

## Gene Section

### Mini Review

# CBL (Cas-Br-M (murine) ecotropic retroviral transforming sequence)

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Published in Atlas Database: September 1999

Online updated version : <http://AtlasGeneticsOncology.org/Genes/CBLID171.html>  
DOI: 10.4267/2042/37531

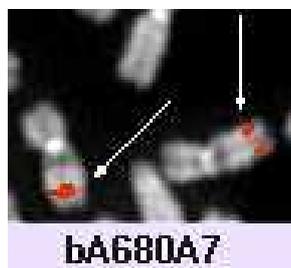
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## Identity

**Other names:** CBL2

**HGNC (Hugo):** CBL

**Location:** 11q23-q25



CBL (11q23) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

## DNA/RNA

### Transcription

10.5 kb; 2718 bp open reading frame.

## Protein

### Description

906 amino acids; 115 kDa; the evolutionarily conserved amino-terminal region of CBL is composed of three interacting domains: a four-helix bundle (4H), an EF-hand calcium binding domain, and a divergent SH2 domain; the three domains together form an integrated phosphoprotein-recognition module; this aminoterminal region is followed by a central Ring finger with a Cys3HisCys4 motif and a carboxy-

terminal region with multiple proline-rich sequences, a putative leucine zipper and several potential tyrosine phosphorylation sites.

### Expression

Ubiquitous but predominant in hematopoietic cells.

### Localisation

Cytoplasmic; cellular activation induces translocation of CBL to the plasma membrane or cytoskeleton.

### Function

CBL has been shown to have a negative regulatory activity in protein tyrosine kinase-mediated signaling pathways; CBL overexpression inhibits cell growth resulting from activation of the EGF and PDGF receptors (EGFR, PDGFRa, PDFFRb) and enhances ubiquitination and degradation of these receptors; CBL also negatively regulates the tyrosine phosphorylation of ZAP70 substrates in T cells.

## Mutations

### Germinal

The fragile site FRA11B has been localized to a stretch of CCG trinucleotides found in the 5' part of the CBL gene and has been involved in the pathogenesis of a proportion of inherited Jacobsen syndroms (OMIM 147791) which have a del(11)(q23qter) telomeric of an expansion of the stretch of CCG triplets. SOMATIC in 9% of the genetically unstable sporadic gastrointestinal tumors, an extension of an ATG trinucleotide repeat with no translation shift was detected in the coding region of CBL; this alteration was not present in cancers without the mutator phenotype

## Implicated in

**Gastrointestinal tumors (see above)**

## References

Langdon WY, Hartley JW, Klinken SP, Ruscetti SK, Morse HC 3rd. v-cbl, an oncogene from a dual-recombinant murine retrovirus that induces early B-lineage lymphomas. Proc Natl Acad Sci U S A. 1989 Feb;86(4):1168-72

Blake TJ, Shapiro M, Morse HC 3rd, Langdon WY. The sequences of the human and mouse c-cbl proto-oncogenes show v-cbl was generated by a large truncation encompassing a proline-rich domain and a leucine zipper-like motif. Oncogene. 1991 Apr;6(4):653-7

Jones C, Penny L, Mattina T, Yu S, Baker E, Voullaire L, Langdon WY, Sutherland GR, Richards RI, Tunnacliffe A.

Association of a chromosome deletion syndrome with a fragile site within the proto-oncogene CBL2. Nature. 1995 Jul 13;376(6536):145-9

Calin G, Herlea V, Barbanti-Brodano G, Negrini M. The coding region of the Bloom syndrome BLM gene and of the CBL proto-oncogene is mutated in genetically unstable sporadic gastrointestinal tumors. Cancer Res. 1998 Sep 1;58(17):3777-81

Liu YC, Altman A. Cbl: complex formation and functional implications. Cell Signal. 1998 Jun;10(6):377-85

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*This article should be referenced as such:*

Rosnet O. CBL (Cas-Br-M (murine) ecotropic retroviral transforming sequence). Atlas Genet Cytogenet Oncol Haematol. 1999; 3(3):130-131.

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