Leukaemia Section
Short Communication

t(9;22)(p24;q11.2) BCR/JAK2

Tatiana Gindina

Cytogenetics Lab, Raisa Gorbacheva Memorial Institute of Children's Oncology, Hematology and Transplantation at First Pavlov St. Petersburg State Medical University, Saint-Petersburg, Russia; tatgindina@gmail.com

Published in Atlas Database: February 2018
Online updated version: http://AtlasGeneticsOncology.org/Anomalies/t0922p24q11ID1331.html
DOI: 10.4267/2042/69827

This article is an update of:
Bohlander SK. t(9;22)(p24;q11.2). Atlas Genet Cytogenet Oncol Haematol 2006;10(2)

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2019 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Abstract

Review on t(9;22)(p24;q11.2) BCR/JAK2, with data on clinics, and the genes involved.

Keywords
Chromosome 9; Chromosome 22; t(9;22)(p24;q11.2); BCR; JAK2.

Identity

G-banded chromosomes showing t(9;22)(p24;q11.2)

Clinics and pathology

Disease
Atypical chronic myeloid leukemia (CML), Myeloproliferative neoplasm, unclassifiable; Myelodisplastic/myeloproliferative neoplasm, unclassifiable; Acute myeloid leukemia, NOS; B lymphoblastic leukaemia/lymphoma, NOS; Burkitt lymphoma.
The translocation t(9;22)(p24;q11.2) JAK2/BCR was found in 11 cases. There were seven patients with myeloproliferative disorders [Griesinger et al., 2005; Lane et al., 2008; Impera et al., 2011; Belesso et al., Elnaggar et al., 2012; Xu et al., 2013; Schwaab et al., 2014], one patient with AML [Cirmena et al., 2008]. ALL was diagnosed in 2 patients [Tirado et al., 2010; Cuesta-Dominguez et al., 2012], Burkitt lymphoma in one patient [Cook et al., 2004]. Should be noted, in a case of Burkitt lymphoma that the molecular study was not been performed. In one patient with ALL, the JAK2/BCR fusion has been proved by molecular methods, but in another one this fusion was not established.

Epidemiology
Median patient's age was 51 (range 14-84) years. Sex ratio was 2 male : 1 female patients.

Treatment
Some patients with the myeloproliferative disease had a response to hydroxyurea and/or interferon alfa and achieved partial or complete remission [Griesinger et al., 2005; Impera et al., 2011; Xu et al., 2013]. One patient had a good response to ruxolitinib but relapsed after 18 months [Schwaab et al., 2014]. No patients, who achieved remission of the disease after treatment with tyrosine kinase inhibitors [Griesinger et al., 2005; Impera et al., 2011; Belesso et al., 2013].
Allogeneic and autologous hematopoietic stem cell transplantation was performed for four and one patient, respectively [Cirmena et al., 2008; Tirado et al., 2010; Belesso et al., 2013; Scwaab et al., 2014; Cuesta-Dominguez et al., 2012].

**Prognosis**

Until recently, the prognosis and therapeutic options for patients with BCR/JAK2 fusion genes were rather different. The fusion genes are seen in cases with an aggressive clinical course with rapid progression, usually within the first two years after diagnosis [Griesinger et al., 2005; Impera et al., 2011; Belesso et al., 2013]. In some patients, long-term survival frequently has been achieved after autologous or allogeneic SCT [Tirado et al., 2010; Cuesta-Dominguez et al., 2012].

**Cytogenetics**

**Cytogenetics molecular**

FISH with a BCR/ABL1 probe (dual color dual fusion) will show a split of the BCR signal but no fusion signals and two normal ABL1 signals. FISH with a JAK2 probe (break-apart) will display a split of one JAK2 signal (one co-localized green/red signal corresponding to the regular gene copy, and one red signal and one green signal, suggesting a breakpoint within the JAK2 locus).

**Additional anomalies**

Six patients had translocation t(9;22)(p24;q11.2) as a sole aberration [Griesinger et al., 2005; Cirmena et al., 2008; Lane et al., 2008; Tirado et al., 2010; Belesso et al., 2013]. In one patient the additional chromosomal aberrations, such as 7q deletion and trisomy 19 were found at blast crisis [Griesinger et al., 2005]. An insertion ins(22;9)(q11;p13p24) was found in 1 patient [Xu et al., 2013]. A three-way translocation with the participation of chromosomes 9, 22 and 18 was observed in 2 cases [Impera et al., 2011; Scwaab et al., 2014]. In a case of atypical Burkitt lymphoma, the translocation t(9;22)(p24;q11.2) was accompanied by t(8;14)(q24;q32) [Cook et al., 2004].

**Result of the chromosomal anomaly**

**Hybrid gene**

**Note**

The chimeric transcripts display the fusion of the first exon of BCR to exon 19 or exon 17 or exon 15 of JAK2, respectively [Xu et al., 2013; Scwaab et al., 2014; Cuesta-Dominguez et al., 2012; Elnaggar et al., 2012; Impera et al., 2011]. Another variant, with fusion of BCR exon 14 to JAK2 exon 11, has been reported in one patient with acute myeloid leukemia [Cirmena et al., 2008]. Only the BCR/JAK2 fusion transcript was detected. The reciprocal JAK2-BCR fusion transcript could not be amplified.

**Detection**

The fusion transcript can be detected by RT-PCR using the 5’ BCR sense primer: 5’-cagacagcaagctcttc-3’ (bp 1602-1622) and the 3’ JAK2 antisense primer: 5’-ctatccagctccacacac-3’ (bp 3100-3081). A PCR product of 300 bp should be expected. Please note that since only one case is known, the breakpoints may vary slightly in future...
cases. This might necessitate the design of different primers.

**Fusion protein**

**Note**
The fusion protein was not detected on Western blots.

**Description**
The BCR/JAK2 protein contains the BCR coiled-coil domain fused to the JH1-tyrosine-kinase domain of JAK2.

**Oncogenesis**
It has been demonstrated by preclinical studies that the kinase domain of JAK2 is activated through oligomerization mediated by the coiled-coil domain of BCR, as occurred in the constitutive activation of BCR/ABL. The BCR/JAK2 induces STAT5 activation and elicits BCRxL gene expression. These factors promote tumorigenic properties and lead to increased cell survival [Cuesta-Dominguez et al., 2012].

**References**


Elnaggar MM, Agersborg S, Sahoo T, Girgin A, Ma W, Rakkhit R, Zorzilla I, Leal A. BCR-JAK2 fusion as a result of a translocation (9;22)(p24;q11 2) in a patient with CML-like myeloproliferative disease Mol Cytogetnet

Griesinger F, Hennig H, Hillmer F, Podleschny M, Steffens R, Pies A, Wörmann B, Haase D, Bohlander SK. A BCR-JAK2 fusion gene as the result of a t(9;22)(p24;q11 2) translocation in a patient with a clinically typical chronic myeloid leukaemia Genes Chromosomes Cancer

Impera L, Lonoce A, Fanfulla DA, Moreihon C, Legros L, Raynaud S, Storlazzi CT. Two alternatively spliced 5'BCR/3'JAK2 fusion transcripts in a myeloproliferative neoplasm with a three-way t(9;18;22)(p23;p11 3;q11 2) translocation

Lane SW, Fairbairn DJ, McCarthy C, Nandini A, Perry-Keene J, Kennedy GA. Leukaemia cutis in atypical chronic myeloid leukaemia with a t(9;22) (p24;q11 2) leading to BCR-JAK2 fusion Br J Haematol


This article should be referenced as such: