

inv(7)(p15q34)

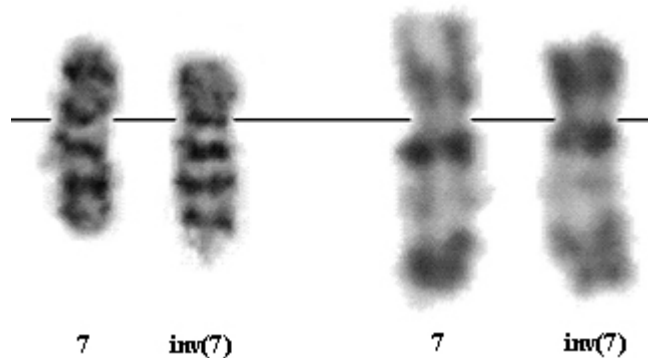
t(7;7)(p15;q34)

Clinics and Pathology

Disease	T cell acute lymphoblastic leukemia (T-ALL) and non-Hodgkin lymphoma (T-NHL)
Phenotype / cell stem origin	T lineage; occurs at early stage of T cell development (CD2-, CD4+, CD8-)
Epidemiology	3.5 % of T-ALL or T-NHL
Clinics	hepato and/or splenomegaly, lymphadenopathy, mediastinal mass, moderate WBC count (15 to 100 X 10 ⁹ /l)
Cytology	FAB L1 or L2

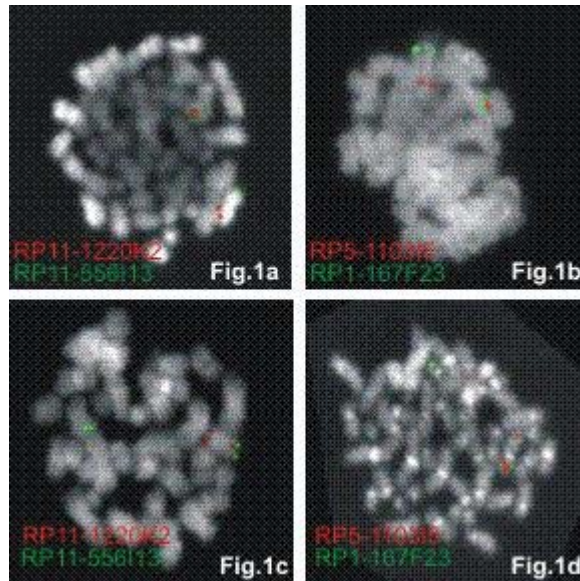
Cytogenetics

Cytogenetics This rearrangement remains undetected in poor quality metaphases.
Morphological In less condensed, well banded metaphases, the abnormality may be suspected as del(7)(p15) or clearly as an inv(7)(p15q34).



inv (7)(p15q34) G- banding (left) and R- banding (right)

Cytogenetics Molecular inv(7)(p15q34) and t(7;7)(p15;q34) can be detected by FISH using either TRB and HOXA flanking probes which gives a split signal of both probes in these cases. A fusion signal will be detected when combining the proximal TCR/distal HOXA flanking or the distal TCR/proximal HOXA flanking FISH probe.



FISH results of inv(7)(Fig.1a and b) and t(7;7)(Fig.1c and d) case using TRB flanking (Fig.1a and 1c) and HOXA (Fig.1b and 1d) flanking probes

Probes TRB flanking probes: RP11-1220K2 and RP11-556I13
 HOXA flanking probes: RP1-167F23 and RP5-1103I5

Additional anomalies most patients show no additional karyotypic abnormalities

Genes involved and Proteins

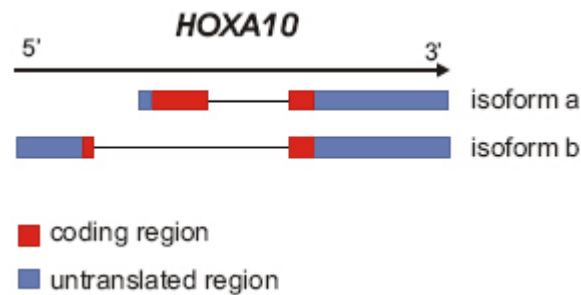
Note Chromosomal disruption of the HOXA gene cluster (7p15) following chromosomal rearrangement, leads to upregulation of HOXA gene expression, which are normally weakly expressed in T-ALL. Further studies are needed to determine the various patterns of HOXA gene upregulation but from present data, HOXA10 seems most consistently involved in keeping with the breakpoint position near HOXA9. The upregulation of HOXA10 expression is thought to result from enhancers embedded within the TRB locus, which is translocated upstream from these genes. Upregulation of HOXA genes has also been described for other subgroups of T-ALL i.e. the [CALM-AF10](#) and [MLL](#) rearranged T-ALLs indicating a more general role for HOXA genes in T-ALL development.

HOXA, together with HOXB, HOXC and HOXD, belongs to the class I homeobox genes and comprises 11 HOXA cluster genes : HOXA1, HOXA2, HOXA3, HOXA4, HOXA5, HOXA6, HOXA7, HOXA9, HOXA10, HOXA11, HOXA13. Given the breakpoint position 5' to HOXA10 and its consistent overexpression in all TRB-HOXA rearranged cases, we currently assume that this gene exerts a specific oncogenic effect in this subgroup of T-ALLs.

Gene Name HOXA10 (alias : PL, HOX1.8, HOX1H, HOX1)

Location 7p15

Note DNA-binding transcription factor which regulates gene expression, morphogenesis, and differentiation. More specifically, it may function in fertility, embryo viability, and regulation of hematopoietic lineage commitment. Two transcript variants encoding different isoforms have been found for this gene. HOXA10 expression is normally present in hematopoietic stem cells and developing T-cells with decreasing expression as T-cells mature.



2 transcripts :

Dna / Rna transcript variant 1 (isoform a) : 2 exons, transcript 2618 bp, protein 393 amino-acids

transcript variant 2 (isoform b) : 2 exons, transcript 2241 bp, protein 94 amino-acids

Protein DNA binding, transcription factor activity

Gene Name [TRB](#)

Location 7q34

Note The human TRB locus at 7q34 spans 620 kb and consists of 82-85 genes. Enhancer sequences have been characterized 5.5kb 3' from TRBC2.

Protein Proteins encoded by the TRB locus are the T-cell receptor beta chains

Result of the chromosomal anomaly

Fusion

Protein Description no fusion protein, but ectopic expression of HOXA10

Oncogenesis Little is known about the target genes for HOXA10. Cyclin-dependent kinase inhibitor [p21](#) (alias CDKN1A,CIP1,WAF1) was shown to be a transcriptional target of HOXA10 in differentiating myelomonocytic cells. However, a potential role of p21 in HOXA10 driven oncogenesis has not been proved so far. In vitro transfection experiments with HOXA9 and HOXA10 showed upregulation of several genes of the Wnt pathway (Wnt10b, Frizzled1, Frizzled5) which are essential in hematopoietic stem cell renewal.

External links

Other database	inv(7)(p15q34)	Mitelman database (CGAP - NCBI)
Other database	t(7;7)(p15;q34)	Mitelman database (CGAP - NCBI)
Other database	t(7;7)(p15;q34)	CancerChromosomes (NCBI)

To be noted

translocations involving the TRB genes frequently result from errors of the recombinase enzyme complex (RAG1, RAG2, etc.), responsible of the Immunoglobulin and T cell receptor V-J and V-D-J rearrangements.

Additional cases are needed to delineate the epidemiology of this rare entity:

you are welcome to submit a paper to our new [Case Report section](#).

Bibliography

p21 is a transcriptional target of HOXA10 in differentiating myelomonocytic cells

Bromleigh VC, Freedman LP.

Genes Dev 2000 Oct 15; 14(20): 2581-2586.

Medline [11040212](#)

Homeobox gene expression profile in human hematopoietic multipotent stem cells and T-cell progenitors: implications for human T-cell development.

Taghon T, Thys K, De Smedt M, Weerkamp F, Staal FJ, Plum J, Leclercq G.

Leukemia 2003 Jun; 17(6): 1157-1163.

Medline [12764384](#)

Activation of stem-cell specific genes by HOXA9 and HOXA10 homeodomain proteins in CD34+ human cord blood cells.

Ferrell CM, Dorsam ST, Ohta H, Humphries RK, Derynck MK, Haqq C, Largman C, Lawrence HJ.

Stem Cells 2005 May; 23(5): 644-655.

Medline [15849172](#)

HOXA genes are included in genetic and biologic networks defining human acute T-cell leukemia (T-ALL).

Soulier J, Clappier E, Cayuela JM, Regnault A, Garcia-Peydro M, Dombret H, Baruchel A, Toribio ML, Sigaux F.

Blood 2005 Jul 1; 106(1): 274-286.

Medline [15774621](#)

A new recurrent inversion, inv(7)(p15q34) leads to transcriptional activation of HOXA10 en HOXA11 in a subset of T-cell acute lymphoblastic leukemias.

Speleman F, Cauwelier B, Dastugue N, Cools J, Verhasselt B, Poppe B, Van Roy N, Vandesompele J, Graux C, Uyttebroeck A, Boogaerts M, De Moerloose B, Benoit Y, Selleslag D, Billiet J, Robert A, Huguet F, Vandenberghe P, De Paepe A, Marynen P, Hagemeijer A.

Leukemia 2005; 19 (3): 358-366.

Medline [15674412](#)

Contributor(s)

Written 10- Barbara Cauwelier, Nicole Dastugue, Anne Hagemeijer, Frank
2005 Speleman

Citation

This paper should be referenced as such :

Cauwelier B, Dastugue N, Hagemeijer A, Speleman F .

inv(7)(p15q34),t(7;7)(p15;q34). Atlas Genet Cytogenet Oncol Haematol. October 2005 .

URL : <http://AtlasGeneticsOncology.org/Anomalies/t0707p15q34ID1384.html>

© *Atlas of Genetics and Cytogenetics in Oncology and Haematology*
