

## Details of the numbers of patients and controls with copy number loss in each subtelomeric region

Establishment of a mechanistic basis underlying the pathogenesis of high-risk leukemia associated with chromosomal translocation and inversion

### Professor YAMAMOTO, Masayuki

Professor Masayuki Yamamoto and Lecturer Mikiko Suzuki at Tohoku University Graduate School of Medicine discovered a mechanism to activate EVI1 proto-oncogene in leukemia associated with chromosomal translocation and inversion between 3q21 and 3q26. The chromosomal rearrangements induce overexpression of EVI1 proto-oncogene located on 3q26, which results in leukemia with poor prognosis. Prof. Yamamoto et al. generated a novel leukemia mouse model recapitulating the human inverted allele between 3q21 and 3q26 by linking two bacterial artificial chromosome (BAC) clones of a human genome library and found that GATA2 gene distal hematopoietic enhancer on 3q21 induces EVI1 gene overexpression specifically in hematopoietic stem and progenitor cells, which leads to leukemogenesis. The results provide new strategies for therapies that target gene-regulatory regions activating proto-oncogenes, in addition to those that target proto-oncogenes. The results of this research were published in *Cancer Cell* and an illustration representing the concept of this study were selected as a cover of the journal.

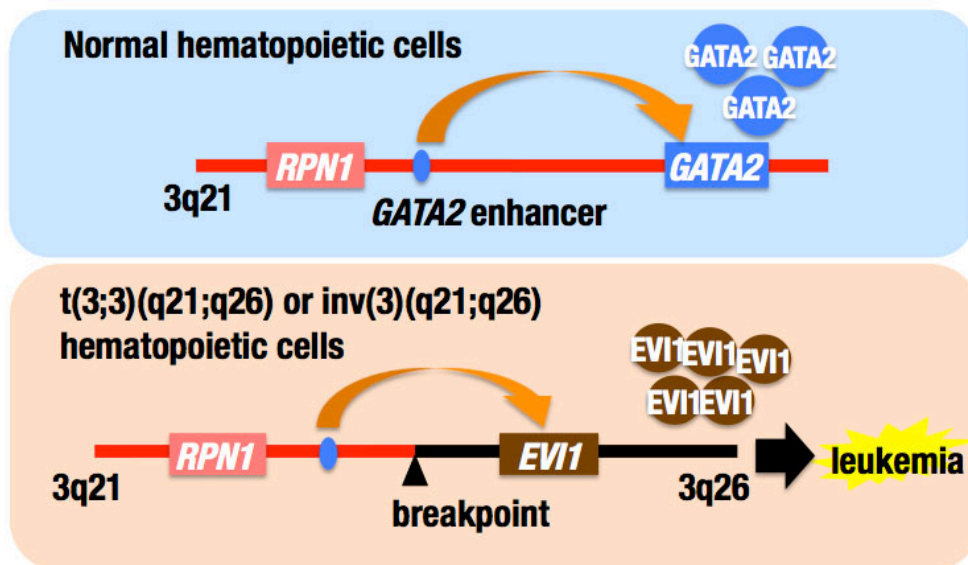


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**Figure.** A mechanistic basis underlying EVI1 proto-oncogene overexpression and leukemogenesis. The GATA2 gene enhancer on 3q21, which activates GATA2 gene expression in normal hematopoietic stem/progenitor cells (an upper panel), is brought into close proximity to the EVI1 proto-oncogene on 3q26 and activates its expression in cells with chromosomal translocation and inversion between 3q21 and 3q26 (an lower panel), which leads to leukemogenesis.

### A remote GATA2 hematopoietic enhancer drives leukemogenesis in *inv(3)(q21;q26)* by activating EVI1 expression.

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