

慶 應 医 学 会 例 会

下記により例会を開催いたしますので、多数ご来聴ください。

記

日 時 2017 年 12 月 1 日 (金) 17 : 00

場 所 東校舎 1F セミナールーム

演 題 **A non-catalytic function of MLL/SET H3K4
methyltransferase in acute myeloid leukemia cells**

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Epigenetic regulations of chromatin state by mediator enzymes play an important role in the control of gene expression during normal development and cancer. The disease-specific transcriptional regulation is an attractive therapeutic target and there is an increasing demand for identification of target molecule as well as development of epigenetic drugs. MLL/SET methyltransferases catalyze methylation of histone 3 lysine 4 and play critical roles in development and cancer. We assessed MLL/SET proteins and found that SETD1A is required for survival of acute myeloid leukemia (AML) cells. Mutagenesis studies and CRISPR-Cas9 domain screening, showed the enzymatic SET domain is not necessary for AML cell survival but that a newly identified region, termed the FLOS (Functional Location on SETD1A) domain, is indispensable. The FLOS domain acts as a Cyclin K-association site that is required for chromosomal recruitment of Cyclin K, and for DNA repair-associated gene expression in S phase. These data identify a connection between the chromatin regulator SETD1A and the DNA damage response that is independent of histone methylation, and suggests that targeting SETD1A and Cyclin K complexes may represent a therapeutic opportunity for AML and potentially other cancers.

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(内線 62384)

以上

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