University of Texas at San Antonio

Department of Physics & Astronomy

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Time: 3:00 p.m.-4:00 p.m.

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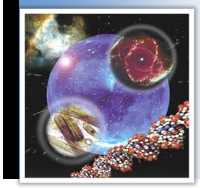
Understanding Macromolecular Function via Direct Visualization using Cryo-Electron Microscopy

Cryo-electron microscopy (Cryo-EM) has become a major tool in the structural characterization of large macromolecular assemblies, their architecture, interactions with different ligands, and the regulation of their function. I will present two different examples of how cryo -EM is being used in my lab to understand the molecular mechanisms of complex biological systems.

During division the eukaryotic cell needs to accurately segregate its genetic material between daughter cells. This process involves the interaction of the microtubule mitotic spindle with special regions on chromosomes called kinetochores. Errors, which result in misplaced chromosomes, can lead to cancer or death. We have visualized the interaction of microtubules with two kinetochore components, the yeast Dam1 and the human Ndc80 complexes, using cryo-electron microscopy and image reconstruction. Interestingly, both complexes oligomerize on the surface of the microtubule, a property that is essential for their capacity for harness the energy of microtubule depolymerization for chromosome movement.

Bacteria acquire resistance to viruses by integrating short fragments of foreign DNA into Clustered Regularly Interspaced Short Palindromic Repeats (CRISPRs), which serve as molecular vaccination cards CRISPRs are transcribed and the processed into a library of short CRISPR-derived RNAs (crRNAs). These crRNAs are incorporated into a large surveillance complex called Cascade, required for protection against bacteriophage. We have determined the structure of the complex and shown that the crRNA is displayed along a helical arrangement of protein subunits that protect the crRNA from degradation, while maintaining availability for base pairing. Binding of complementary nucleic acid triggers a concerted conformational change that may serve to recruit a nuclease for destruction of invading nucleic acid sequences.



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