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Leukaemia Section
Short Communication

dic(9;17)(p13;q11) PAX5/TAOK1

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Abstract

Short communication on dic(9;17)(p13;q11) PAX5/TAOK1, with data on clinics, and the genes implicated.

Clinics and pathology

Disease

Acute lymphoblastic leukemia (ALL)

Epidemiology

Only one case to date, a 3-year old girl with a pre-B-ALL (Coyaud et al., 2010).

Cytogenetics

Additional anomalies

There was a +X and additional rearrangements.

Genes involved and proteins

PAX5

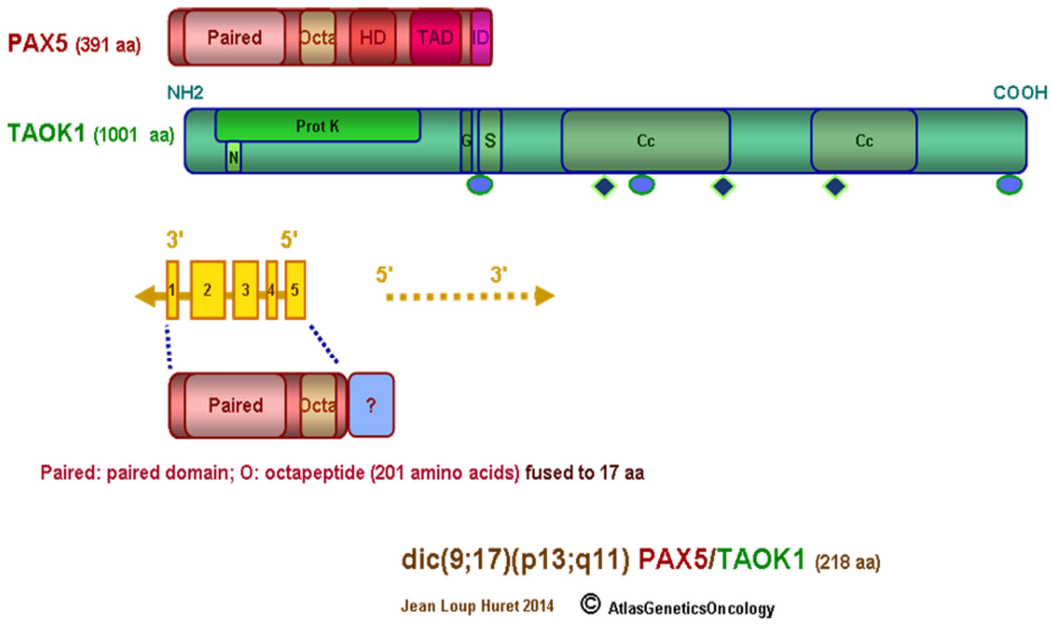
Location
9p13.2

Protein
391 amino acids; from N-term to C-term, PAX5 contains: a paired domain (aa: 16-142); an octapeptide (aa: 179-186); a partial homeodomain (aa: 228-254); a transactivation domain (aa: 304-359); and an inhibitory domain (aa: 359-391). Lineage-specific transcription factor; recognizes the concensus recognition sequence GNCCANTGAAGCGTGAC, where N is any nucleotide. Involved in B-cell differentiation. Entry of common lymphoid progenitors into the B cell lineage depends on E2A, EBF1, and PAX5; activates B-cell specific genes and repress genes involved in other lineage commitments. Activates the surface cell receptor CD19 and repress FLT3. Pax5 physically interacts with the RAG1/RAG2 complex, and removes the inhibitory signal of the lysine-9-methylated histone H3, and induces V-to-DJ rearrangements. Genes repressed by PAX5 expression in early B cells are restored in their function in mature B cells and plasma cells, and PAX5 repressed (Fuxa et al., 2004; Johnson et al., 2004; Zhang et al., 2006; Cobaleda et al., 2007; Medvedovic et al., 2011).

TAOK1

Location
17q11.2

Protein
1001 amino acids (aa); from N-term to C-term, TAOK1 contains: a protein kinase domain (aa 28-281), a nucleotide binding site (aa 34-42), a poly-Glu stretch (aa 330-334), a Ser-rich region (aa 347-379), and coiled coil domains (aa 458-651; 754-877). Phosphorylation on Ser/Thr followed by Gln are the following: SQ motifs: aa 363-364; 554-555; 990-991, TQ motifs: aa 502-503; 643-644; 785-786 (Raman et al., 2007).
TAOK1 is a serine/threonine-protein kinase. TAOK1 has the ability to phosphorylate MARK1 (MAP/Microtubule affinity-regulating kinase 1, 1q41), a kinase regulating microtubule dynamics and cell polarity (Timm et al., 2003). TAOK1 regulates apoptotic morphology via C-Jun N-terminal kinases (MAPK8, 10q11.22; MAPK9, 5q35.3; MAPK10, 4q21.3) and ROCK1 (Rho-associated, coiled-coil containing protein kinase 1, 18q11.1) (Zihni et al., 2006).



PAX5-TAOK1 translocation protein.

TAOK1 alters actin cytoskeletal organization and binds to microtubules, regulating their organization and stability (Zihni et al., 2006). The TAO kinases (TAOK1; TAOK2, 16p11.2; TAOK3, 12q24.23) mediate the activation of p38 (MAPK11, 22q13.33; MAPK12, 22q13.33; MAPK13, 6p21.31; MAPK14, 6p21.31) in response to various genotoxic stimuli.

ATM (ataxia telangiectasia mutated, 11q22.3) phosphorylates the TAO kinases. TAO kinases are regulators of p38-mediated responses to DNA damage and are intermediates in the activation of p38 by ATM (Hutchison et al., 1998; Raman et al., 2007).

TESK1 (testis-specific kinase 1, 9p13.3) binds to and inhibits TAOK1. The elevation of TAOK1 results in microtubule disruption. SPRED1 (sprouty-related, EVH1 domain containing 1, 15q14) - TESK1 binding causes inhibition of TESK1, making F-actin fibers dynamic (Johne et al., 2008). Taok1 controls epithelial morphogenesis by promoting Fas2 (Fasciclin 2, the insect homologue of NCAM1 (neural cell adhesion molecule 1, 11q23.2)) endocytosis in Drosophila melanogaster (Gomez et al., 2012).

Result of the chromosomal anomaly

Hybrid gene

Description

Fusion of PAX5 exon 5 to TAOK1 intron 19-20, but in reverse orientation. Transcript with exon 1B to exon 5 of PAX5, and an additional sequence of 54 bp.

Fusion protein

Description

Predicted fusion protein of 218 amino acids. The predicted fusion protein contains the DNA binding paired domain of PAX5 (201 aa) and 17 amino acids.

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