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Leukaemia Section

Short Communication

t(1;1)(p36;q41) DUSP10/PRDM16

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Abstract

Review on t(1;1)(p36;q41) DUSP10/PRDM16 translocations, with data on clinics, and the genes involved.

Keywords

chromosome 1; t(1;1)(p36;q41); PRDM16; DUSP10

Clinics and pathology

Disease

Acute myeloid leukemia.

Clinics

A 25-year-old male patient presented acute monoblastic leukemia without differentiation (FAB type M5a) (Noguchi et al 2007).).

Cytogenetics

Cytogenetics morphological

The der(1)t(1;1)(p36.3;q41) was the sole abnormality.

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).

DUSP10 (dual specificity phosphatase 10)

Location

1q41

Protein

482 amino acids. DUSP10 is a MAP kinase phosphatase. DUSP10 inactivate p38MAPK signaling by dephosphorylation. Activation/phosphorylation of the p38MAPK pathway inhibits tumor formation (the p38MAPK subfamily is composed by four members: MAPK11, MAPK12, MAPK13 and MAPK14). DUSP10 mRNA levels were lower in prostate cell lines derived from malignant tumor (Nonn L,

2011). High DUSP10 expression in colorectal cancer was found associated with improvement in survival. DUSP10 negatively regulates intestinal epithelial

cell growth and acts as a suppressor for colorectal cancer (Png et al., 2016).
DUSP10 polymorphisms influence the risk of developing colorectal cancer. DUSP10 was found expressed in meningiomas of all grades. DUSP10 expression with deactivation of p38MAPK may contribute to the pathogenesis of meningiomas (Johnson et al., 2016).
AGR2, a protein known to be overexpressed in various human cancers and to provide a poor prognosis, up-regulates DUSP10 which subsequently inhibits p38MAPK, prevents TP53 activation by phosphorylation, and provides a poor prognosis in ER+breast cancer (Hrstka et al., 2016).
mTORC2 (MTOR protein complex 2) binds and phosphorylates DUSP10, which blocks DUSP10 turnover resulting in inactivation of p38MAPK signaling. DUSP10 protein levels and phosphorylation is increased inglioblastoma multiforme tumors (Benavides-Serrato et al., 2014).
MIR92A/DUSP10/JNK signaling: MIR92A targets DUSP10 (DUSP10 inhibits JKN signaling (MAPK8, MAPK9 and MAPK10, also called JNK1,2,3) to promote JNK signaling, which promotes pancreatic cancer cell proliferation. (He et al., 2014).

Result of the chromosomal anomaly

Hybrid gene

Description

5' DUSP10 - 3' PRDM16. The splice junction was in intron 1 of DUSP10 and in exon 4 of PRDM16.

Fusion protein

Description

The breakpoint within PRDM16 induced the disruption of the PRDI-BF1-RIZ1 homologous (PR) domain.

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