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Leukaemia Section

Mini Review

t(1;14)(q21;q32) IRTA1/IGH

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Identity

Note:

This translocation with IRTA1 involvement is different from t(1;14)(q21;q32) with BCL9 involvement, from the t(1;14)(q21;q32) with FCGR2B involvement, and from the t(1;14)(q21;q32) with MUC1 involvement.

Clinics and pathology

Disease

Multiple Myeloma and B-cell non-Hodgkins lymphoma.

Epidemiology

Rare. 2 published cases: 1 in a multiple myeloma cell line. The second in a case of gastric diffuse large B-cell lymphoma (DLBCL).

Prognosis

Unknown.

Genetics

Note

The t(1;14) interrupts the IRTA gene locus (Immunoglobulin superfamily Receptor Translocation Associated gene locus) which spans approximately 250kb, between the IRTA1 and IRTA2 genes.

Genes involved and proteins

IRTA1

Location

1q21

DNA/RNA

IRTA1 localises to the IRTA gene locus. Three IRTA1 transcripts of 2.5kb, 2.7kb and 3.5kb are possible due to alternate usage of 3 polyadenylation sites.

Protein

The three alternate IRTA1 transcripts give rise to the same putative 515 amino acid protein.
The protein shows a signal peptide, four extracellular Ig-type domains carrying three potential asparagaine (N)-linked glycosylation sites, a 16 amino acid transmmbrane and a 106 amino acid cytoplasmic domain with three putative consensus Src-homology 2 SH2 binding domains.
These domains show similarity to both ITAM (Immunoreceptor Tyrosine-based Activation Motifs) and ITIM (Immunoreceptor Tyrosine-based Inhibition Motifs). The function of the protein is unknown.
It is expressed in marginal zone B cells. In the extracellular domain IRTA1 protein shows homology to Ig superfamily receptors (47% identity and 51% similarity) and Fc receptor family (37% identity and 50% similarity). In the intracellular domain, IRTA1 shows striking homology to PECAM1 (31% identity and 45% homology).

IGH

Location

14q32

Result of the chromosomal anomaly

Fusion protein

Description

Expression of IRTA1 fusion proteins. In the first case

described the t(1;14) juxtaposes the IRTA1 gene to the C alpha constant gene in the same transcriptional orientation on the der(14) chromosome. An IRTA1/C alpha fusion protein results from this. The predicted fusion protein fuses the signal peptide and first two extracellular residues of IRTA1 to the C alpha encoded transmembrane and cytoplasmic domains.

Overexpression of IRTA1 was not observed in other myeloma or lymphoma cell lines, regardless of the status of its chromosomal band 1q21.

More recently long distance inverse PCR cloning identified a second case of IRTA1 translocation to IGH switch sequence (Switch gamma 3) in a case of gastric DLBCL.

In contrast, IRTA2 gene (located telomeric of IRTA1 in the IRTA gene locus) shows frequent deregulation in Burkitt lymphoma and Multiple Myeloma cell lines with 1q21 abnormalities (mostly duplications or unbalanced translocations that lead to trisomy or tetrasomy 1q).

IRTA1 is normally expressed in marginal zone B cells while IRTA2 is selectively expressed in centrocytes, marginal zone B cells and immunoblasts.

IRTA1 and 2 have been independently cloned as FcRH4 and FcRH5 (Fc Receptor Homologues) from a human lymph node cDNA library.

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