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Leukaemia Section

Short Communication

t(2;9)(p24;p13) PAX5/KIDINS220

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Abstract

Review on t(2;9)(p24;p13), with data on the genes involved

Keywords
Chromosome 2; Chromosome 9;

Clinics and pathology

Disease

B acute lymphoblastic leukemia

Phenotype/cell stem origin

Immunophenotyping revealed that the leukemic blasts were positive for CD10, CD19, CD34, CD58, CD66c, CD38, CD79a, and HLA-DR.

Epidemiology

Only one case to date: a 7-year-old boy (Sakamoto et al, 2016).

Treatment

The patient achieved first complete remission under the extremely high-risk protocol (JACLS ALL-02), he underwent allogeneic HSCT due to a poor response to initial induction therapy. However, the patient relapsed and died in 5 years after the initial diagnosis (Sakamoto et al. ,2017).

Cytogenetics

Cytogenetics morphological

G-banding analysis showed a normal karyotype. It is a cryptic translocation, not visible with conventional cytogenetics.

Genes involved and proteins

KIDINS220

Location 2p24

Note
Kinase D-interacting substrate of 220 kDa.

Protein
KIDINS220 gene encodes a transmembrane protein that is a mediator of multiple receptor signaling pathways, interacts with both T- and B-cell receptors, and is necessary for sustained extracellular signal-regulated kinase (ERK) signaling.

PAX5

Location 9p13

Protein
PAX5 gene encodes a member of the paired box family of transcription factors.
PAX5 is the B-cell lineage specific activator protein that is expressed at early stages of B-cell differentiation.
PAX5 rearrangements induce a differentiation block in B lymphocytes.

Result of the chromosomal anomaly

Hybrid gene

Description
PAX5/KIDINS220

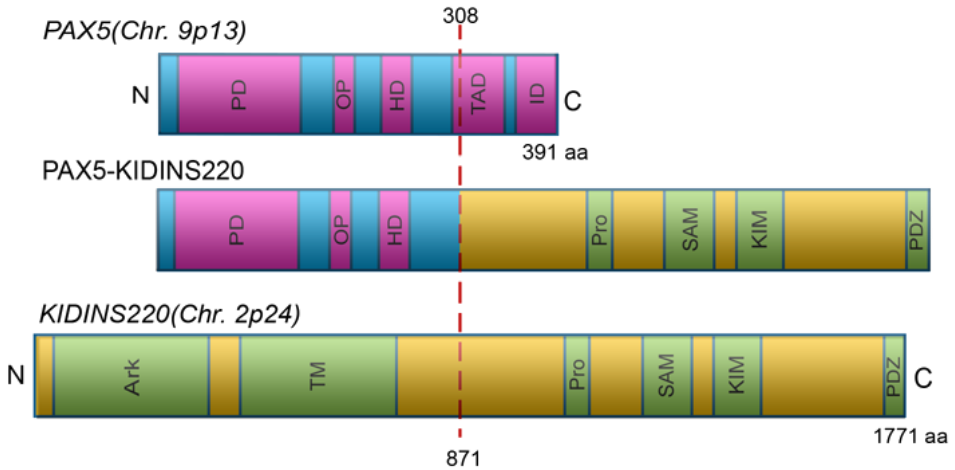

Figure 1. Structure of the PAX5/KIDNS220 fusion protein. PD, paired domain; OP, octapeptide domain; HD, homeodomain; TAD, transactivation domain; ID- inhibitory domain; Pro, proline-rich domain; SAM, sterile alpha motif domain; KIM, kinesin light chain-interacting motif; PDZ, PDZ-binding motif; Ank, ankyrin repeat; TM, transmembrane region.

Transcript

Nucleotide sequence analyses revealed that PAX5 exon 7 was fused in-frame to KIDINS220 exon 20.

Fusion protein

Description

The PAX5 protein is fused in-frame to KIDINS220 at amino acids 306 and 871, respectively, resulting in the preservation of the N-terminal region of PAX5, including the DNA-binding domain, and the C-terminal region of KIDINS220, including several protein-protein interaction domains (Sakamoto et al., 2017). The PAX5/KIDINS220 fusion protein preserves the DNA-binding domain of PAX5 and growth promotion activities of KIDINS220.

Oncogenesis

The PAX5/KIDINS220 fusion protein plays a dual role in leukemogenesis: first, the fusion protein likely induces a block in the differentiation of B lymphocytes by inhibition of wild-type PAX5 function; second, it possibly enhances ERK signaling pathway activation through KIDINS220, resulting in increased proliferation and a survival advantage for leukemic cells. Functional studies need to be performed to determine the precise function of PAX5/KIDINS220 fusion (Sakamoto et al., 2017).

References

Sakamoto K, Imamura T, Kanayama T, Yano M, Asai D, Deguchi T, Hashii Y, Tanizawa A, Ohshima Y, Kiyokawa N, Horibe K, Sato A. Ph-like acute lymphoblastic leukemia with a novel PAX5-KIDINS220 fusion transcript. Genes Chromosomes Cancer. 2017 Apr;56(4):278-284

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