Tata Institute of Fundamental Research
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Seminar

Motion, regulation, recognition in specialized nucleosome formation

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The basis of a successful cell division is the faithful segregation of the sister chromatids during mitosis and meiosis, a process driven by the formation of the kinetochore complex on the centromere. Centromeres in most eukaryotes are identified by the formation of specialized nucleosome(s) where the Histone 3 (H3) is replaced by a unique variant CENP-A (Centromeric protein-A). Histone variant CENP-A^{Cse4} is required for kinetochore assembly and is an epigenetic marker for centromere identity in budding yeast. The regulation of the cellular levels of Cse4 is primarily achieved by ubiquitin-mediated proteolysis. However, the structural transitions needed for centromere localization and its interaction with regulatory components are poorly understood. Using various biophysical techniques we showed that soluble Cse4 can exist in a 'closed' conformation, inaccessible to various regulatory components. We also characterized its interaction with obligate partner H4, which stabilizes Cse4, ensuring an 'open' state that will lend itself to proteolysis and allow interaction with kinetochore proteins. Our dynamic model shows allosteric effect of H4 binding on Cse4 N-terminus, which is required for interaction with centromeric components. The specific requirement of H4 binding for the conformational regulation of Cse4 suggests a novel structure-based regulatory mechanism for Cse4 localization and prevention of premature kinetochore assembly.

Wednesday, Nov 22nd 2017

04:00 PM (Tea/Coffee at 03:30 PM)

Auditorium, TIFR-H (FReT-B)