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/KIDINS220 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

This article should be referenced as such: