Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

BCL11B (B-cell lymphoma/leukaemia 11B)

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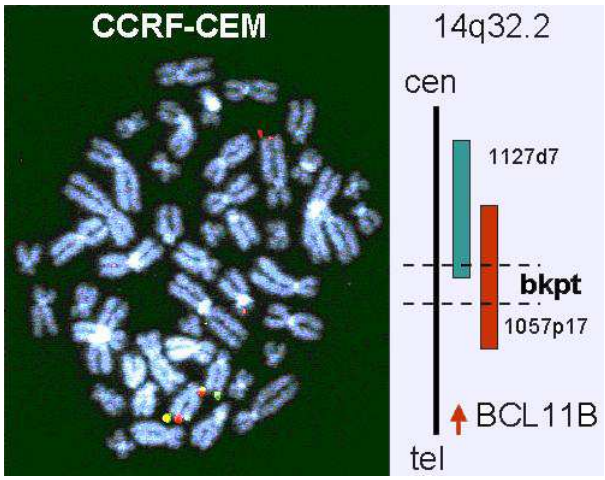
Identity

Other names: CTIP2 (Ctip-2) chicken ovalbumin upstream promoter transcription factor (COUP-TF)-interacting protein; Rit1 zinc finger protein hRit1 alpha (not to be confused with RIT1 on chr. 1q22)

HGNC (Hugo): BCL11B

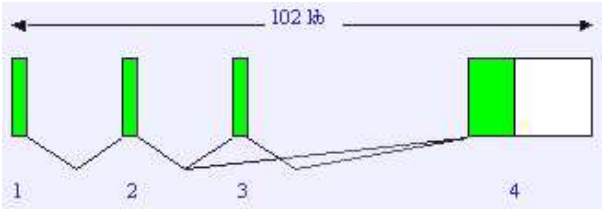
Location: 14q32.2



Note

BCL11B (14q32.2): FISH with RP11 BAC clones 1127d7 (green label) and 1057p17 (red label) showing split signal as indicated above right (dotted lines). Observe telomeric part of chr 14 translocated to the der(5) as revealed by the red doublet signal. The der(14) partner in turn receives a microinsertion containing material from chr 5. Analysis was performed on the pediatric T-ALL cell line CCRF-CEM which carries t(5;14)(q35.1;q32) resulting in ectopic expression of of NKX2-5 (2Mbp telomeric of, and closely related to, the standard partner gene TLX3 at 5q35) by juxtaposition with the far downstream region of BCL11B.

DNA/RNA



Description

ORF comprises 4 exons, exon 3 being alternately spliced, while the 3' part of exon 4 is untranslated. Alternative splice variants due to presence (var.1) or absence (var.2) of exon 3.

Transcription

In a telomeric --> centromeric orientation.

Protein

Description

894 amino acids, 95.5 kDa; contains 6 krueppel-like Zn-finger domains and a proline-rich region

Expression

Normal expression in thymus and brain; malignant expression in T-cell neoplasia and Ewing-family tumors.

Localisation

Inner nuclear membrane; colocalization with heterochromatin protein (HP1) and histone deacetylase SIRT1 suggests role as transcriptional repressor.

Function

Poorly defined; transcriptional repressor; developmentally regulates thymic differentiation and survival; inhibits HIV-1 Tat transactivation and repression of viral replication.

Homology

BCL11A on chromosome 2p13.

Mutations

Somatic

Unrecorded in humans. Biallelic mutation/deletion in mouse thymic lymphomas induced by ionizing radiation.

Implicated in

T-cell acute lymphoblastic leukemia (T-ALL) with t(5;14)(q35;q32) --> TLX3 - BCL11B

Disease

First detected as translocation partner of TLX3 (alias HOX11L2) in 15-20% pediatric cortical T-ALL with possible male bias; subsequently confirmed in adult T-ALL, albeit less frequently.

Prognosis

May be poor via strong cytogenetic assocation with TLX3 which reportedly confers adverse prognosis.

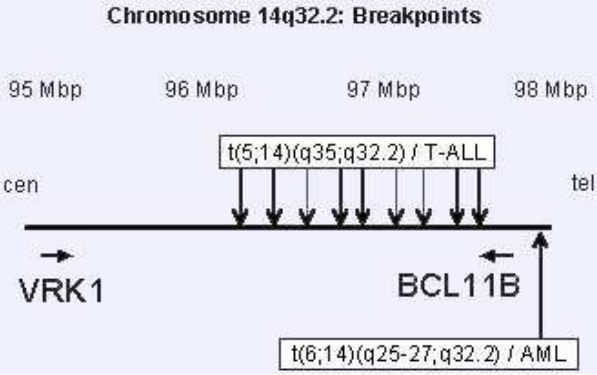
Cytogenetics

Additional known recurrent rearrangements reportedly absent from t(5;14) patients.

Oncogenesis

Distal regulatory elements drive ectopic expression of TLX3 in T-ALL and possibly other related NK-family Hox genes, viz. NKX2-5. Tumor suppressor role reported in mouse yet to be confirmed in man.

Breakpoints



Note

t(5;14) breakpoints are widely scattered over 1.2 Mbp downstream of BCL11B probably targeting distal enhancer(s) posited to lie in the "gene desert" separating BCL11b from VRK1. This region has been recently shown to carry multiple Dnase-I sensitive sites in T-cells which may represent a locus control region. The solitary AML breakpoint lies upstream of BCL11B and its significance has yet to be established.

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