CDB SEMINAR

Makiko Iwafuchi-Doi

University of Pennsylvania, Perelman School of Medicine, USA

Wednesday, September 13, 2017
16:00~17:00 Seminar Room A7F

Developmental Role and Mechanistic Insight into Chromatin Opening by Pioneer Factor FoxA

Gene regulation occurs in the context of chromatin, the complex of DNA and histone proteins that makes up nucleosomes, where linker histones stabilize a repressive, closed configuration. A distinct combination of transcription factors is necessary to elicit cell fate changes in embryonic development and cellular reprogramming. Within each group of fate-changing transcription factors, a subset called "pioneer factors" are dominant in their ability to engage silent chromatin and recruit other transcription factors, thereby imparting a new function to regulatory DNA sequences. However, the molecular mechanisms by which pioneer factors open chromatin remains unclear. Here we demonstrate that a pioneer factor FoxA, but not ATP-dependent chromatin remodelers, opens chromatin compacted with linker histones, which then allows chromatin remodelers to further open chromatin. We identified a chromatin opening domain in FoxA C-terminus that potentially interacts with core histones. When we deleted the chromatin opening domain in the mouse FoxA2 genomic locus, but kept the other FoxA2 parts intact, including the DNA binding and transactivation domains, chromatin opening and embryonic development were markedly affected. These studies provide mechanistic insight into chromatin opening and can ultimately enhance our ability to control chromatin state at will.

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Chromatin Scanning by Dynamic Binding of Pioneer Factors.
Mol Cell. 2016 Jun 2;62(5):665-7. Review.

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The Pioneer Transcription Factor FoxA Maintains an Accessible Nucleosome Configuration at Enhancers for Tissue-Specific Gene Activation.
Mol Cell. 2016 Apr 7;62(1):79-91.

Host:
Mitsuru Morimoto
Lung Development, CDB
mmorimoto@cdb.riken.jp
Tel: 078-306-3199 (ext:1602)