BNIP3 (Bcl-2/adenovirus E1B 19kD-interacting protein 3)

Sang-Gi Paik, Hayyoung Lee

Department of Biology, School of Biosciences and Biotechnology, Chungnam National University, Daejeon 305-764, Korea

Published in Atlas Database: October 2007

Online updated version: http://AtlasGeneticsOncology.org/Genes/BNIP3ID822ch10q26.html

DOI: 10.4267/2042/38517

This work is licensed under a Creative Commons Attribution-Non-commercial-No Derivative Works 2.0 France Licence.

© 2008 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Hugo: BNIP3
Other names: NIP3
Location: 10q26.3

DNA/RNA

14.23 kb on reverse strand; 6 exons

Transcription

mRNA in MCF-7 cells are 1.7 kb (major) and 1.5 kb (minor) and 1.3 kb (minor).

Protein

194 amino acids; 1 BH3 domain and 1 TM domain; BH3 only Bcl2 family member. The TM domain and C-terminal tail are essential for mitochondrial membrane localization and proapoptotic function. The predicted molecular weight is 21.5 kDa. BNIP3 migrates as 30 kDa monomeric form and 60 kDa dimeric form on SDS-PAGE.

Expression

BNIP3 is detected in mouse oviduct, uterus, spleen, lung, stomach, brain, seminal, lacrimal, submaxillary, heart, kidney, liver. It can be detected in cell lines such as HeLa, 293T, RAW264.7 and K562 cells. Its expression can be induced in both normal and cancer tissues that experience hypoxia or hypoxia-like conditions. Other stimuli, such as nitric oxide or arsenic trioxide, are also reported to induce BNIP3 expression.

Localisation

Outer mitochondrial membrane.

Function

Proapoptotic protein; BNIP3 leads to opening of the mitochondrial permeability transition pore (PTP) thereby abolishing the proton electrochemical gradient and this is followed by chromatin condensation and DNA fragmentation. BNIP3 leads necrosis-like apoptosis. Unusually to the other Bcl-2 family proteins, the BNIP3-induced cell death depends not on BH3 domain but on C-terminal TM domain. BNIP3-induced cell death is known to be independent the nuclear translocation of AIF. However, whether caspase activation and cytochrome c release are involved in the cell death remains controversial. BNIP3 can induce autophagy. However whether the consequence of the autophagy is the cell death or survival remains to be established.

Since BNIP3 is induced by hypoxia through transcription factor HIF-1, it was postulated to play a role in hypoxia-induced cell death. Hypoxia-induced acidosis augments the proapoptotic function of BNIP3.

Homology

The close homologue: BNIP3L/BNIP3a/Nix/B5 (8q21).
The BH3-only Bcl2 family members: BBC3/PUMA (19q13), BCL2L11/BIM/BOD (2q13), BID (22q11), BIK/NBK/BBC1 (22q13), BLK (8q23), BMF (15q14), HRK/DP5/BID3 (12q24), PMAIP1/NOXA (18q21).

**Implicated in**

**Pancreatic cancer**

Prognosis

Pancreatic adenocarcinoma is highly resistant to chemical and radiation therapy, and has an extremely poor prognosis. Reduced expression of BNIP3 increased resistance to gemcitabine and 5-fluoro-uracil (5-FU) and showed a good correlation with reduced patient survival.

Oncogenesis

In most cases of pancreatic adenocarcinoma, BNIP3 expression was not detected even in response to hypoxia. The promoter of BNIP3 is located within a CpG island and is methylated in most pancreatic cancer cell lines. Restoration of BNIP3 expression by the methyltransferase inhibitor, 5-aza-deoxycytidine, showed a good correlation with reduced patient survival.

**Colorectal cancer**

Oncogenesis

Methylation of BNIP3 in 66% of primary colorectal cancer.

**References**


Bruick RK. Expression of the gene encoding the proapoptotic Nip3 protein is induced by hypoxia. Proc Natl Acad Sci USA 2000;97:9082-9087.


This article should be referenced as such: