

Gene Section

Mini Review

BCL10 (B-cell CLL/lymphoma 10)

Pei Lin

Department of Hematopathology, University of Texas-MD Anderson Cancer Center Houston, Texas, 77030 USA (PL)

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Identity

Other names: Bcl-10; CARMEN; CIPER; CLAP; Cellular-E10; c-E10; cCARMEN; hCLAP; mE10

HGNC (Hugo): BCL10

Location: 1p22.3

DNA/RNA

Description

12,308 bases, 4 exons, Transcription: 4.2 kb.

Transcription

Transcription produces 4 alternatively spliced variants and 1 unspliced form with 2,974 bps or 2,819 bps.

Protein

Description

233 amino acids with a molecular weight of 26252 Da.

Expression

BCL10 is expressed in all normal and malignant tissues. In the lymphoid tissue, it is highly expressed in the germinal center but low in the mantle zone, and intermediate in the marginal zone. BCL10 is likely to play a role in the normal development of the germinal center.

Localisation

BCL10 resides in the cytoplasm or perinuclear region of normal cells.

Function

BCL10 functions normally as a proapoptotic

protein through caspase recruitment domain (CARD) at the amino terminal and activation of NF-kappaB pathway. This activity requires oligomerization via the CARD domain and interaction between BCL10 and other CARD domain containing proteins including CARD9, CARD10, CARD11 and CARD14.

Homology

Equine herpesvirus-2 E10 gene.

Implicated in

1p rearrangement/non-hodgkin lymphoma

Disease

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma).

Phenotype stem cell origin: Marginal zone B-cells.

Epidemiology: Commonly seen in MALT lymphoma involving stomach (approximately 4%) and lung (approximately 9%). Uncommon in MALT lymphoma involving other sites.

Evolution: MALT lymphoma may evolve to diffuse large B-cell lymphoma.

Prognosis

Generally indolent.

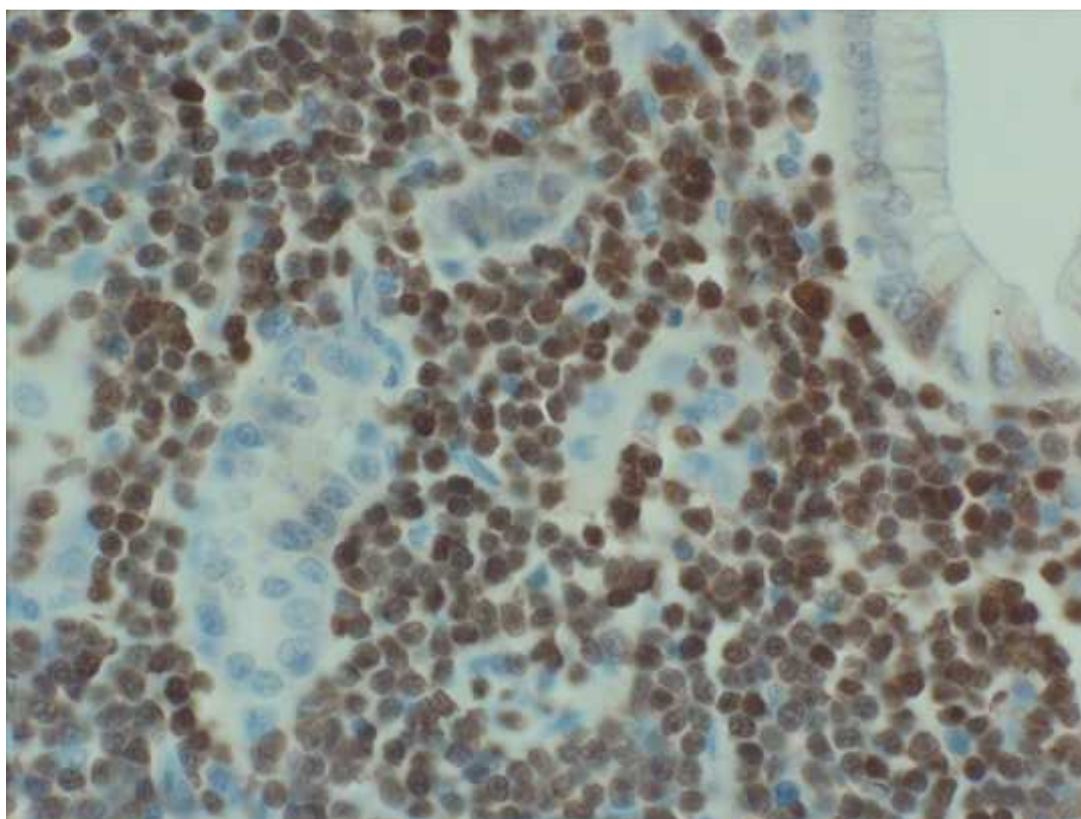
Cytogenetics

In t(1;14)(p22;q32). The gene on 14q32 is IgH. The breakpoint on 1p22 involves a recurrent breakpoint upstream of the promoter of BCL10.

Hybrid/Mutated gene

BCL10-IgH.

The translocation t(1;14)(p22;q32) is associated



MALT lymphoma expressing BCL10 (courtesy of Dr. Du M-Q).

with frameshift mutation of BCL10 and truncation of BCL10 protein distal to CARD. The mutant type of BCL10 enhances cell survival and proliferation through activation of NF-kappaB pathway. MALT lymphomas without BCL10 rearrangement may also carry BCL10 mutation however.

Abnormal protein

MALT lymphomas with t(1;14)(p22;q32) demonstrate strong nuclear BCL10 staining regardless of BCL10 mutation status. MALT lymphoma without t(1;14)(p22;q32) may also show strong nuclear staining. So a strong nuclear BCL10 staining is not always a presumptive evidence of t(1;14)(p22;q32). This pattern is different from the weak cytoplasmic expression observed in normal germinal center B-cells.

Oncogenesis

Loss of CARD domain through translocation and mutations lead to loss of proapoptotic activity. In addition, MALT1 and BCL10 may synergize in the activation of NF-kappaB leading to enhanced cell survival and downstream activation of anti-apoptotic/proliferative signals.

Various cancers

Disease

BCL10 mutations have also been described in

follicular lymphoma, Sezary syndrome, malignant mesothelioma, germ cell tumor, and colon cancer.

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