SLAC COLLOQUIUM SERIES

# Visualizing Structure, Dynamics and Interactions of Macromolecules Controlling the Reading of our Genes

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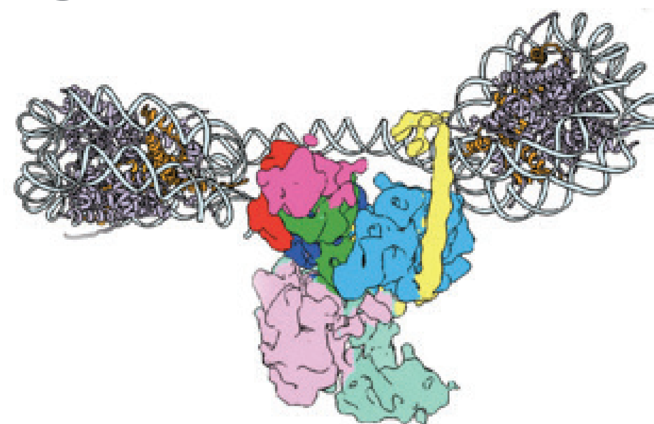

**Abstract:**
Cryo-electron microscopy (cryo-EM) is a technique capable of visualizing challenging systems that otherwise defy structural characterization, as it overcomes the need for crystallization, requires only small sample amounts, and has the potential to deal with and describe compositional and conformational mixtures. Therefore, cryo-EM can be used to investigate complete and fully functional complexes in different functional states, providing a richness of biological insight. Recent technical advances have dramatically increased its applicability, throughput and achievable resolution. My lab is using cryo-EM in the study of complex machinery involved in the regulation of gene expression in humans. Covalent modification of the N-terminal tails of histone proteins that package DNA in nucleosomes in eukaryotes, is a fundamental mechanism of epigenetic gene regulation. Histone modifying enzymes catalyze the deposition or removal of these histone marks, which can in turn be bound by specific recognition modules within larger protein assemblies that serve gene regulatory functions. Trimethylation of lysine 27 on histone H3 (H3K27me3), catalyzed by polycomb repressive complex 2 (PRC2), leads to gene silencing of developmental and cell fate determining genes within multicellular organisms. We have obtained cryo-EM structures of human PRC2 in two distinct, active states, while in complex with its cofactors JARID2 and AEBP2. We have also visualized how human PRC2 engages with a complex chromatin substrate. Our analysis defines the complete architecture of a functionally relevant PRC2 and provides a structural framework to understand its regulation by cofactors and histone tails.

April 30, 2018, Kavli Auditorium, Refreshments and Colloquium Start at 3:45pm