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Leukaemia Section

Mini Review

t(7;9)(q34;q34)

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Clinics and pathology

Disease

Specifically associated with T-cell Acute Lymphoblastic Leukemia (T-ALL).

Note

This translocation is related to Notch1 (TAN1) dysregulation. Mutation or chromosomal rearrangements of Notch gene have not yet been identified outside of T-ALL but Notch1 was recently studied by immunohistochemistry in various subsets of human lymphomas. Strong staining was found in Hodgkin¹s lymphoma (HL) and anaplastic large cell lymphoma (ALCL) but much additional works is needed to determine whether Notch signaling is necessary for HL and ALCL growth and survival.

Phenotype/cell stem origin

T lineage. CD4+ CD8+ double positive stage.

Epidemiology

Rare: < 1% among T-ALL.

Cytogenetics

Cytogenetics morphological

9q34 is a partner of 7q34. The other partners are 1p34, 1p32, 9q32, 10q24, 11p13, 15q22, 19p13

Additional anomalies

In T- lymphoblastic cell lines: polyploidy, inv(2)(p22;q11), inv(14)(q11;q32), del(6)(q23q27), del(4)(q13q35)

Genes involved and proteins

TCRB: T-cell receptor beta-chain gene on 7q35

Location

7q35

DNA/RNA

The TRB locus spans 685 Kb. The locus contains 2 types of coding elements: TCR elements (64-67 variable genes TRBV, 2 clusters of diversity, joining and constant segments) and 8 trypsinogen genes. A portion of the TCRB locus has been duplicated and translocated to the chromosome 9 at 9p21.

Protein

T cell receptor beta chains.

NOTCH1 alias TAN1 (translocation-associated Notch homolog)

Location

9q34.3

Note

Notch receptors are highly conserved transmembrane glycoproteins that regulate the morphogenesis through a signaling pathway with pleiotropic effects of apoptosis, proliferation and cellular differenciation. At least one Notch homolog is expressed in human bone marrow CD34+ cells, on the basis of this finding; it is likely that members of Notch family, including TAN1, may be involved in mediating cell-fate decisions during hematopoiesis.

DNA/RNA

DNA size: 49715 bases.

Protein

Size: 2256 amino acids, 272550 Da. Functions as a receptor for membrane-bound ligands Jagged1.

Result of the chromosomal anomaly

Hybrid gene

Description

The t(7;9) disrupts the Notch1 gene, fusing the 3¹end portion encoding its intracellular domain (ICN) to enhancer and promoter elements of the T cell receptor (TCRB). This results in overexpression of a constitutively active form of Notch activating genes that inhibit cell differenciation.The t(7;9)(q34;q34) results in a serie of tumor specific 5¹deleted Notch1 mRNA transcripts. All known beakpoints fall within a single intron in the coding sequence for the EGF repeat 34 of Notch1. The t(7 ;9) truncated transcripts encode ICN1-like polypetides (ICN = intracellular portion of Notch receptor). These polypeptides localize to the nucleus and structurally resemble ICN1. The intracellular portion of Notch1 contains six ankyrin repeats that are similar to those found in cytoplasmic I kappa B proteins or I kappa B are specific inhibitors of nuclear factor NFKappa B transcription factors.

Fusion protein

Oncogenesis

On primary effect of constitutive Notch 1 activation is the maturation arest of T lymphoblastes at the CD4+ CD8+ double positive stage but recent works suggest that Notch contributes to T cell transformation by influencing proliferation and survival, rather than merely blocking differenciation.

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