“Toward understanding Structural and Molecular Sociology of Life”

: Integrative Structural Studies on Neurodegenerative Disease Proteins

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Proteins are molecular machines in cells to maintain life. These molecular machines are often composed of many different proteins. However, little is known about the complexity and diversity of protein complexes and supramolecular structures in-cell and their functions.

My research focuses on three areas 1) to understand molecular mechanism of epigenetic gene regulation focusing on nucleosome assembly, modification and recognition, 2) to understand the mechanism by which neurodegenerative disease proteins cause the diseases, and lastly 3) to understand structural and molecular sociology of protein complexes in diverse organisms and cells via a comparative and comprehensive analysis.

Among these research programs, here, I will present our on-going integrative structural studies on a neurodegenerative disease protein-Huntington’s disease protein. Huntington’s disease (HD) is caused by mutation causing polyglutamine (PolyQ) tract expansion in huntingtin protein. We analyzed the structural and functional changes caused by PolyQ expansion in protein via an integrative structural approach including cryo-electron microscopy, mass spectrometry, small angle x-ray scattering and molecular dynamics modeling as well as biochemical approaches. Our data shows that the polyQ expansion at the N-terminus of the protein affects global structural and functional changes in the protein, which is involved in the HD pathology. Furthermore, we are seeking to develop means to regulate the structure and function of huntingtin protein, which might lead to develop therapeutics for the devastating HD.