40th IRCMS Seminar

Date: **July 17, 2018 (Tue)**

Time: 16:00-17:00

Venue: 1F Meeting Lounge
International Research Center
for Medical Sciences(IRCMS)

Speaker: **Dr. Takayuki Hoshii, Ph.D.**
Scientist I
Department of Pediatric Oncology, Dana-Farber Cancer Institute,
Division of Hematology/Oncology, Boston Children's Hospital,
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Title: **Identification and targeting of the transcriptional vulnerabilities in leukemia**

Abstract: 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 a 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. We also identified FLOS subunits for DNA repair-associated gene expression in S phase. These data indicate a connection between the chromatin regulator SETD1A and the DNA damage response, and suggests that targeting newly identified SETD1A complexes may represent a therapeutic opportunity for AML and other cancers.

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