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Wednesday, July 5, 2023

14:00-15:00

1F Auditorium, DB Building C, Kobe / Broadcast online via Zoom

Zoom meeting URL will be announced on the event day by e-mail.

※Non-BDR members: Please register from the following link.

<https://krs1.riken.jp/m/bdrseminarregistration> (Registration deadline July 3)

Chromatin compaction measured by single-cell imaging predicts epigenetic memory

Summary

Epigenetic memory, mitotically stable changes in gene expression mediated by chromatin modifications, is ubiquitous across many dynamical biological systems, and used to remember past signals, such as differentiation, infection, or metabolic stress. Repressive chromatin modifications are thought to compact chromatin to silence gene expression. However, the dynamics of chromatin state remains unknown, especially whether chromatin compaction remains after epigenetic memory establishment and whether compaction is correlated with gene silencing or epigenetic memory. Here, we used multiplexed DNA FISH to measure 3D chromatin structure changes after direct recruitment and release of chromatin regulators to a reporter gene. KRAB recruitment, known to cause epigenetic memory, leads to chromatin compaction across tens of kilobases that is retained in stably silenced cells even after KRAB release. Silencing by histone deacetylase HDAC4 does not lead to epigenetic memory nor large-scale compaction, suggesting transcriptional silencing is not sufficient to induce chromatin compaction at the tens of kilobases scale. Compaction arises at the average level, but chromatin structure is heterogeneous in single cells, with open and compacted conformations present in both active and silent cells. By varying the duration of KRAB recruitment and using KRAB mutants with partial loss of function, we generate cell populations with different percentages of stably silenced cells (i.e., epigenetic memory), and find that chromatin compaction upon recruitment quantitatively predicts the epigenetic memory weeks later. Finally, this quantitative connection also holds in a natural gene regulatory context: chromatin compaction at the Nanog locus predicts mouse ES cell fate commitment. These findings suggest that chromatin compaction upon transient epigenetic silencing is predictive of future gene expression.