The 467th IMEG Seminar

【Date】 Jul. 3 (Mon), 2023 17:30～18:30

【Venue】 Conference room, 1st floor,
Institute of Molecular Embryology and Genetics (IMEG),
Kumamoto University

【Title】 Stem cell potency and cellular identify in the germline

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【Abstract】

Spermatogonial stem cells (SSCs) support life-long fertility in adult males by balancing self-renewal and differentiation to produce haploid gametes in a slow-cycling cell population. However, it remains unknown how long-term SSC potency in adults is molecularly regulated. We discover that an epigenetic regulator, Polycomb repressive complex 1 (PRC1), shields SSC potency, maintains slow cycling, and directs commitment to differentiation during steady-state spermatogenesis in adults. Our quantitative epigenomic profiling uncovers PRC2-mediated H3K27me3 as a hallmark of SSC potency. Indeed, spermatogonial differentiation is accompanied by a global loss of H3K27me3. Loss of PRC1 impairs global deposition of H3K27me3, leading to precocious activation of the spermatogonial differentiation program and ectopic activation of somatic genes in undifferentiated spermatogonia. Importantly, unlike other tissue-specific stem cells where PRC1 promotes cell cycle progression, PRC1 functions as a negative regulator of the SSC cell cycle that maintains slow cycling. Our findings have implications for how epigenetic regulators can be tuned to regulate stem cell potency, the cell cycle, and differentiation to ensure life-long fertility in adult males. Further, by performing a high-resolution Hi-C analysis of representative stages of mouse spermatogenesis, we found that 3D chromatin predetermines gene expression programs required for spermatogenesis. We propose that CTCF-mediated 3D chromatin underlines epigenetic priming to direct unidirectional differentiation in the male germline.

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