東京農業大学　生物資源ゲノム解析センター　特別講演

日時:2015 年 11 月 12 日(木)16:00~17:30　会場:講義棟 633 教室

Medical Genetics, University of British Columbia

Prof. Matthew C. Lorincz

“Impact of LTR Retrotransposons on the Transcriptome and Methylome in Mouse Oocytes”

DNA methylation is highly dynamic in mammalian development. Following the wage of DNA demethylation that takes place in PGCs, de novo methylation in the female germline takes place after birth in growing germinal vesicle oocytes (GVOs). Curiously, while DNA methylation levels overall are significantly higher in sperm than in oocytes, analysis of the methylation state of CpG Islands (CGIs) using whole genome bisulphite sequencing identified 1,329 oocyte-specific CGI DMRs but only 349 sperm-specific CGI DMRs. Transcription-coupled de novo methylation mediated by oocyte-specific transcription units may explain the significantly higher number of methylated CGIs in GVOs. Indeed DNMT3A and DNMT3L are required for de novo methylation of intragenic regions in GVOs, as well as imprinted and non-imprinted CGIs, indicating that transcription per se is broadly required for de novo methylation in oocytes. Retrotransposons constitute >40% of the human and mouse genomes. A subset of these intracellular parasites, including specific long terminal repeat (LTR) elements, are transcriptionally active only at specific developmental stages. RNAseq analysis of GVOs reveals that the mouse transposon (MT) family of non-autonomous mammalian apparent LTR retrotransposons (MaLRs), the most abundant ERV family in the mouse, is the most highly transcribed family in growing oocytes, but inert in the male germline. I will present our recent work indicating that transcription emanating from MT LTRs is likely responsible for transcription-coupled de novo methylation of a significant fraction of the intergenic methylation observed in oocytes, including many CGIs and a subset of gametic imprinted DMRs. Furthermore, using a novel bioinformatics approach applied to paired-end RNAseq data, we identified dozens of genes that are driven by chimaeric transcripts initiating in LTRs, including many genes shown previously to play important roles in oocyte function. Taken together, these observations reveal that retrotransposons have a profound effect on the methylome, imprintome and transcriptome in the mammalian germline.

RIKEN Center for Integrative Medical Sciences (IMS)

Dr. Jafar Sharif

“Role of reader proteins that recognize ubiquitinated uH2A for Polycomb-mediated gene silencing”

Polycomb group (PcG) proteins comprise mainly two distinct repressive modules, namely, Polycomb Repressive Complex 1 (PRC1) and 2 (PRC2), which mediate gene silencing via ubiquitination of histone H2A (uH2A) and histone H3 lysine 27 trimethylation (H3K27me3), respectively. Such transcriptional repression by PcG complexes plays a major role to keep developmental genes at a "poised" state in embryonic stem (ES) cells. According to the established model, H3K27me3 deposition by PRC2 recruits PRC1 to induce uH2A-mediated chromatin compaction. Interestingly, this notion has been recently challenged by several papers showing that PRC1 recruitment could in turn bring PRC2, most likely through recognition of uH2A. Indeed, recent reports have revealed that JARID2 and AEBP2, two proteins included in the PRC2 complex, facilitate PRC2 recruitment by recognizing uH2A. Intriguingly, H3K27me3 marks were reduced but not completely removed in Jarid2 knockout ES cells, indicating that other recruiter(s) could also play a role to bring PRC2 by recognizing uH2A. We have recently found that PRC2 recruitment and H3K27me3 deposition in PcG-target loci substantially depend on a uH2A reader, which is not part of either PRC1 or PRC2, and is paradoxically well-known for its functions in DNA methylation. Our study thus reveals a new role for epigenetic reader/regulator proteins that are not included in the classical PcG complexes but nonetheless possess the ability to profoundly affect PRC recruitment and downstream gene silencing.

英語でのセミナーとなります。お問い合わせは小林までお願いします。

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