

Leukaemia Section

Short Communication

t(1;7)(p36;p12) IKZF1/PRDM16

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Abstract

Review on t(1;7)(p36;p12) translocations, with data on clinics, and the genes involved.

Keywords

chromosome 1; chromosome7; t(1;7)(p36;p12); PRDM16; IKZF1

Clinics and pathology

Disease

A t(1;7)(p36;p12) was found in a case of myelodysplastic syndrome (MDS) (Duhoux et al., 2012).

Clinics

A 66-year-old male patient who died 49 months after diagnosis.

Cytogenetics

Cytogenetics morphological

A +8 was present.

Genes involved and proteins

PRDM16 (PR domain containing 16)

Location

1p36.32

DNA/RNA

11 splice variants

Protein

1276 amino acids and smaller proteins. Contains a N-term PR domain; 7 Zinc fingers, a proline-rich

domain, and 3 Zinc fingers in the C-term. Binds DNA. Transcription activator; PRDM16 has an intrinsic histone methyltransferase activity. PRDM16 forms a transcriptional complex with CEBPB. PRDM16 plays a downstream regulatory role in mediating TGFB signaling (Bjork et al., 2010). PRDM16 induces brown fat determination and differentiation. PRDM16 is expressed selectively in the earliest stem and progenitor hematopoietic cells, and is required for the maintenance of the hematopoietic stem cell pool during development. PRDM16 is also required for survival, cell-cycle regulation and self-renewal in neural stem cells (Chuikov et al., 2010; Kajimura et al., 2010; Aguilo et al., 2011; Chi and Cohen, 2016).

IKZF1 (Ikaros family zinc finger 1)

Location

7p12.2

DNA/RNA

Numerous splice variants

Protein

519 amino acids. Contains 6 Zn fingers (act as DNA-binding domain, and dimerization domain). Transcription regulator. IKZF1 is involved in chromatin remodeling complexes, such as nucleosome-remodeling and histone deacetylation (NuRD), and can both enhance and repress gene transcription. IKZF1 plays a key role in hematopoietic stem cell maintenance, B- and T-lymphopoiesis, erythropoiesis and the fetal-to-adult hemoglobin switch.

ETV6 and IKZF1 are components of a network of heptad transcription factors (ERG, FLI1, GATA2, LMO2, LYL1, RUNX1, and TAL1 (SCL)). This heptad acts in combination to regulate genes in

hematopoietic stem and progenitor cells) that regulate the expression of a number of hematopoietic genes and whose high expression in acute myeloid leukemia is associated with poor prognosis (Unnikrishnan et al., 2016). IKZF1 deletions are associated with unfavorable prognosis in childhood B-cell precursor acute lymphoblastic leukemia (ALL) (Boer et al., 2016), and is associated with a higher relapse risk and worse survival in adults with common B-cell ALL (Yao et al., 2016). IKZF1 mutations were found in cases of common variable immunodeficiency syndrome with progressive B lymphopenia and an increased risk of acute lymphoblastic leukemia (Kuehn et al., 2016).

Result of the chromosomal anomaly

Hybrid gene

Description

5' IKZF1 - 3' PRDM16

Transcript

IKZF1 exon 3 joined to PRDM16 exon 3.

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