UC RIVERSIDE

BCH 252 Seminar Series

Xinyi Chen, Biochemistry & Molecular Biology Graduate Student, UC Riverside

Seminar Title: "Structural basis for the H2AK119ub1-specific DNMT3A-nucleosome interaction"

Abstract: Isoform 1 of DNA methyltransferase DNMT3A (DNMT3A1) specifically recognizes nucleosome monoubiquitylated at histone H2A lysine-119 (H2AK119ub1) for establishment of DNA methylation. Mis-regulation of this process may cause aberrant DNA methylation and pathogenesis. However, the molecular basis underlying DNMT3A1−nucleosome interaction remains elusive. Here we report the cryo-EM structure of DNMT3A1's ubiquitin-dependent recruitment (UDR) fragment complexed with H2AK119ub1-modified nucleosome. DNMT3A1 UDR occupies an extensive nucleosome surface, involving the H2A-H2B acidic patch, a surface groove formed by H2A and H3, nucleosomal DNA, and H2AK119ub1. The DNMT3A1 UDR's interaction with H2AK119ub1 affects the functionality of DNMT3A1 in cells in a context-dependent manner. Our structural and biochemical analysis also reveals competition between DNMT3A1 and JARID2, a cofactor of polycomb repression complex 2 (PRC2), for nucleosome binding, suggesting the interplay between different epigenetic pathways. Together, this study reports a molecular basis for H2AK119ub1-dependent DNMT3A1−nucleosome association, with important implications in DNMT3A1-mediated DNA methylation in development.

Tuesday, November 5th, 2024 12:00 p.m. - 12:50 p.m. PST

In-Person: Genomics Auditorium 1102A

Host: Dr. Xuan Liu