Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Leukaemia Section

Mini Review

t(1;9)(q24;q34)

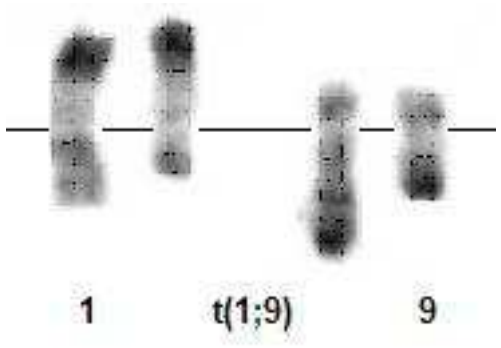
Etienne De Braekeleer, Marc De Braekeleer

Inserm U613, Laboratoire de Cytogénétique, Faculté de Médecine et des Sciences de la Santé, Université de Bretagne Occidentale, 22, av. Camille Desmoulins, CS 93837, F-29238 Brest cedex 3, France

Published in Atlas Database: November 2007

Online updated version: http://AtlasGeneticsOncology.org/Anomalies/t0109q24q34ID2109.html
DOI: 10.4267/2042/38611

Identity



R-banded karyotype showing the t(1;9)(q24;q34) translocation.

Clinics and pathology

Disease

B-cell acute lymphoblastic leukemia.

Epidemiology

Only 1 case to date, a 11-year-old boy.

Prognosis

Complete remission was obtained and a bone marrow transplantation was performed.

Cytogenetics

Cytogenetics, molecular

LSI bcr/abl dual extra-signal (ES) color probe (Abbott, Rungis, France) and BAC Probes.

Probes

RP11-83J21 (chromosome 9) and RP11-232M22, RP11-928F1, RP11-138P14, RP11-652E14, RP11-64D9 (chromosome 1).
All the probes that were used to find the breakpoint on der(1).

Genes involved and Proteins

ABL1 (Abelson Murine Leukemia Viral Oncogene Homolog 1)

Location: 9q34

DNA / RNA

The ABL gene is aproximately 225 kb in size and is expressed as a 7-kb mRNA transcript, with alternatively spliced first exons, exons 1b and 1a, respectively, spliced to the common exons 2-11. Exon 1b is approximately 200 kb 5-prime of exon 1a.

Protein

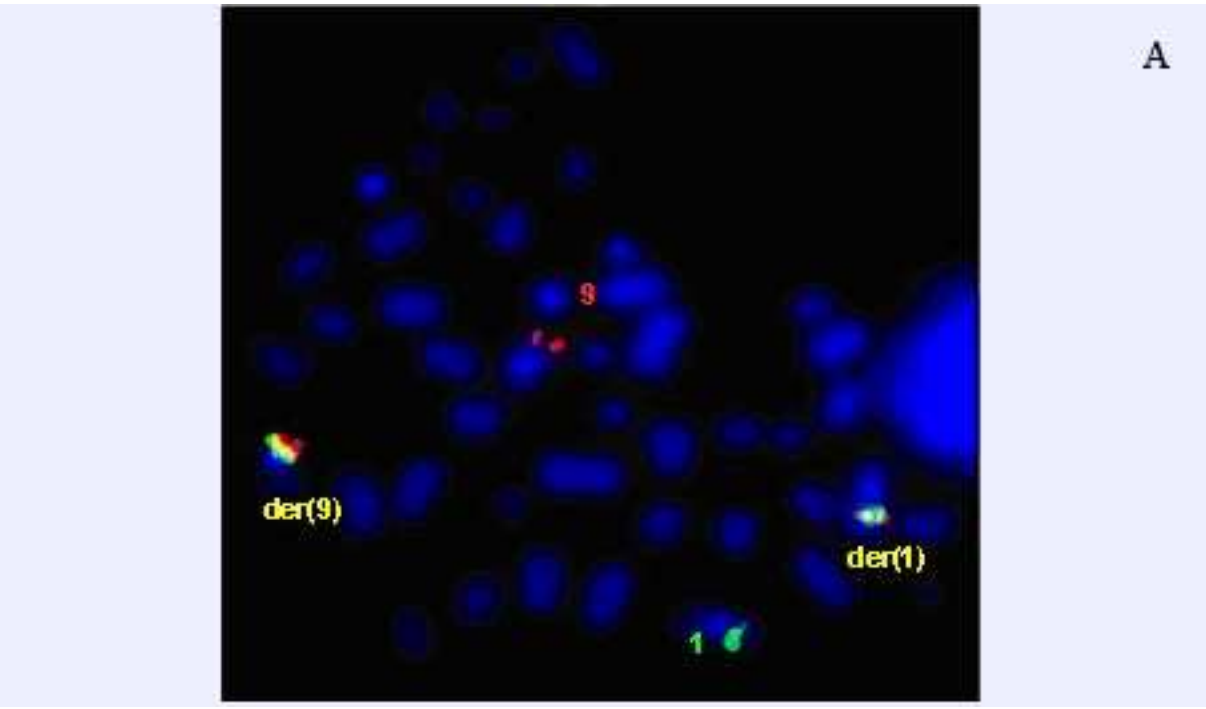
The 145-kD ABL protein is classified as a nonreceptor tyrosine kinase. When the N-terminal region of the ABL protein is encoded by exon 1a, the protein is believed to be localized in the nucleus, while when encoded by exon 1b, the resulting N-terminal glycine would be myristylated and thus postulated to direct that protein to the plasma membrane.

RCSD1 (RCSD Domain-Containing Protein 1)

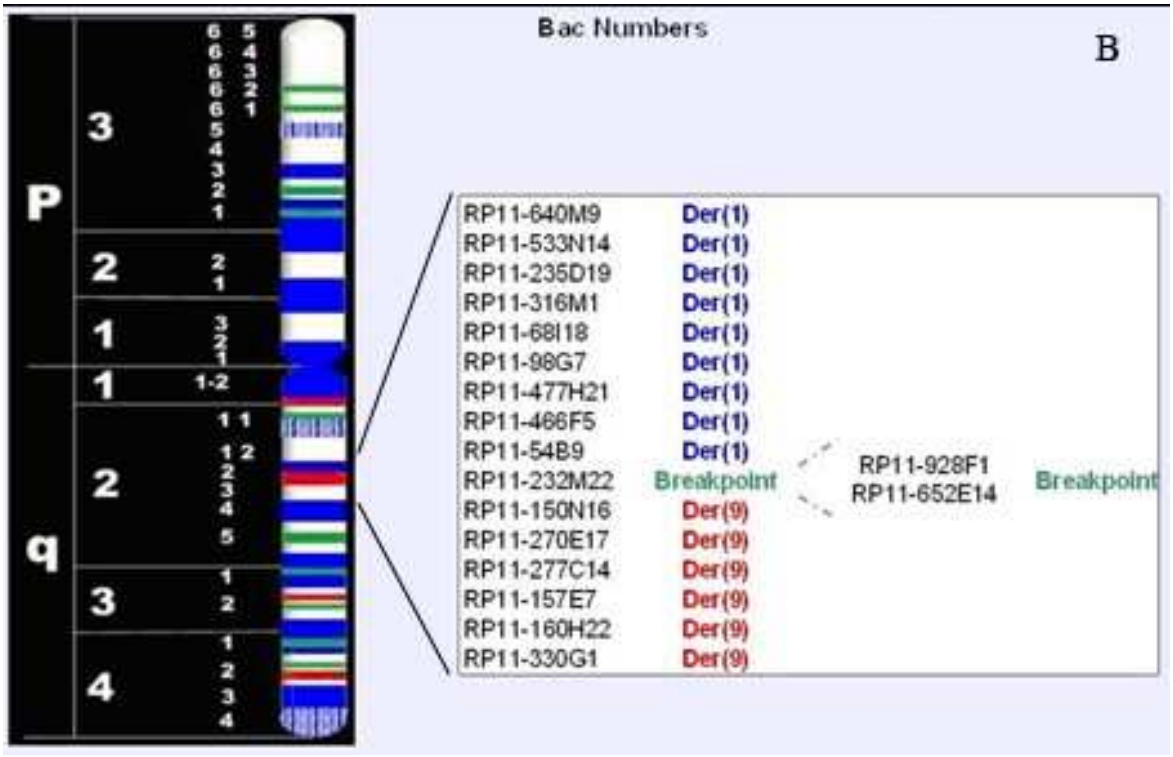
Location: 1q24

DNA / RNA

Eyers et al. (2005) cloned for the first time the human RCSD1, which they called CAPZIP. A 416-amino acid protein was deduced and they calculated a molecular mass of 44.5 kD. Northern blot analysis resulted in a major 3.4-kb transcript and a minor 7-kb transcript that is highly expressed in skeletal muscle and weakly in cardiac muscle. CAPZIP is detected in several lymphoid organs, including spleen, thymus, peripheral blood leukocytes, lymph node, and bone marrow.



A: Dual-color FISH using RP11-83J21 (labeled in spectrum orange) and RP11-232M22 (labeled in spectrum green) showing two fusion genes. FISH, fluorescence in situ hybridization.



B: Probes.

Protein

Eyers et al. (2005) found many properties of rabbit Capzip. It interacted specifically with the F-actin capping protein CapZ. This protein was phosphorylated by: MAPKAPK2 and SAPK3 (MAPK12), on ser108 by SAPK3 and SAPK4 (MAPK13) and on ser68, ser83, and ser216 by JNK1 alpha-1 (MAPK8) in vitro. This team also found that stress induced by hyperosmotic shock and anisomycin, a protein synthesis inhibitor, stimulated the phosphorylation of CAPZIP in human

cell lines and induced the dissociation of CAPZIP from CAPZ in Jurkat human T cells. This phenomenon may regulate the ability of CapZ to remodel actin filament.

Results of the chromosomal anomaly

Hybrid gene

Description

The 3' region of ABL1 is translocated on the 5' region of RCSD1 on the der(1) and the 3' region of RCSD1 is translocated on the 5' region of ABL1 on der(9).

Detection protocole

FISH detection.

Fusion protein

Description

The fusion gene is predicted to encode an aberrant tyrosine kinase.

Oncogenesis

The RCSD1 gene, which codes a protein kinase substrate, CapZIP (CapZ-interacting protein), is found in immune cells, splenocytes and muscle. It is possible that the interaction between CapZIP and CapZ affects the cell ability to remodel actin filament assembly.
CapZIP is phosphorylated when cells are exposed to various cellular stresses, which activate the kinase cascade. The interaction between CapZIP and CapZ would be lost when CapZIP is phosphorylated. So, RCSD1 would be involved in the remodeling of the actin cytoskeleton, which is an important step in mitosis. The probable formation of the ABL1-RCSD1 fusion gene could result in an alteration of the cellular function by affecting the cytoskeleton regulation, which could be an important step in leukemogenesis.

References

Eyers CE, McNeill H, Knebel A, Morrice N, Arthur SJC, Cuenda A, Cohen P. The phosphorylation of CapZ-interacting protein (CapZIP) by stress-activated protein kinases triggers its dissociation from CapZ. Biochem J 2005;389:127-135.

De Braekeleer E, Douet-Guilbert N, Le Bris M-J, Berthou C, Morel F, De Braekeleer M. A new partner gene fused to ABL1 in a t(1;9)(q24;q34)-associated B-cell acute lymphoblastic leukemia. Leukemia 2007;21:2220-2221.

This article should be referenced as such:
De Braekeleer E, De Braekeleer M. t(1;9)(q24;q34). Atlas Genet Cytogenet Oncol Haematol.2008;12(6):466-468.