学 位 論 文 の 要 約

博士の専攻分野の名称　博士（理学）　　　　氏名　ノウローズ　セジュティ

学 位 論 文 題 名

Study of the Effect of Tubulin C-terminal Tail on Mechanical Properties of Microtubule and Interaction with its Associated Motor Protein
(微小管の機械的特性および関連モータータンパク質との相互作用に対する
チューブリン C 末端尾部の効果研究)

Microtubules (MTs), polymerized from αβ tubulin heterodimers, are essential for cellular functions like maintaining cell shape, cell movement, mitosis, intracellular cargo transport, etc. Each tubulin is composed of an ordered core and an extended flexible segment called the C-terminal tail (CTT). Both the ordered core and the disordered CTT of tubulin undergo modifications while MTs perform their diversified functions. Compared to the tubulin cores, the CTTs that protrude from the MT surface are more prone to such modifications.
Previous studies show that the removal or addition of one or more residues on the CTT can alter the MT properties and interaction with its associated proteins, for example, dynein, tau, etc. However, the effect of the absence of the CTT on MTs mechanical properties, for example, bending rigidity and their interaction with one of the most studied motor proteins, kinesin remains elusive. In this dissertation, I examined the influence of CTTs in altering the bending rigidity of MTs and investigated their potential role in modulating the interaction between MTs and kinesin.
To investigate the effect of CTT on the mechanical properties of MTs and their interaction with kinesin, the CTT was removed by treating the native tubulin with a digestive enzyme, subtilisin. The removal of CTT was confirmed using SDS-PAGE and MALDI-TOF mass spectroscopy techniques. To understand the effect of CTT on MT bending rigidity, the persistence lengths of MTs polymerized from native and modified tubulin were determined. Further, the bending rigidity was estimated by studying the response of both the MTs to mechanical stress, in this case, compressive stress. Both the MTs show buckling behavior when gradual compressive stress is applied. By analyzing the wavelengths of buckled MTs, their bending rigidity has been estimated. The bending rigidity is found to be altered in the absence of CTT. This study will provide better opportunities to exploit MTs in biomechanical applications where the tuning of mechanical properties of microtubules is important. To study the role of CTT on the interaction of MTs with its motor protein kinesin, kinesin-driven cargo (quantum dot) transport has been demonstrated along MTs polymerized from native and modified tubulins in the presence of ATP. By analyzing the kinesin-driven cargo velocity along both the MTs, I found that the removal of the tubulin CTTs altered the motility of kinesin along MTs. Molecular Dynamics (MD) simulations of the tubulin-kinesin complex with and without CTT were conducted to reveal the altered interaction energies between tubulin dimer and kinesin in the absence and presence of CTT. These results complement the experimental findings and highlight the impact of CTT on tubulin-kinesin binding. These results may provide new insight into MT-kinesin interaction potentially leading to finding the cause and prevention of neurodegenerative diseases.