

Gene Section

Mini Review

RCHY1 (ring finger and CHY zinc finger domain containing 1)

Wenrui Duan, Miguel A Villalona-Calero

Comprehensive Cancer Center, 1230 JCHRI, 300 West 10th Ave, Columbus, Ohio 43210, USA

Published in Atlas Database: March 2006

Online updated version: <http://AtlasGeneticsOncology.org/Genes/RCHY1ID43012ch04q21.html>
DOI: 10.4267/2042/38321

This work is licensed under a Creative Commons Attribution-Non-commercial-No Derivative Works 2.0 France Licence.
© 2006 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Hugo: RCHY1

Other names: PIRH2; ARNIP; CHIMP; RNF199; ZNF363; PRO1996; DKFZp586C1620

Location: 4q21.1

DNA/RNA

Description

The gene encompasses 32 kb of DNA; 9 exons.

Transcription

4.3 kb nucleotides mRNA. 783 bp open reading frame.

Protein

Description

261 amino acids; 32 kDa protein.

Expression

RCHY1 expresses at higher level in liver, testis and heart. Lower expression is detected in lung, brain, muscle and spleen. RCHY1 is overexpressed in non-small cell lung cancers.

Localisation

The localization of RCHY1 protein in human lung tumors was evaluated immunohistochemically. RCHY1 protein was found primarily in the cytoplasm and membrane and a small portion in the nucleus of malignant cells.

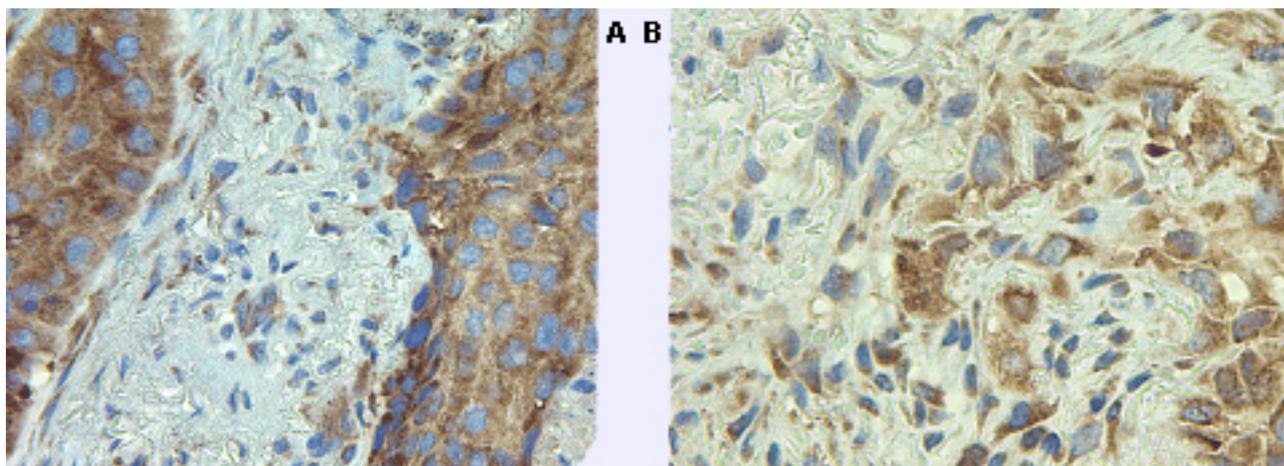
Function

RCHY1 is an ubiquitin-protein E3 ligase that promotes p53 degradation. The RCHY1 gene encodes a RING-H2 domain-containing protein with intrinsic ubiquitin-protein ligase activity. It has been reported that

RCHY1(Pirh2) physically interacts with p53 and promotes ubiquitination of p53 independently of Mdm2. RCHY1 was also reported to be transactivated by the p53 product in MEFs, murine proB cell BaF3 and human BJT fibroblasts cells. Therefore, like MDM2, RCHY1 participates in an autoregulatory feedback loop that controls p53 function. Expression of RCHY1 decreased the level of p53 protein, while abrogation of endogenous RCHY1 expression increased the level of p53. Furthermore, RCHY1 represses p53 functions, including p53-dependent transactivation and growth inhibition. RCHY1 is overexpressed in both human and murine lung cancers by comparing Pirh2 mRNA and protein level between lung neoplastic tissues and uninvolved adjacent lung tissue. The increased RCHY1 protein could cause degradation of wild type p53 and reduce the tumor suppression function in tumor cells.

It has been reported that coexpression of RCHY1(ARNIP) and androgen receptor (AR) in COS-1 cells reduces the interaction between AR N- and C-terminus. The RING-H2 domain of the RCHY1 functions as an ubiquitin-protein ligase in vitro in the presence of a specific ubiquitin-conjugating enzyme, Ubc4-1. Mutation of a single cysteine residue in the RCHY RING-H2 domain (Cys145Ala) abolished this E3 ubiquitin ligase activity. Fluorescent protein tagging studies revealed that AR-RCHY1 interaction was hormone-independent in COS-1 cells, and suggest that co-localization of both AR and RCHY1 to the nucleus upon androgen addition may allow RCHY1 to play a role in nuclear processes.

It has been reported that wild-type RCHY1 is an unstable protein with a short half-life and coexpression of TIP60 enhances RCHY1 protein stability and alters RCHY1 subcellular localization. In addition, MVP (measles virus phosphoprotein) is able to specifically



Immunohistochemical detection of human RCHY1 protein in non-small cell lung cancers. (A) squamous cell carcinoma, and (B) large cell carcinoma.

interact with and stabilize the RCHY1 by preventing its ubiquitination. It has been reported that the RCHY1 also interacts with NTKL-BP1 (N-terminal kinase-like protein-binding protein 1) proteína.

Homology

It belongs to the ring finger ubiquitin protein E3 ligase family. Containing Conserved RING-finger Domain (residues 145-186) and CHY zinc finger (residues 20-94).

Mutations

Note: Unknown.

Implicated in

Non-Small Cell Lung Cancer

Disease

Lung cancers are pathologically classified as small cell lung cancer and non-small cell lung cancer (non-small cell lung cancer includes large cell carcinomas, squamous cell carcinomas and adenocarcinomas).

Oncogenesis

RCHY1 protein is overexpressed in about 84% human lung cancers compared to uninvolved lung tissue. The RCHY1 protein was also elevated in about 93% of murine lung tumors. Because RCHY1 is an ubiquitin-protein ligase that promotes p53 protein degradation,

the increased RCHY1 expression could play an important role in lung tumorigenesis.

References

- Beitel LK, Elhaji YA, Lumbroso R, Wing SS, Panet-Raymond V, Gottlieb B, Pinsky L, Trifiro MA. Cloning and characterization of an androgen receptor N-terminal-interacting protein with ubiquitin-protein ligase activity. *J Mol Endocrinol* 2002;29:41-60.
- Leng RP, Lin Y, Ma W, Wu H, Lemmers B, Chung S, Parant JM, Lozano G, Hakem R, Benchimol S. Pirh2, a p53-induced ubiquitin-protein ligase, promotes p53 degradation. *Cell* 2003;112:779-791.
- Duan W, Gao L, Druhan LJ, Zhu WG, Morrison C, Otterson GA, Villalona-Calero MA. Expression of Pirh2, a newly identified ubiquitin protein ligase, in lung cancer. *J Natl Cancer Inst* 2004;96:1718-1721.
- Logan IR, Sapountzi V, Gaughan L, Neal DE, Robson CN. Control of human PIRH2 protein stability: involvement of TIP60 and the proteasome. *J Biol Chem* 2004;279:11696-11704.
- Zhang L, Li J, Wang C, Ma Y, Huo K. A new human gene hNTKL-BP1 interacts with hPirh2. *Biochem Biophys Res Commun* 2005;330:293-297.
- Chen M, Cortay JC, Logan IR, Sapountzi V, Robson CN, Gerlier D. Inhibition of ubiquitination and stabilization of human ubiquitin E3 ligase PIRH2 by measles virus phosphoprotein. *J Virol* 2005;79:11824-11836.

This article should be referenced as such:

Duan W, Villalona-Calero MA. RCHY1 (ring finger and CHY zinc finger domain containing 1). *Atlas Genet Cytogenet Oncol Haematol.*2006;10(3):173-174.