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Leukaemia Section

Short Communication

t(9;12)(q34;p13)

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Clinics and pathology

Disease

Described in only 6 cases; acute lymphoblastic leukemia (ALL), acute non lymphocytic leukemia (ANLL) and chronic myeloid leukemia (CML).

Prognosis

Numbers small, but one CML case had allogeneic BMT and is in complete remission, the remaining cases had rapid disease progression and died of shortly after diagnosis.

Cytogenetics

Cytogenetics morphological

t(9;12)(q34;p13), cryptic at the cytogenetic level.

Variants

t(9;12;14)(q34;p13;q22) and complex insertions of ETV6 into ABL.

Genes involved and proteins

ABL

Location: 9q34

DNA/RNA

ETV6 is fused to exon 2 of ABL in the three cases described.

Protein

Tyrosine kinase, localized primarily to the nucleus.

ETV6

Location: 12p13

DNA/RNA

9 exons; alternate splicing.

Protein

Contains Helix-Loop-Helix (HLH) at N-terminal end and ETS DNA binding domain at C-terminal end; wide expression; nuclear localization; ETS- related transcription factor.

Result of the chromosomal anomaly

Hybrid gene

Description

5' ETV6–3' ABL; two different fusion breakpoints have been described; ETV6 exon 4 fused in frame to ABL exon 2 (Type A) and ETV6 exon 5 fused in frame to ABL exon 2 (Type B); ETV6 maintains the HLH domain and ABL the tyrosine kinase domain.

Fusion protein

Description

a 155 kDa protein in Type A, 180 kDa protein in Type B; has elevated tyrosine kinase activity, localized in the cytoplasm and co-localizes with the actin filaments of the cells.

Oncogenesis

The HLH domain of ETV6 induces oligomerization, which results in the constitutive activation of the kinase domain of ABL; this is thought to result in phosphorylation of JAK2 and activation of the STAT pathway.
Biological activity very similar to BCR-ABL.

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