Leukaemia Section
Short Communication

\(t(9;15)(p13;q24)\) PAX5/PML

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Abstract
Short Communication on \(t(9;15)(p13;q24)\) PAX5/PML, with data on clinics, and the genes implicated.

Identity

Note
The translocation is noted with various breakpoints on chromosome 15, ranging from q22 to q25 (this is reminiscent of the \(t(15;17)\) PML/RARA).

Clinics and pathology

Disease
B-cell acute lymphoblastic leukemia (B-ALL)

Epidemiology
Two cases to date, a 9-month old girl and a 1.5-year old boy, both with a CD10+ ALL (Nebral et al., 2007; Nebral et al., 2009).

Prognosis
A patient remains in complete remission 84 months from diagnosis, while the other one had a testicular relapse 2 years after diagnosis and died.

Cytogenetics

Cytogenetics morphological
The translocation was the sole abnormality.

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 consensus 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).
PML

**Location**
15q24.1

**Protein**
882 amino-acids (aa) and shorter isoforms with distinct C terminus sequences; from N-term to C-term, PML contains: a proline rich domain (aa 3-46); a zinc finger (RING finger type) (aa 57-92); two zinc fingers (B-box types) (aa 124-166 and aa 183-236); a coiled coil made of hydrophobic aa heptad repeats (aa 228-253); an interaction domain with PER2 (aa 448-555); a nuclear localization signal (aa 476-490); a proline rich domain (aa 504-583); a serine rich domain (aa 506-540); and a sumo interaction motif (aa 556-562). The RING finger, B-boxes, and coiled-coil region form a tripartite motif known as the TRIM or the RBCC motif, and is associated with E3 ubiquitin ligase activity. PML is the organizer of nuclear domains called nuclear bodies, which recruit a wide variety of proteins, most often sumoylated. PML is involved in DNA damage response, cell division control, chromosome instability, and is a clock regulator via regulation of PER2 expression. PML has pro-apoptotic functions, induces senescence, inhibits angiogenesis and cell migration (Grignani et al., 1996; Chen et al., 2012; de Thé et al., 2012).

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**
Fusion of PAX5 exon 6 to PML exon 2.

**Fusion protein**

**Description**
1099 amino acids. The predicted fusion protein contains the DNA binding paired domain of PAX5 (260 aa from PAX5) and most of PML (839 aa).

**References**


This article should be referenced as such: