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# Leukaemia Section
## Short Communication

# t(5;9)(q14.1;p24) SSBP2/JAK2

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## Abstract

Review on t(5;9)(q14.1;p24) SSBP2/JAK2, with data on clinics, and the genes implicated.

## Identity

**Other names**
SSBP2-JAK2 fusion

## Clinics and pathology

### Disease

B-lymphoblastic leukemia/lymphoma

### Phenotype/cell stem origin

CD45+(dim), TdT+, CD34+(subset), HLA-DR+, CD19+, CD10+, and CD20+(variable) with weak aberrant expression of the myeloid markers CD13 and CD33; no expression of surface immunoglobulin, T lymphoid, and other myeloid and monocytic markers.

### Epidemiology

One reported case; 39-year-old male presenting with a white blood cell count of $400x10^9$/L with 98% blasts (Poitras et al., 2008).

### Treatment

Prednisone, vincristine, doxorubicin, asparaginase, and high-dose methotrexate; achieved complete remission after 30 days of cytoreductive chemotherapy; also received prophylactic intrathecal chemotherapy and cranial radiation.

### Prognosis

Rapid systemic relapse; 8 months after initial diagnosis the patient died from progressive disease.

## Cytogenetics

**Note**
t(5;9) detected in 19 of 20 GTG-banded metaphase cells analyzed from a 24-hr unstimulated bone marrow culture.

### Cytogenetics molecular

The breakpoint on chromosome 9p was found to be distal to band p23 by FISH mapping on abnormal metaphase. The breakpoint was found to reside within the JAK2 locus by hybridizing a BAC spanning the JAK2 gene (RP11-927h16; nucleotides 4965192-5138016), which produced signals on both der(9) and der(5) chromosomes. Additional FISH mapping localized the chromosome 5 breakpoint to a 57.5 kb interval at 5q14.1 spanning SSBP2, with RP11-120L4 (nucleotides 80698679-80848640) and RP11-147O19 (nucleotides 80861153-81023195) flanking the breakpoint; the presence of the SSBP2-JAK2 transcript was confirmed by RT-PCR.

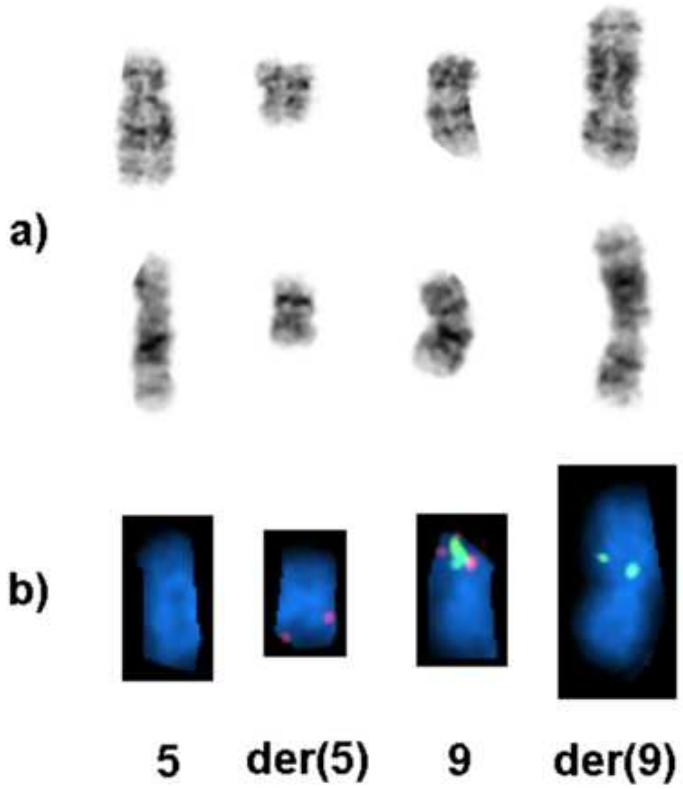
### Additional anomalies

With disease progression, a subsequent sample revealed additional chromosome aberrations: 46,XY,t(5;9)(q14.1;p24.1) [cp10]/46,idem, t(1;13)(p22;q32), t(15;20)(q15;q13)[3]/46,idem,t(1;3)(p36;p21),del(12)(q12q13)[cp7].

## Genes involved and proteins

### SSBP2

**Location**
5q14.1




**a).** Partial GTG-banded karyotypes showing the t(5;9)(q14.1;p24.1). **b).** Partial FISH analysis showing the 5'JAK2 hybridization signal on der(5), the 3'JAK2 hybridization signal on der(9) and an intact JAK2 hybridization signal on the normal chromosome 9.

**DNA/RNA**
17 exons.

**Protein**
Single-stranded DNA-binding complex; plays role in the maintenance of genome stability.

### *JAK2*

**Location**
9p24

**DNA/RNA**
24 exons.

**Protein**
Tyrosine kinase; cytokine receptor signaling.

## Result of the chromosomal anomaly

### *Hybrid gene*

**Description**
5'SSBP2-3'JAK2.

**Transcript**
RT-PCR using the forward primer in exon 3 of SSBP2 and the reverse primer in exon 12 of JAK2 yielded three discrete products of 465 bp, 375 bp, and 290 bp; sequencing revealed that each contained the same 3' JAK2 sequences (exon 11 and downstream 3' sequence), but different joining 5' SSBP2 sequences (junction occurred at the 3' end of SSBP2 exons 5, 4, and 3, respectively termed T1-T3).

### *Fusion protein*

**Description**
It is predicted that T1 and T2, which are both in-frame, will encode SSBP2-JAK2 fusion proteins containing the SSBP2 Lissencephaly type I-like homology (LisH) motif as well as the JH2 and JH1 domains of JAK2; the T3 fusion is out of frame and may encode a truncated SSBP2 protein with a COOH-terminal deletion of the proline-rich, glycine-rich, and downstream regions.

**Oncogenesis**
Other JAK2 fusions with other partners genes PCM1 (8p22), BCR (22q11.2) and ETV6 (12p13) lead to dimerization of adjacent, receptor-associated JAKs, and ensuing auto- and trans-phosphorylation causing constitutive kinase activation (Lacronique et al., 1997); it is predicted that the LisH (Lissencephaly type I-like homology) motif in SSBP2 may permit a similar mechanism of JAK2 activation.

# To be noted

**Note**

JAK2 fusion proteins have been described in several hematopoietic neoplasms including acute leukemias and myeloproliferative neoplasms. The fusion partners reported in B-lineage acute lymphoblastic leukemia (ALL) include ETV6 (Peeters et al., 1997), PCM1 (Reiter et al., 2005), PAX5 (Nebral et al., 2009), BCR and STRN3 (Roberts et al., 2012). It is thought that these fusions result in constitutive JAK2 tyrosine kinase activity, and it is predicted that patients with B-ALL exhibiting one of these fusions may respond to JAK2 inhibitors (Lacronique et al., 1997; Roberts et al., 2012). This is clinically relevant given that at least the PAX5-JAK2, BCR-JAK2 and STRN3-JAK2 fusions have been associated with a group of high-risk B-lineage ALLs known as BCR-ABL1 negative ALL or "Ph-like ALL", which are characterized by a gene expression profile similar to BCR-ABL1-positive ALL, an alteration of IKZF1, and poor prognosis (Roberts et al., 2012). The translocation described herein describes an additional JAK2 fusion protein in B-lineage ALL (SSBP2-JAK2) (Poitras et al., 2008).

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