

# 学位論文の要旨

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<p>主論文の題名</p> <p><i>Bahcc1</i> is critical for the aberrant epigenetic program in a mouse model of <i>MLL-ENL</i>-mediated leukemia</p> <p>主論文の要旨</p> <p>In leukemogenesis, genotoxic stress in hematopoietic stem and progenitor cells (HSPCs) drives individual context-dependent programs of malignant transformation. In light of the various differentiation stages of HSPCs based on a recently revised definition using CD150/CD48, our analyses showed that a subpopulation of long-term-repopulating HSCs was most susceptible to <i>MLL-ENL</i>-mediated transformation. An analysis of the molecular mechanism identified <i>Bromo-adjacent homology domain and coiled-coil containing 1</i> (<i>Bahcc1</i>), which encodes a reader molecule of trimethylated histone H3 lysine 27 (H3K27me3), as a candidate gene involved in distinct susceptibility to leukemic transformation. Interestingly, <i>Bahcc1</i> was previously reported to be highly expressed in acute myeloid leukemia (AML) with an unfavorable prognosis, including some cases of <i>MLL</i>-rearranged AML. We found that <i>MLL-ENL</i> upregulated <i>Bahcc1</i> through binding to its promoter, and that <i>Bahcc1</i> was involved in <i>MLL-ENL</i>-mediated immortalization at least partly through repression of H3K27me3-marked <i>Cdkn1c</i>. Analyses using bone marrow transplantation in mice showed that depletion of <i>Bahcc1</i> suppressed the leukemogenic activity of <i>MLL-ENL</i>. These findings shed light on the distinct immortalization potential of HSPCs and suggest a novel <i>MLL-fusion-Bahcc1</i> axis, which may lead to development of molecular targeted therapy against <i>MLL-fusion</i>-mediated leukemia.</p>			