

Gene Section

Mini Review

BIRC6 (baculoviral IAP repeat-containing 6)

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Identity

Hugo: BIRC6

Other names: Baculoviral IAP repeat-containing ubiquitin-conjugating enzyme (BRUCE); Baculoviral IAP repeat-containing 6 (Apollon); FLJ13726; FLJ13786; KIAA1289

Location: 2p22

Local order: CARD12 (caspase recruitment domain family member 12) {encoded on minus strand, 32.303.029-32.344.427}; YPF4 (YIP1 domain family member 4) {32.356.483-32.385.159}; BIRC6 {32.435.234-32.697.467}; TTC27 (tetratricopeptide repeat domain 27) {32.706.633-32.899.620}; LTBP1 (latent transforming growth factor beta binding protein 1) {33.025.896-33.478.077}.

DNA/RNA

Description

The BIRC6 gene comprises 75 exons resulting in a transcript of 16066 bps. The ATG is in the first exon.

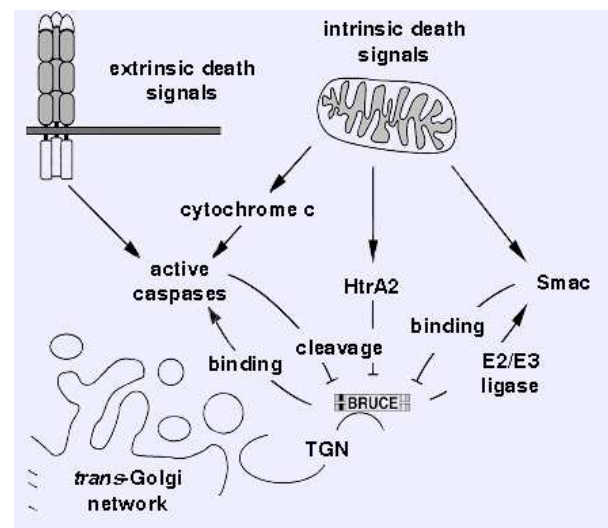
Transcription

Only one variant of BIRC6 has been found so far which comprises 14490 bps. There are several synonymous and nonsynonymous SNPs reported for BIRC6 (E589K, L1742F, R2187T, T2646S, T3708N, E3864K, Q4323H, N4324Y, S4325C, N4326T, P4329R).

Pseudogene

Not known. There is evidence for a processed pseudogene in *M. musculus*.

Protein



BRUCE is component of the apoptosis regulatory network. Multiple protein-protein interactions allow a switch from apoptosis inhibition to inactivation in later steps in apoptosis. BRUCE's action on activated caspases and other pro-apoptotic molecules might be restricted to the trans-Golgi network and the vesicular system.

Description

BIRC6 contains two functionally validated domains: A N-terminal BIR repeat (SMART SM00238, aa: 256-332) and a C-terminal UBC domain (SMART SM00212, aa: 4548 - 4712). The BIR repeat is needed for interactions with caspases and IAP-binding motif (IBM) containing proteins (HtrA2, Smac). The UBC domain can form a thiolester linkage with ubiquitin transferred by E1.

Between aa 1589-1633 a coiled-coil region can be found.

Expression

BRUCE is highly expressed in brain, testis, lymphatic cells and secretory organs and also found in any other tissue. It is highly expressed in the mouse embryos up to E11 and then transcript levels drop.

Localisation

Localized to membranes of the trans Golgi network (TGN) and the endosomal system.

Function

BRUCE is a peripheral membrane protein of the trans-Golgi network that protects cells from apoptosis by functioning as an inhibitor of apoptosis protein (IAP). BRUCE can bind and inhibit activated caspases CASP-3, CASP-6, CASP-7, CASP-8 and CASP-9. Furthermore it ubiquitylates caspase-9, HtrA2 (a pro-apoptotic serine protease) and DIABLO/Smac (a competitor for caspase-IAP interactions) thereby most likely targeting them for proteasomal degradation. The ubiquitylation reactions do not require an ubiquitin E3 ligase making BRUCE a chimeric E2/E3 ubiquitin ligase.

Homology

ubc-17 (*C. elegans*)
IAP6 (*A. gambiae*)
Bruce (*D. melanogaster*)
BIRC6 (*X. tropicalis*)
Birc6 (*M. musculus*).

Mutations

Note: There are several synonymous and nonsynonymous SNPs reported for BIRC6 (E589K, L1742F, R2187T, T2646S, T3708N, E3864K, Q4323H, N4324Y, S4325C, N4326T, P4329R).

Implicated in

Overexpression of BRUCE is found in several cancer cell lines (brain SF-268, SNB-78 - ovarian cancer OVCAR-8).

High level expression of BRUCE in these cell lines seems to correlate with their resistance to apoptotic reagents. Furthermore, bone marrow cells of myelodysplastic syndromes exhibit significant expression of BIRC6.

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