

Seminar

Weavers of Actin Cytoskeletal Networks: Structural Insights into Arp2/3 Complex Activation by Nucleation Promoting Factors

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The polymerisation of actin filament networks is crucial for cellular processes such as motility, morphogenesis, endocytosis, and DNA repair. This tightly regulated process depends on the nucleation of new actin filaments, a critical step enabling precise control over filament formation. Central to this process is the Arp2/3 complex, a ubiquitous actin nucleator whose activity is meticulously controlled by nucleation promoting factors (NPFs). Dysregulation of Arp2/3-mediated actin nucleation is implicated in cancers and developmental disorders. Despite extensive research, the mechanism of Arp2/3 complex activation by NPFs and the initiation of actin polymerisation remained elusive due to the lack of structural information on the activated complex. Moreover, how these NPFs dictate different actin architectures are still not clearly understood. To address this gap, we utilised cryo-Electron Microscopy (cryo-EM) to determine high-resolution structures of the activated Arp2/3 complex. Our findings not only provide insights into the active conformation of this key actin nucleator but also reveal specific conformational changes and molecular interactions that occur during activation and how different NPFs influence the architecture of actin assembly in cells. By elucidating the molecular mechanisms underlying Arp2/3 complex activation and actin polymerisation, our study contributes to a deeper understanding of cellular processes and may offer new avenues for therapeutic intervention in diseases associated with dysregulated actin dynamics.

Friday, Aug 2nd 2024

16:00 Hrs (Tea / Coffee 15:45 Hrs)

Auditorium, TIFR-H