Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Leukaemia Section

Mini Review

t(7;14)(p15;q11)

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Clinics and pathology

Disease

T- Acute lymphoblastic leukemia (T-ALL).

Phenotype / cell stem origin

T lineage TCR gamma delta +, CD4/8 double positive (DP), CD1a- immunophenotype.

Epidemiology

1 case reported.

Clinics

FABL1 or L2. The index case had hepatosplenomegaly without mediastinal involvement.

Cytogenetics

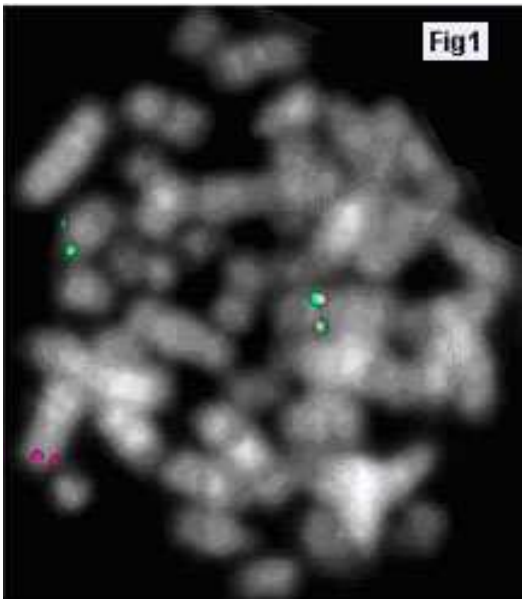

Fig1: FISH hybridization result using a TCRA/D distal (Green) and HOXA proximal (orange) FISH probes showing a fusion signal in 6 of 8 mitosis.

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

This case also expressed (by RQ-PCR) a CALM-AF10 fusion transcript (t(10;11)(p13;q14-21)).

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 (intronic region)

Location: 7p15
Note: 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.

TCRD

Location: 14q11
Note: 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.

Results of the chromosomal anomaly

Hybrid gene

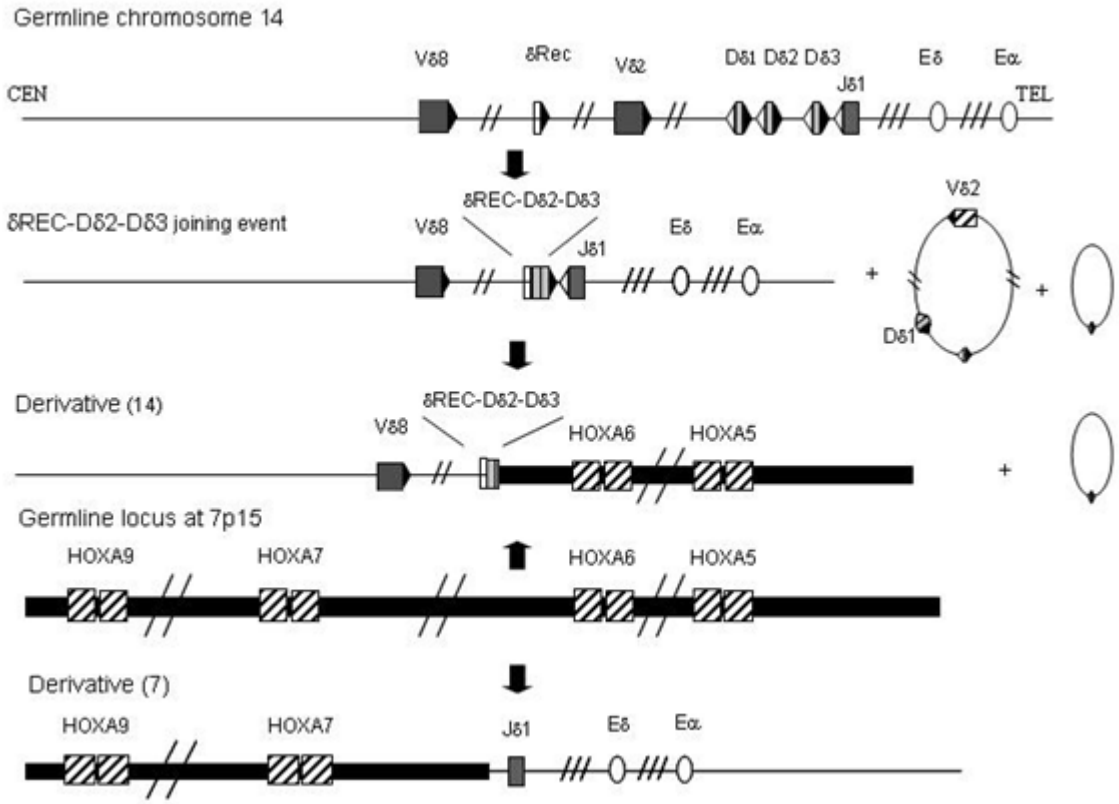

Fig2: Sequence of events leading to the final translocation. Exons are represented by boxes. Triangles represent RSS and show their orientation. E=enhancer.

Fusion protein

Fig3: The nucleotide sequence of both derivatives implicated in the t(7 ;14) translocation. Underscored are RSS or RSS-like sequence in the vincinity of the breakpoints. In lower case letters: non templated nucleotides at the junction.

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.

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