

## Gene Section

### Mini Review

# BAG3 (Bcl-2 associated athanogene 3)

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### Identity

**Hugo:** BAG3

**Other names:** BAG-3; BIS; CAIR-1

**Location:** 10q26.11

### DNA/RNA

#### Description

The gene encompasses 26449 bases, 4 exons.

#### Transcription

2608 nucleotides mRNA.

### Protein

#### Description

575 amino acids. 74 kDa protein, belonging to the evolutionary conserved family of BAG domain-containing proteins.

#### Expression

BAG3 protein is constitutively expressed in muscle and a few other normal cell types, and in some tumors; its expression can be induced by stressors in a number of cell types.

#### Localisation

BAG3 is a cytoplasmatic protein, particularly concentrated in the rough endoplasmic reticulum; a slightly different molecular weight, a doublet form or a nuclear localisation can be observed in some cell types and/or following cell exposure to stressors.

#### Function

Through its BAG domain, BAG3 protein binds with high affinity to the ATPase domain of Hsc70 and regulates its chaperone activity in a Hip-modulated manner; through its PXXP region, BAG3 binds to the

SH3 domain of PLC-gamma and forms an epidermal growth factor (EGF)-regulated ternary complex; the proline-rich repeat appears to be involved in regulating cell adhesion and migration, through an indirect effect on focal adhesion kinase (FAK) and its downstream partners; BAG3 knockout mice develop a fulminant myopathy; downmodulation of BAG3 protein levels enhance cell apoptotic response to several inducers, while hyperexpression protects cells from apoptosis.

#### Homology

Other members of BAG family.

### Mutations

**Note:** Unknown.

### Implicated in

#### ***B*-chronic lymphocytic leukaemia**

##### Disease

Expression of BAG3 gene in leukaemic cell samples from a study on 24 B-CLL-affected patients was detected by RT-PCR and immunofluorescence. Downmodulation of its levels by antisense ODNs resulted in enhancing cytochrome c release, caspase 3 activation and appearance of hypodiploid elements in response to fludarabine.

#### ***Childhood acute lymphoblastic leukemia***

##### Disease

Expression of BAG3 gene in leukaemic cell samples from a study on 11 ALL- affected patients was detected by immunofluorescence. Downmodulation of its levels by antisense ODNs resulted in stimulating caspase 3 activity and enhancing by more than 100% the percentages of apoptotic elements in primary cultures, either untreated or incubated with cytosine arabinoside.

## Thyroid carcinomas

### Disease

BAG3 was expressed in human thyroid carcinoma cell lines; small interfering RNA-mediated downmodulation of its levels significantly enhanced NPA cell apoptotic response to TRAIL. The protein was not detectable in 19 of 20 specimens of normal thyroid or goiters, whereas 54 of 56 analyzed carcinomas (15 follicular carcinomas, 28 papillary carcinomas, and 13 anaplastic carcinomas) were clearly positive for BAG3 expression.

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