Johns Hopkins University

Department of Biology Seminar Series

Thursdays, 4:00pm

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

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

April 20th, 2023 - Mudd 100

Melissa Harrison

Department of
Biomolecular Chemistry

University of
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Host: Bob Johnston

"Pioneers, settlers and life on the OregonR trail: transcriptional regulation during development"

The DNA genome is differentially interpreted over development, ensuring expression of genes where and when they are needed. My long-standing interests focus on this essential biological process and the mechanisms by which the cis-regulatory modules that govern gene expression are reprogrammed to cause dramatic changes in cell fate. Leveraging the strengths of the Drosophila system, we are defining the fundamental mechanisms that drive conserved developmental transitions. We identified specialized transcription factors, termed pioneer factors, that control these transitions. Pioneer factors are distinctive in that, unlike other transcription factors, they bind to DNA in the context of nucleosomes. This feature allows them unique access to the genome and helps to redefine the chromatin accessibility landscape. Because of their ability to reprogram cell fate, mis-expression of pioneer factors are correlated with numerous different cancers. Nonetheless, the specific functions of pioneer factors that enable efficient reprogramming and the biological barriers that restrict it remain unclear. We defined the essential role of pioneer factors in the rapid and efficient reprogramming that follows fertilization as the genomes of the specialized germ cells are unified to generate an entirely new organism. Using the power of the early embryo, we uncovered key properties of pioneer factors in defining both the active and silent genome. We further defined roles for pioneer factors in stem-cell populations, allowing us to define universal mechanisms that regulate cell-fate transitions. Building on the systems we developed, we continue to address fundamental questions regarding how multiple pioneer factors cooperate to allow for efficient genome reprogramming, what cell-type-specific features regulate pioneer activity, and how dysregulation of gene expression leads to disease. Understanding how specialized factors structure the genome to promote gene expression programs necessary for cell-fate specification will have important implications for understanding both normal development and how mis-regulation leads to disease.