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Gene Section
Mini Review

BOK (Bcl2-related ovarian killer)

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Identity

Hugo: BOK
Other names: Mtd (Matador); BOKL; BCL2-like 9; BCL2L9; MGC4631
Location: 2q37.3
Local order: LOC728248; STK25; BOK; THAP4; ATG4B.

DNA/RNA

Description

The gene encompasses 15,361 bp of DNA with 5 exons.

Transcription

Alternative splicing results in expression of two mRNA variants. The full-length (Bok-L) mRNA comprises 2.6 kb with the 639 bp open reading frame. The truncated form (Bok-S) results from skipping of exon three and a deletion of 43 bp in the Bok-L coding region. It has been shown that transcription activity of the Bok gene depends on expression of p53 and can be directly regulated at the gene promoter level by E2F transcription factors during cell cycle progression.

Protein

Description

A Bok transcript was initially isolated from a rat ovarian fusion cDNA library. Sequencing of this transcript has revealed that full-length BOK protein consists of 213 amino acids and contains three conserved BCL2 homology regions BH1, BH2, and BH3 in addition to a C-terminal transmembrane domain. BOK-S that results from the alternative splicing has its N-terminal BH3 domain part fused to the C-terminal part of the BH1 region. Using the yeast two-hybrid system, it has been demonstrated that, although the BH domains composition of BOK-L protein was similar to that of BAX and BAK, it interacted only with MCL-1, BHRF1, and BCL2A1/BFL-1 but not other anti-apoptotic multidomain BCL-2 family members.

Expression

Bok mRNA was isolated from the ovarian cDNA library. Results of Northern blot analysis revealed high expression levels of Bok mRNA in the reproductive tissues, such as ovary, testis, and uterus. Using in situ hybridization the authors localized Bok mRNA in granulosa cells. However, Bok expression is also evident in other mammalian tissues, such as brain, liver, thymus, lung, heart, kidney intestinal epithelium and lymphoid tissues.

Localisation

Intracellular localization of BOK protein remains to be clarified. Results of different studies suggest either its mitochondrial or cytosolic and nuclear localization.

Function

BOK promotes both caspase-dependent and caspase-independent apoptosis at the level of mitochondria in various cell types by promoting the release of pro-apoptotic mitochondrial factors to the cell cytosol. Inhibition of BOK induction using siRNA markedly decreases p53-dependent cell death. However, a specific mechanism, by which BOK increases mitochondrial membrane permeability, remains unknown. Apoptosis induced by BOK overexpression cannot be inhibited by Bcl-2 or Bcl-XL suggesting a unique role for BOK in apoptosis. A recent report indicates that BOK may cooperate with a BH3-only member, NOXA in p53-dependent apoptosis induced by DNA damage in human neuroblastoma cells, where it substitutes for a function of pro-apoptotic BAX.

Homology

Evolutionary conserved from fly to human.

Mutations

Note: Unknown.

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