Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Leukaemia Section
Short Communication

t(1;1)(q24;q25) RCSD1/ABL2, inv(1)(q24q25) RCSD1/ABL2

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Published in Atlas Database: October 2018
Online updated version : http://AtlasGeneticsOncology.org/Anomalies/inv1q24q25RCSD1ABL2ID1831.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/70529/10-2018-inv1q24q25RCSD1ABL2ID1831.pdf
DOI: 10.4267/2042/70529

Abstract

Review on t(1;1)(q24;q25)/inv(1)(q24q25), with data on clinics, and the genes involved

Keywords
RCSD1, ABL2, B-cell acute lymphoblatic leukemia

Clinics and pathology

Disease

B-lymphoblastic leukemia, BCR-ABL1-like (WHO, 2016).

Epidemiology

Only 2 cases described: a 20-years-old man (Roberts et al, 2014; Raca et al., 2015; Roberts et al., 2017) and a second patient without further data (case A530 in Boer et al., 2017). These cases were first classified as B-ALL, and reclassified later as "B-ALL, BCR-ABL1-like" after characterization [CHU1]of the RCSD1/ABL2 fusion.
The RCSD1/ABL2 case described by Roberts et al, 2014 was part of a study of 1665 B-ALL cases, three of which with ABL2 fusions. In the case described in Boer et al., 2017, the RCDS1/ABL2 fusion case was identified in a series of 77 BCR-ABL1-like B-ALL cases.

Treatment

The 20-year-old case received induction therapy with vincristine/peg-asparaginase/daunorubicin/prednisone with intrathecal cytorabine and methotrexate; there was no response post induction at days 15 and 29). Additional therapy included Cytoxan, cytarabine, 6-mercaptopurine, decadron, vincristine, peg-asparaginase and intrathecal therapy with methotrexate (8-week cycle) and produced a morphologic remission but high-level minimal residual disease (MRD) was detected by flow cytometry.
The patient received a hematopoietic stem cell transplant (total body irradiation and etoposide based preparative regimen) from an unrelated donor (Raca et al., 2015). The other case was treated according to the ALL10-HR protocol. There was a good response to prednisone, and high MRD (Boer et al., 2017).

Evolution

The 20-year-old case was in complete remission 8 month post-transplant and with no evidence of MRD (Raca et al., 2015). The other patient has been followed up for 3-4 years (Boer et al., 2017).

Prognosis

The two cases showed a IKZF1 deletion. Roberts et al. showed a tyrosine kinase inhibitors sensitivity when the RCSD1/ABL2 fusion was tested in Ba/F3 cells and in vivo mice models, and dasatinib was proposed to be evaluated in the future treatment of BCR-ABL1-like B-ALL with ABL-class fusions, especially for RCSD1/ABL2 fusion)(Roberts et al, 2017)

Cytogenetics

Cytogenetics morphological

This abnormality was not detected by conventional cytogenetic in any of the two cases. A complex rearrangement necessarily occurs because the two genes are in opposite directions of transcription.

Cytogenetics molecular

The rearrangement can be detected by molecular cytogenetics or other molecular technics.

Genes involved and proteins

RCSD1

Location 1q24.2

Protein

416 amino acids. RCSD1 is also called CAPZIP. CapZ-interacting protein, implication in cytoskeleton regulation and cell migration. RCSD1 is a mediator of non-canonical Wnt/JNK signalling. It interacts with the actin capping protein CapZ (CAPZA1, CAPZA2, CAPZB: capping actin protein of muscle Z-line subunits alpha 1, alpha 2 and beta). RCSD1 Binds CapZ to prevent CapZ from binding to the actin cytoskeleton. The T-cell costimulatory receptor CD28 phosphorylation regulates RCSD1 (Hempel et al. 2017: Tian et al. 2015).

ABL2

Location 1q25.2

Protein

1182 amino acids. ABL2 is also called ARG. ABL2 is a member of the ABL family of tyrosine kinases. ABL kinases have been found to play essential roles for the downstream signaling of the T- and B-cell receptors. ABL1 and ABL2 have both overlapping and distinct functions. The two proteins diverge in their C-terminal halves: ABL2 contains two F-actin binding domains and a microtubule-binding domain and is a key regulator of actin cytoskeletal remodeling. ABL2 acts as negative regulator of signaling downstream of the kinase activity of the transmembrane receptor protein tyrosine kinase FLT3: it partially blocks FLT3-induced AKT phosphorylation (Jacobsen et al., 2018; Kazi et al., 2017). ABL2 gene is often implicated in solid tumors.

Result of the chromosomal anomaly

Hybrid gene

Description

5'RCSD1 (exon 3) - 3'ABL2 (exon 5).

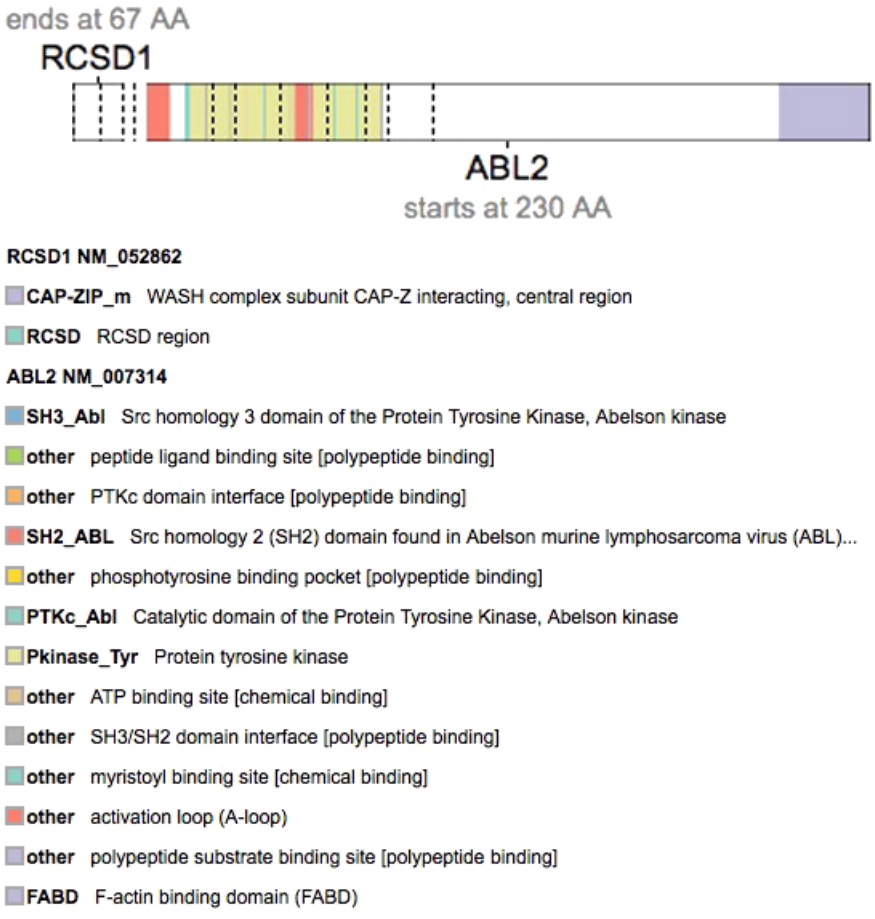

Figure 1. RCSD1/ABL2 fusion protein, according to https://pecan.stjude.cloud/proteinpaint/ABL2

Fusion protein

Description

The transcript retains the tyrosine kinase domain of ABL2 and a portion of the SH2 domain, but not the NH2-terminal SH3 domain (Raca et al., 2015).

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This article should be referenced as such:

Gaillard B. t(1;1)(q24;q25) RCSD1/ABL2 inv(1)(q24q25) RCSD1/ABL2. Atlas Genet Cytogenet Oncol Haematol. 2019; 23(9):274-276.