

## Gene Section

### Mini Review

# FNIP1 (folliculin interacting protein 1)

Laura S Schmidt

Laboratory of Immunobiology, National Cancer Institute Frederick, Bldg 560, Rm 12-69, Frederick, MD 21702, USA

Published in Atlas Database: July 2007

Online updated version: <http://AtlasGeneticsOncology.org/Genes/FNIP1ID44003ch5q23.html>

DOI: 10.4267/2042/38472

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:** FNIP1

**Other names:** KIAA1961; MGC 667

**Location:** 5q23.3

### DNA/RNA

#### Description

The FNIP1 gene consists of a 6655 nt mRNA (using NM 133372 derived from AC005593.1, DQ145719.1, AC008695.9 and AL832008.1, the coding sequence extends from nt143 to nt3643) and contains 18 coding exons. The initiation codon is located within exon 1.

#### Transcription

Northern blot analysis revealed an about 7 kb FNIP1 mRNA transcript that was expressed in most major adult tissues, with strongest expression in heart, liver and placenta, and expression in kidney and lung, tissues involved in the Birt-Hogg-Dube' syndrome phenotype (see below). Several alternate transcripts lacking one or more exons have been reported. Transcript 1 is the full-length isoform. Transcript 2 lacks exon 7 (NM 001008738).

### Protein

#### Description

The FNIP1 protein contains 1166 amino acids and has an estimated molecular weight of 130 kDa.

#### Localisation

Epitope-tagged FNIP1 expressed in HeLa cells localized exclusively in the cytoplasm.

#### Function

Coimmunoprecipitation studies to elucidate the function of folliculin (FLCN) (encoded by the tumor suppressor gene, BHD/FLCN, which is mutated in the Birt-Hogg-Dube' syndrome) identified a novel folliculin-interacting protein, FNIP1, which interacts through the C-terminus of FLCN. FNIP1 overexpression enhanced phosphorylation of FLCN and phospho-FLCN preferentially bound to FNIP1. FNIP1 is a novel protein with no domains to suggest function. By coimmunoprecipitation studies FNIP1 was also found to interact with the heterotrimer, 5'AMP-activated protein kinase (AMPK), a key molecule for energy sensing and a negative regulator of mTOR (mammalian target of rapamycin). AMPK, which



bound to FNIP1, was preferentially in its phosphorylated (active) form and FNIP1 could act as a substrate for AMPK phosphorylation both in vitro and in vivo. Inhibition of AMPK kinase activity resulted in reduced FNIP1 protein expression in HEK293 cells suggesting that phosphorylation of FNIP1 by AMPK may enhance protein stability. These data suggest that FNIP1 and its interacting partner, FLCN, may be involved in energy and nutrient-sensing through the AMPK and mTOR signaling pathways. FNIP1 was also shown to interact with HSP90 by coimmunoprecipitation in HEK293 cells.

### Homology

A comparison of FNIP1 proteins across species identified 5 blocks of conserved sequence with at least 35% similarity. FNIP1 homologs have been identified in *Mus musculus*, *Gallus gallus*, *Xenopus tropicalis*, *Danio rerio*, *Drosophila melanogaster* and *Caenorhabditis elegans*.

## Implicated in

### **Birt-Hogg-Dube'(BHD) syndrome**

**Note:** FNIP1 interacts with FLCN, encoded by a novel tumor suppressor gene, BHD/FLCN, which is mutated in the germline of patients with BHD syndrome.

### Disease

Genodermatosis characterized by the triad of benign tumors of the hair follicle, spontaneous pneumothorax and kidney tumors.

## References

- Nagase T, Kikuno R, Ohara O. Prediction of the coding sequences of unidentified human genes. XXII. The complete sequences of 50 new cDNA clones which code for large proteins. *DNA Res* 2001;8:319-327.
- Baba M, Hong SB, Sharma N, Warren MB, Nickerson ML, Iwamatsu A, Esposito D, Gillette WK, Hopkins RF, Hartley JL, Furihata M, Oishi S, Zhen W, Burke TR, Linehan WM, Schmidt LS, Zbar B. Folliculin encoded by the BHD gene interacts with a binding protein, FNIP1, and AMPK, and is involved in AMPK and mTOR signaling. *Proc Natl Acad Sci USA* 2006;103:15552-15557.

---

*This article should be referenced as such:*

Schmidt LS. FNIP1 (folliculin interacting protein 1). *Atlas Genet Cytogenet Oncol Haematol.*2008;12(1):39-40.

---