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

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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)

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

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</thead>
<tbody>
<tr>
<td>3</td>
<td>M/29</td>
<td>T-ALL</td>
<td>46,XY,t(7;14)(p15;q11),t(10;11)(p14;q21),add(18)(q23)</td>
<td>HOXA-TRA/D CALM-AF10</td>
</tr>
<tr>
<td>5</td>
<td>9/M</td>
<td>T-ALL</td>
<td>46,XY,del(6)(q14q21),t(7;14)(p15;q11.2),del(9)(p13)/92,1derx2</td>
<td>HOXA-TRA/D</td>
</tr>
<tr>
<td>1</td>
<td>M/51</td>
<td>Mycosis fungoides/Sezary syndrome</td>
<td>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</td>
<td>TRA+, TRG+</td>
</tr>
</tbody>
</table>


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.

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**


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