



第 387 回 つくば分子生命科学セミナー

TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR

演題 : The epigenetic role of TET2 proteins in the development of myeloid leukemia

演者 : Dr. Kazuyuki Yamagata

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日時 : 2013年11月21日 (木) 17:00-18:00

会場 : イノベーション棟 1階 105 会議室

セミナーは日本語です。 This seminar will be held in Japanese

How do gene mutations lead to cancer? Myeloid leukemia (ML) is a type of blood cancer where normal myeloid differentiation is impaired, and multiple gene mutations have been identified in myeloid leukemia patients to contribute to cancer initiation and/or progression. Hematopoiesis and myeloid differentiation are well understood, providing researchers a handle to define the roles of the identified genetic mutations. Among those identified are the TET oncogene family member 2 (TET2) mis-sense mutations, found in several independent cohorts of patients with massive myeloproliferative disorders. However, the mechanism by which TET2 mutations cause ML is completely unknown. TET1, an ortholog of TET2, catalyzes the conversion of 5-methylcytosine (5mC) in DNA to 5-hydroxymethylcytosine (hmC), which hints that epigenetic regulation plays critical roles for leukemia development caused by TET2 mutations. Importantly, approximately ~30 % of the missense mutations in affected persons are clustered in a cysteine-rich (CR) region, whose function has remained elusive.

Here we identify the CR region as a nucleosome-binding module. Mutation of the CR region affects its nucleosome binding. Using microscale thermophoresis, we screened histone tail peptides and identified potential binding partner(s) for the CR. CR mutations which lack H3-binding still possess enzymatic activity of the conversion from 5mC to hmC *in vitro*, but this function is strongly impaired *in vivo*. These findings indicate oncogenic mutations in the CR region of TET2 impair its nucleosome-binding activities, which may contribute towards the development of leukemia.

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