

Leukaemia Section

Short Communication

t(7;14)(p15;q11) TRD/HOXA10

Adriana Zamecnikova

Kuwait Cancer Control Center, Department of Hematology, Laboratory of Cancer Genetics, Kuwait; annaadria@yahoo.com

Published in Atlas Database: October 2017

Online updated version : <http://AtlasGeneticsOncology.org/Anomalies/t0714p15q11ID1435.html>

Printable original version : <http://documents.irevues.inist.fr/bitstream/handle/2042/69018/10-2017-t0714p15q11ID1435.pdf>

DOI: 10.4267/2042/69018

This article is an update of :

Bergeron J, Macintyre E, Asnafi V. t(7;14)(p15;q11). Atlas Genet Cytogenet Oncol Haematol 2006;10(4)

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2018 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Abstract

Review on t(7;14)(p15;q11) TRD/HOXA10, with data on clinics.

KEYWORDS

Chromosome 7; Chromosome 14; TRD ; HOXA10; T-cell lymphoblastic leukaemia

Clinics and pathology

Disease

T-cell Acute lymphoblastic leukemia (T-ALL)

Phenotype/cell stem origin

T lineage TCR gamma delta +, CD4/8 double positive (DP), CD1a- ; FAB L1 or L2. Immunophenotype.

Epidemiology

2 patients diagnosed with T-cell acute lymphoblastic leukemia: a 29-years old male (Asnafi et al., 2003) and a 9- years old male (Mahlow et al., 2015). In addition, 3 more cases with t(7;14)(p15;q11) have been described: a 51-years old male with mycosis fungoides/Sezary syndrome and TRA+ rearrangement (Santos et al., 1990), a 31-year old female with T-ALL (Garipidou et al., 1991) and a 46-years old female with refractory anemia with excess of blasts and rearranged HOXA9 (Chen et al., 2005) (Table 1).

Table 1. Reported cases with t(7;14)(p15;q11)

	Sex/Age	Diagnosis	Karyotype	Genes involved
4	F/46	RAEB	46,XX,t(7;14)(p15;q11),+8	HOXA9/?
2	F/31	T-ALL	46,XX,t(7;14)(p15;q11),add(18)(q23)	?

t(7;14)(p15;q11) TRD/HOXA10

3	M/29	T-ALL	46,XY,t(7;14)(p15;q11),t(10;11)(p14;q21),add(18)(q23)	HOXA-TRA/D CALM-AF10
5	9/M	T-ALL	46,XY,del(6)(q14q21),t(7;14)(p15;q11.2),del(9)(p13)/92,idemx2	HOXA-TRA/D
1	M/51	Mycosis fungoides/ Sezary syndrome	41-45,X,-Y,add(5)(q33),+7,t(7;14)(p15;q11),-8,-10,del(10)(p13),del(11)(q21q23),del(12)(p13),add(14)(q11),add(15)(q15),inc	TRA+, TRG+

1. Santos et al., 1990; 2. Garipidou et al., 1991; 3. Asnafi et al., 2003; 4. Chen et al., 2005; 5. Mahlow et al., 2015. **Abbreviations:** M: male; F: female; T-ALL: T-cell acute lymphoblastic leukemia, RAEB: refractory anemia with excess of blasts.

Cytogenetics

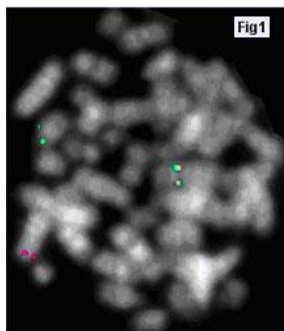


Figure 1. FISH hybridization result using a TCRA/D distal (Green) and HOXA proximal (orange) FISH probes showing a fusion signal - Courtesy Julie Bergeron, Elizabeth Macintyre, Vahid Asnaf.

Cytogenetics molecular

Balanced t(7;14)

Der(7): Intronic region of HOXA locus on 7p15 between HOXA6 and HOXA7 genes fused with Jd1 segment of TCRD on 14q11.

Der(14): DREC segment on chromosome 14q11 rearranged with Dd2 and Dd3 segments and fused to the telomeric part of HOXA locus on 7p15

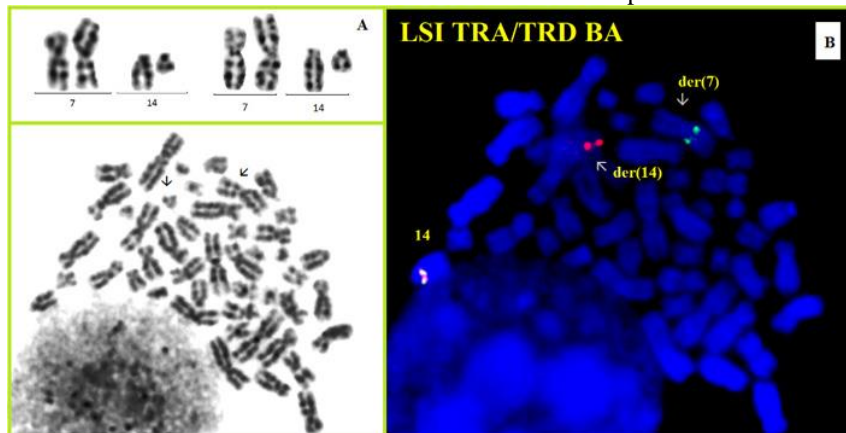


Figure 2. (A) Partial karyotypes showing t(7;14)(p15.2;q11.2). (B) Fluorescence in situ hybridization with LSI TCRA/D break apart probe (Vysis, Abbott Molecular, US) showing TCRA/D rearrangement as a result of t(7;14)(p15.2;q11.2) - Courtesy Adriana Zamecnikova.

Additional anomalies

The case described by Asnafi et al. 2003 also expressed (by RQ-PCR) a CALM-AF10 fusion transcript (t(10;11)(p13;q14-21)). Associated with 6q and 9p deletion in the other T-ALL case with fusion of HOXA-TCRA/D gene regions (Mahlow et al., 2015).

Variants

Variant translocation cases are reported: 9 cases of T-ALLs having the HOXA locus translocated to TCRB in a t(7;7). The breakpoints on 7p15 in those HOXA-TCRB cases are more centromeric, close to HOXA9

Genes involved and proteins

HOXA@

Location

7p15
HOXA6 and HOXA7 lie at 6,9kb from each other on 7p15

Protein

Various HOXA genes act as transcription factors playing important roles in the differentiation and

commitment processes of embryonic and hematopoietic cells.

TRD (T cell Receptor Delta)

Location

14q11.2

Breakpoint on der(7) lie 5' from Jd1. Breakpoint on der(14) lies 12 nucleotides 5' of the 3' end of the DREC segment.

Protein

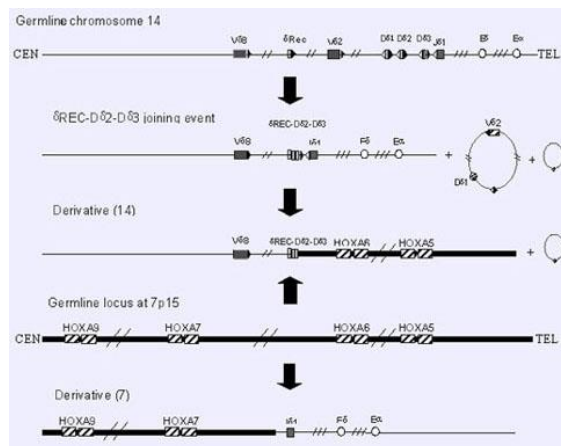
Protein encoded by the TCRD locus are the T-cell receptor chains.

Result of the chromosomal anomaly

Fusion protein



Figure 4. The nucleotide sequence of both derivatives implicated in the t(7;14) translocation. Underscored are RSS or RSS-like sequence in the vicinity of the breakpoints. In lower case letters: non templated nucleotides at the junction- Courtesy Julie Bergeron, Elizabeth Macintyre, Vahid Asnafi.



Description

No fusion protein. Overexpression of HOXA genes as a result of the translocation with TCRD was expected, as it was demonstrated to be the case in HOXA-TCRB T-ALLs. However this case had a CALM-AF10 fusion in the same leukemic clone. CALM-AF10 is already known to be associated with HOXA cluster global overexpression. The HOXA pattern of expression in this case was similar to other CALM-AF10 T-ALL.

Oncogenesis

Probable, as several HOX/HOXA genes have been implicated in leukemic processes.

References

Armstrong SA, Staunton JE, Silverman LB, Pieters R, den Boer ML, Minden MD, Sallan SE, Lander ES, Golub TR, Korsmeyer SJ. MLL translocations specify a distinct gene expression profile that distinguishes a unique leukemia. *Nat Genet.* 2002 Jan;30(1):41-7

Asnafi V, Beldjord K, Libura M, Villarese P, Millien C, Ballerini P, Kuhlein E, Lafage-Pochitaloff M, Delabesse E, Bernard O, Macintyre E. Age-related phenotypic and oncogenic differences in T-cell acute lymphoblastic leukemias may reflect thymic atrophy. *Blood.* 2004 Dec 15;104(13):4173-80

Asnafi V, Radford-Weiss I, Dastugue N, Bayle C, Leboeuf D, Charrin C, Garand R, Lafage-Pochitaloff M, Delabesse E, Buzyn A, Troussard X, Macintyre E. CALM-AF10 is a common fusion transcript in T-ALL and is specific to the TCRgammadelta lineage. *Blood.* 2003 Aug 1;102(3):1000-6

Bergeron J, Clappier E, Cauwelier B, Dastugue N, Millien C, Delabesse E, Beldjord K, Speleman F, Soulier J, Macintyre E, Asnafi V. HOXA cluster deregulation in T-ALL associated with both a TCRD-HOXA and a CALM-AF10 chromosomal translocation. *Leukemia.* 2006 Jun;20(6):1184-7

Chen B, Zhao WL, Jin J, Xue YQ, Cheng X, Chen XT, Cui J, Chen ZM, Cao Q, Yang G, Yao Y, Xia HL, Tong JH, Li JM, Chen J, Xiong SM, Shen ZX, Waxman S, Chen Z, Chen SJ. Clinical and cytogenetic features of 508 Chinese patients with myelodysplastic syndrome and comparison with those in Western countries. *Leukemia.* 2005 May;19(5):767-75

Dik WA, Brahim W, Braun C, Asnafi V, Dastugue N, Bernard OA, van Dongen JJ, Langerak AW, Macintyre EA, Delabesse E. CALM-AF10+ T-ALL expression profiles are characterized by overexpression of HOXA and BMI1 oncogenes. *Leukemia.* 2005 Nov;19(11):1948-57

Garipidou V, Secker-Walker LM. The use of fluorodeoxyuridine synchronization for cytogenetic investigation of acute lymphoblastic leukemia. *Cancer Genet Cytogenet.* 1991 Mar;52(1):107-11

Mahlow J, Ebrahim S, Mohamed AN. T-cell acute lymphoblastic leukemia with t(7;14)(p15;q11.2)/HOXA-TCRA/D and biallelic deletion of CDKN2A. Case report and literature review. <http://atlasgeneticsoncology.org/Reports/t0714p15q11MahlowID100075.html>

Marculescu R, Le T, Simon P, Jaeger U, Nadel B. V(D)J-mediated translocations in lymphoid neoplasms: a functional assessment of genomic instability by cryptic sites *J Exp Med* 2002 Jan 7;195(1):85-98

Milne TA, Briggs SD, Brock HW, Martin ME, Gibbs D, Allis CD, Hess JL. MLL targets SET domain methyltransferase activity to Hox gene promoters *Mol Cell* 2002 Nov;10(5):1107-17

Santos M, Benitez J, Rivas C. Possible correlation between a specific alteration t(7;14) and the rearrangement of TCR observed in a Sézary's syndrome *Cancer Genet Cytogenet* 1990 Jun;46(2):281-3

Soulier J, Clappier E, Cayuela JM, Regnault A, Garcia-Peydró M, Dombret H, Baruchel A, Toribio ML, Sigaux F. HOXA genes are included in genetic and biologic networks defining human acute T-cell leukemia (T-ALL) *Blood* 2005 Jul 1;106(1):274-86

Speleman F, Cauwelier B, Dastugue N, Cools J, Verhasselt B, Poppe B, Van Roy N, Vandensompele J, Graux C, Uyttebroeck A, Boogaerts M, De Moerloose B, Benoit Y, Selleslag D, Billiet J, Robert A, Hugué F, Vandenberghe P,

t(7;14)(p15;q11) TRD/HOXA10

De Paepe A, Marynen P, Hagemeijer A. A new recurrent inversion, inv(7)(p15q34), leads to transcriptional activation of HOXA10 and HOXA11 in a subset of T-cell acute lymphoblastic leukemias *Leukemia* 2005 Mar;19(3):358-66

This article should be referenced as such:

Zamecnikova A. t(7;14)(p15;q11) TRD/HOXA10. *Atlas Genet Cytogenet Oncol Haematol.* 2018; 22(12):493-496.
