ASHBi / CiRA JOINT SEMINAR

Epigenetic Regulation of Cell Identity in Tissue Homeostasis and Diseas

Lecturer: **Masaki Yagi, Ph.D.**
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Time 17:00 – 18:00 [JST]

\ No registration required /

Venue CiRA Auditorium
1F, Center for iPS Cell Research and Application Bldg. #1

Abstract

Mammalian development and cellular differentiation are guided by dynamic changes to posttranslational histone modifications, which correlate with specific transcriptional states. Lysine-to-methionine (K-to-M) substitutions of histone H3 have recently emerged as powerful tools to dissect the physiological roles of histone marks. Histone H3 K-to-Mmutants function as dominant alleles that substantially reduce methylation levels at non-mutated copies of histone H3 at specific lysines across the genome without disrupting the respective enzymes. In contrast to methyltransferase knockout models, K-to-M mutations function as hypomorphs, allowing modulation of histone marks in contexts where genetic disruption of the enzyme is deleterious to viability. Building off these observations, we have developed transgenic histone mutant mouse models to perturb H3K4me and H3K27me in an inducible and reversible manner, allowing us to dissect the functional significance of these classic histone modifications in tissue homeostasis and malignant transformation. We have uncovered specific as well as combinatorial roles for H3K4me and H3K27me at different stages of hematopoiesis, suggesting that the expression of certain bivalent genes is crucial for hematopoietic differentiation (Yagi et al., Cell 2025). In addition to elucidating the biological functions of two antagonistic histone marks in hematopoiesis specifically, our work expands our fundamental understanding of how H3K4 and H3K27 methylation including bivalent chromatin may control development, tissue homeostasis and pathogenesis more generally.

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