Johns Hopkins University

Department of Biology Seminar Series

Tuesday, 4:00pm

For more information go to: https://bio.jhu.edu/events

Zoom link: https://zoom.us/j/97925356454?pwd=bjNuTlY1dU9BcXcvRFdleis2TVNadz09

April 23rd, 2024 - Mudd 100

Matthew Wooten

Basic Sciences

Fred Hutchinson Cancer Research Center

Host: Xin Chen

"Visualizing changes in chromatin structure over cellular and developmental time"

Factors that bind DNA and regulate accessibility create distinct chromatin structures that must be preserved to maintain proper gene expression patterns. However, chromatin structure must also change to facilitate cell cycle progression and differentiation. To understand how changes in chromatin structure are regulated during development, I have developed two methods, termed Nascent CUT&Tag and CUT&TIME, that allow me capture transient chromatin structures at discrete temporal windows. During cell cycle progression, DNA replication represents an unparalleled challenge to the maintenance of chromatin structure, as all chromatin factors must be removed from DNA to allow for passage of the replication fork. Transcription factors (TFs) are a critical component of chromatin structure that bind to target motifs to specify and maintain gene expression. As TF binding sites become occluded by nucleosomes following passage of the replication fork, the mechanisms that enable TFs to rebind newly synthesized DNA are unclear. I have developed a method, termed Nascent CUT&Tag, to capture TF binding on newly synthesized DNA and quantitatively track maturation over time. Using Nascent CUT&Tag, I have shown that while certain binding sites rapidly recover TF occupancy, others recover more slowly. Fast recovering sites contain strong TF binding motifs, while slow recovering sites are characterized by degenerate motifs and multiple TF binding events, suggesting that cooperative binding may play a critical role in reestablishing TF binding following passage of the replication fork. In retinal development, multipotent retinal progenitor cells differentiate into distinct cell types. However, the molecular mechanisms that direct retinal progenitors to adopt distinct cell fates remains unclear. To better understand and map developmental trajectories of retinal neurons, I have developed a method, termed CUT&TIME, that allows me to track the historical open chromatin of a progenitor cell during differentiation. Using human retinal organoids, I demonstrate that CUT&TIME can capture the historical chromatin state of retinal ganglion cells. CUT&TIME also reveals that progenitor cells exhibit a unique chromatin landscape defined by broad accessibility across cis regulatory elements. These results indicate that CUT&TIME is a useful tool to characterize and track changes in chromatin structure across development.