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

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, PDGFRα, PDGFRβ) 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 tripletsSOMATIC 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


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


*This article should be referenced as such:*