences
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Seminar

Molecular mechanisms regulating cell fate specification in the developing cerebral cortex

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The cerebral cortex is a complex brain structure that processes higher functions in distinct regions. Broadly, the neocortex is the seat of sensory perception, decision-making, language, while the hippocampus is critical for learning and memory. For these structures to function normally, a precise development of circuitry is essential, which entails a diverse array of neuronal subtypes and glia being generated in a sequential manner. Perturbations of this process can lead to a range of neurological diseases and disability.

I built on earlier work in the lab that demonstrated distinct roles for transcription factor Lhx2 in the development of the neocortex and the hippocampus, respectively. I explored the molecular mechanisms underlying these distinct functions by performing ChIP-seq from embryonic neocortex and hippocampus separately. I identified a range of potential targets, which I explored further in specific contexts, and uncovered novel functions for Lhx2 in the developing brain.

In the neocortical primordium, I showed that Lhx2 is bound to the enhancers of transcription factors required for specification of particular cortical neuronal subtypes. Furthermore, Lhx2 associates with chromatin modifiers, and causes epigenetic changes leading to suppression of select target genes. This is a novel function of Lhx2, as a key regulator of neuronal subtype identity in the neocortex. In the hippocampal primordium, I identified key neurogenic genes to be downstream targets of Lhx2, and showed that they are sufficient to rescue Lhx2 loss of function. Furthermore, a cross-species analysis shows that Lhx2 binds a region that is highly conserved across chick, Xenopus, human, and mouse. Lhx2 may therefore regulate an evolutionarily conserved mechanism in the hippocampus that suppresses astrogliogenesis until neurogenesis is complete.

Thursday, Jan 12th 2017

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

Seminar Hall, TCIS