

Nucleotide-dependent conformational changes in Tubulin dimer and the effects of Mutations: Insights into Microtubule Dynamic Instability

Prof. Sanjib Senapati

Department of Biotechnology, Indian Institute of Technology Madras

Date	:	6 May 2016 (Friday)
Time	:	4:30 – 6:00 p.m.
Venue	:	SCM 809
Language	:	English
Facilitator	:	Prof. Li Min

Abstract

The complex dynamical behavior of microtubules (MTs) is believed to be primarily due to the $\alpha\beta$ -tubulin dimer architecture and its intrinsic GTPase activity. Hence, a detailed knowledge of the conformational variations of isolated α -GTP- β -GTP- and α -GTP- β -GDP-tubulin dimers in solution and their implications to interdimer interactions and stability is directly relevant to understand the MT dynamics. Moreover, the vital role of tubulin dimer in cell division makes it an attractive drug target. Drugs that target tubulin showed significant clinical success in treating various cancers. However, the efficacy of these drugs is attenuated by the emergence of tubulin mutants. In this talk, I will discuss results from molecular dynamics simulations, protein-ligand docking, and free energy calculations to show the conformational variations in $\alpha\beta$ -tubulin dimer in different nucleotide states and correlate the observed changes to MT dynamics. We will also examine the binding of anticancer drugs, taxol and epothilone to the reported point mutants of tubulin and explain the molecular basis of drug resistance. At the end, I will briefly talk about a novel solvent media that can enhance the stability and/or activity of DNA and several proteins.

~ ALL ARE WELCOME ~