

Leukaemia Section

Short Communication

t(9;9)(p13;p24) PAX5/JAK2

del(9)(p13p24) PAX5/JAK2

inv(9)(p13p24) PAX5/JAK2

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Abstract

Short communication on t(9;9)(p13;p24) PAX5/JAK2, with data on clinics, and the genes implicated.

Clinics and pathology

Disease

B-cell acute lymphoblastic leukemia (B-ALL)

Phenotype/cell stem origin

Three cases were CD10+, and one case was Cμ.

Embryonic origin

Only four cases to date (Nebral et al., 2009; Coyaud et al., 2010; Roberts et al., 2012).

Epidemiology

This chromosome abnormality has only been found so far in childhood B-ALL: there were 2 male and 2 female patients, aged 7, 10, 13 and 14 years.

Prognosis

Two of three patients were considered as being at high risk, and one at intermediate risk.

One patient was in complete remission (CR) 65 months after diagnosis, and another one was in a second CR at 10 months+ (Nebral et al., 2009).

Cytogenetics

Cytogenetics morphological

Additional chromosome abnormalities were noted in the two cases with complete data on the karyotypes.

Genes involved and proteins

JAK2

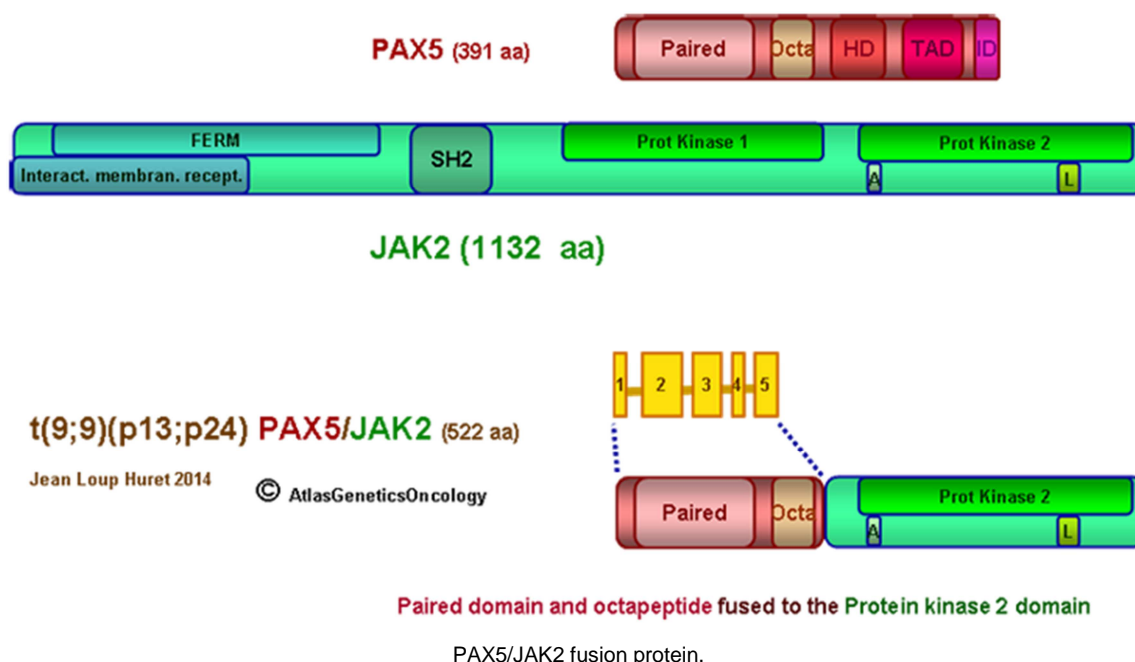
Location

9p24.1

Protein

1132 amino acids (aa); from N-term to C-term, JAK2 contains: an interaction region with cytokine/interferon/growth hormone receptors: aa 1-239, a FERM domain: aa 37-380, a SH2 domain: aa 401-482, two protein kinase domains: aa 545-809 and 849-1124, an ATP nucleotide binding site: aa 855-863, and a loop structure: aa 1056-1078 (JAK2 kinase insertion loop).

JAK homology domains are the following: JH7: aa 25-137; JH6: aa 144-284; JH5: aa 288-309; JH4: aa 322-440; JH3: aa 451-538; JH2: aa 543-824; JH1: 836-1123.



Phosphotyrosines are located at aa 119, 372, 373, 523, 813, 868, 966, 972, 1007, and 1008 (Harpur et al., 1992; Saltzman et al., 1998; Lucet et al., 2006). Protein tyrosine kinase of the non-receptor type that associates with the intracellular domains of cytokine receptors; Mediates signaling transduction.

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).

Result of the chromosomal anomaly

Hybrid gene

Description

Fusion of PAX5 exon 5 to JAK2 exon 19 in each case. Opposite direction is noted by Coyaud et al., 2010.

Fusion protein

Description

522 amino acids (201 from PAX5 and 321 from JAK2).

The predicted fusion protein contains the DNA binding paired domain of PAX5 and the Protein kinase 2 domain from JAK2 (breakpoint at aa 811 or 812 in JAK2).

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