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Short Communication

t(1;2)(p36;p21) THADA/PRDM16

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Abstract

Review on t(1;2)(p36;p21) translocations, with data on clinics, and the genes involved.

Keywords

chromosome 1; chromosome2; t(1;2)(p36;p21); PRDM16; THADA

Clinics and pathology

Disease

A t(1;2)(p36;p21) was found in primary myelofibrosis, myelodysplastic syndrome (MDS) in most cases, and T-cell acute lymphoblastic leukemia (T-ALL).

Phenotype/cell stem origin

At least 3 of the 8 available cases were treatment related myelodysplastic syndromes (t-MDS) (Roulston et al., 1998; Mauritzson et al., 2002; Masuya et al., 2002), and 2 other cases were MDS (Horiike et al., 1988; Storlazzi et al., 2008).

Clinics

A 38-year-old male patient presented with a treatment related myelodysplastic syndrome (t-MDS) evolving towards an acute myeloid leukemia (t-AML). Previous treatment included topoisomerase inhibitors for a Hodgkin disease 36 months before diagnosis of the t-MDS (Roulston et al., 1998). A t-MDS was diagnosed in a 76-year-old female patient previously treated with radiotherapy for uterine cancer 29 years ago. She died 26 months after diagnosis of the t-MDS (Mauritzson et al., 2002). A 49-year-old female patient was diagnosed with t-MDS (FAB refractory anemia (RA)); she had been treated with etoposide 2 years previously for M1-AML; the patient died 6.5 years after onset of the t(1;2). Other chromosome anomalies appeared during course of the disease, as well as an unrelated clone (Masuya et al., 2002). A 67-year-old female patient had a chronic myelomonocytic leukemia (CMML) with a normal karyotype; she received hydroxyurea. Three years later, a refractory anemia with excess of blasts-2 (RAEB-2) and a t(1;2) was diagnosed. The patient died one month later (Storlazzi et al., 2008). Refractory anemia with excess of blasts (RAEB) was diagnosed in a 69-year-old male patient. The patient was still alive 15 months after diagnosis (Horiike et al., 1988). A 63-year old male patient presented with myelofibrosis, and was lost to follow up (Duhoux et al., 2012). A T-cell acute lymphoblastic leukemia (T-ALL) was found in a 1-year-old child (Mathew et al., 2001), and another one in a 79-year old female patient, who died one month after diagnosis (Duhoux et al., 2012).

Genes involved and proteins

Note

In only three cases (the myelofibrosis case, one MDS, and one T-ALL), the genes likely to be involved in the translocation were determined: PRDM16 and probably THADA (Storlazzi et al., 2008; Duhoux et al., 2012).

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).

THADA (THADA, armadillo repeat containing)

Location
2p21

DNA/RNA
19 splice variants

Protein
1953 amino acids and smaller proteins. Contains a poly-lysine stretch, a coiled coil domain, a poly-leucine stretch and a poly-alanine stretch. A strong expression of THADA is seen in pancreas and testis. THADA was found to be a ligand of death receptor DR5 and may be involved in the death receptor pathway and apoptosis. THADA was found to be fused to other partner genes in thyroid adenoma (Rippe et al., 2003).

Result of the chromosomal anomaly

Fusion protein

Oncogenesis
Overexpression of PRDM16, but no significant change in the expression of THADA (Storlazzi et al., 2008; Duhoux et al., 2012)

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