

FLCN Gene

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Folliculin

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1. Normal Function

The *FLCN* gene provides instructions for making a protein called folliculin. Researchers have not determined the protein's function, but they believe it may act as a tumor suppressor. Tumor suppressors help control the growth and division of cells. The folliculin protein is present in many of the body's tissues, including the brain, heart, placenta, testis, skin, lung, and kidney. Researchers have proposed several possible roles for the protein within cells. Folliculin may be important for cells' uptake of foreign particles (endocytosis or phagocytosis). The protein may also play a role in the structural framework that helps to define the shape, size, and movement of a cell (the cytoskeleton) and in interactions between cells. In the lung, it is thought that folliculin plays a role in repairing and re-forming lung tissue following damage.

2. Health Conditions Related to Genetic Changes

2.1 Birt-Hogg-Dubé Syndrome

Several mutations in the *FLCN* gene have been identified in people with Birt-Hogg-Dubé syndrome, a condition characterized by multiple noncancerous (benign) skin tumors, an increased risk of other tumors, and lung cysts. Most of these mutations insert or delete one or more protein building blocks (amino acids) in the folliculin protein. These mutations lead to the production of an abnormally small, nonfunctional version of this protein. Without folliculin, researchers believe that cells can grow and divide uncontrollably to form cancerous or noncancerous tumors. They have not determined how a loss of folliculin increases the risk of lung abnormalities that are often associated with Birt-Hogg-Dubé syndrome.

2.2 Primary Spontaneous Pneumothorax

At least eight mutations in the *FLCN* gene have been found to cause primary spontaneous pneumothorax. This condition occurs when air builds up abnormally in the space between the lungs and the chest cavity (plural space), potentially leading to a partial or complete collapse of the lung. Many of these mutations result in the production of a folliculin protein that is abnormally short and nonfunctional. Researchers have not determined how *FLCN* gene mutations lead to the development of primary spontaneous pneumothorax. One theory is that the altered folliculin protein may trigger inflammation within lung tissue that could lead to the formation of small sacs of air (blebs) in the tissue. These blebs can rupture, causing air to leak into the pleural space. People who have an *FLCN* gene mutation associated with primary spontaneous pneumothorax all appear to develop blebs, but it is estimated that only 40 percent of those individuals go on to have a primary spontaneous pneumothorax.

2.3 Other Cancers

Some gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes, called somatic mutations, are not inherited. Somatic mutations in the *FLCN* gene are probably associated with several types of nonhereditary (sporadic) tumors. Specifically, somatic *FLCN* mutations have been identified in some cases of clear cell renal cell carcinoma (a type of kidney cancer) and in some colon cancers. These mutations may change the structure of the folliculin protein, disrupting its tumor suppressor function. Researchers do not know how *FLCN* mutations lead to these particular forms of cancer.

3. Other Names for This Gene

- BHD

- FLCL
- FLCN_HUMAN
- MGC17998
- MGC23445

References

1. da Silva NF, Gentle D, Hesson LB, Morton DG, Latif F, Maher ER. Analysis of the Birt-Hogg-Dubé (BHD) tumour suppressor gene in sporadic renal cell carcinoma and colorectal cancer. *J Med Genet.* 2003 Nov;40(11):820-4.
2. Fröhlich BA, Zeitz C, Mátyás G, Alkadhi H, Tuor C, Berger W, Russi EW. Novel mutations in the folliculin gene associated with spontaneous pneumothorax. *Eur Respir J.* 2008 Nov;32(5):1316-20. doi: 10.1183/09031936.00132707.
3. Graham RB, Nolasco M, Peterlin B, Garcia CK. Nonsense mutations in folliculin presenting as isolated familial spontaneous pneumothorax in adults. *Am J Respir Crit Care Med.* 2005 Jul 1;172(1):39-44.
4. Kahnoski K, Khoo SK, Nassif NT, Chen J, Lobo GP, Segelov E, Teh BT. Alterations of the Birt-Hogg-Dubé gene (BHD) in sporadic colorectal tumours. *J Med Genet.* 2003 Jul;40(7):511-5.
5. Nickerson ML, Warren MB, Toro JR, Matrosova V, Glenn G, Turner ML, Duray P, Merino M, Choyke P, Pavlovich CP, Sharma N, Walther M, Munroe D, Hill R, Maher E, Greenberg C, Lerman MI, Linehan WM, Zbar B, Schmidt LS. Mutations in a novel gene lead to kidney tumors, lung wall defects, and benign tumors of the hair follicle in patients with the Birt-Hogg-Dubé syndrome. *Cancer Cell.* 2002 Aug;2(2):157-64.
6. Painter JN, Tapanainen H, Somer M, Tukiainen P, Aittomäki K. A 4-bp deletion in the Birt-Hogg-Dubé gene (FLCN) causes dominantly inherited spontaneous pneumothorax. *Am J Hum Genet.* 2005 Mar;76(3):522-7.
7. Schmidt LS, Nickerson ML, Warren MB, Glenn GM, Toro JR, Merino MJ, Turner ML, Choyke PL, Sharma N, Peterson J, Morrison P, Maher ER, Walther MM, Zbar B, Linehan WM. Germline BHD-mutation spectrum and phenotype analysis of a large cohort of families with Birt-Hogg-Dubé syndrome. *Am J Hum Genet.* 2005 Jun;76(6):1023-33.
8. Shin JH, Shin YK, Ku JL, Jeong SY, Hong SH, Park SY, Kim WH, Park JG. Mutations of the Birt-Hogg-Dubé (BHD) gene in sporadic colorectal carcinomas and colorectal carcinoma cell lines with microsatellite instability. *J Med Genet.* 2003 May;40(5):364-7.
9. Vocke CD, Yang Y, Pavlovich CP, Schmidt LS, Nickerson ML, Torres-Cabala CA, Merino MJ, Walther MM, Zbar B, Linehan WM. High frequency of somatic frameshift BHD gene mutations in Birt-Hogg-Dubé-associated renal tumors. *J Natl Cancer Inst.* 2005 Jun 15;97(12):931-5. Erratum in: *J Natl Cancer Inst.* 2005 Jul 20;97(14):1096.
10. Warren MB, Torres-Cabala CA, Turner ML, Merino MJ, Matrosova VY, Nickerson ML, Ma W, Linehan WM, Zbar B, Schmidt LS. Expression of Birt-Hogg-Dubé gene mRNA in normal and neoplastic human tissues. *Mod Pathol.* 2004 Aug;17(8):998-1011.

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