CFTR Gene

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Cystic fibrosis transmembrane conductance regulator

genes

1. Normal Function

The *CFTR* gene provides instructions for making a protein called the cystic fibrosis transmembrane conductance regulator. This protein functions as a channel across the membrane of cells that produce mucus, sweat, saliva, tears, and digestive enzymes. The channel transports negatively charged particles called chloride ions into and out of cells. The transport of chloride ions helps control the movement of water in tissues, which is necessary for the production of thin, freely flowing mucus. Mucus is a slippery substance that lubricates and protects the lining of the airways, digestive system, reproductive system, and other organs and tissues.

The CFTR protein also regulates the function of other channels, such as those that transport positively charged particles called sodium ions across cell membranes. These channels are necessary for the normal function of organs such as the lungs and pancreas.

2. Health Conditions Related to Genetic Changes

2.1. Congenital bilateral absence of the vas deferens

About 80 *CFTR* mutations have been identified in males with congenital bilateral absence of the vas deferens. Most affected males have a mild mutation in at least one copy of the gene in each cell. These mutations allow the CFTR protein to retain some of its function. Some affected males have a mild mutation in one copy of the *CFTR* gene in each cell and a more severe, cystic fibrosis-causing mutation in the other copy of the gene.

Mutations in the *CFTR* gene disrupt the function of the chloride channel, preventing the usual flow of chloride ions and water into and out of cells. As a result, cells in the male genital tract produce mucus that is abnormally thick and sticky. This mucus clogs the tubes that carry sperm from the testes (the vas deferens) as they are forming, causing them to deteriorate before birth. Without the vas deferens, sperm cannot be transported from the testes to become part of semen. Men with congenital bilateral absence of the vas deferens are unable to father children (infertile) unless they use assisted reproductive technologies.

2.2. Cystic fibrosis

More than 1,000 mutations in the *CFTR* gene have been identified in people with cystic fibrosis. Most of these mutations change single protein building blocks (amino acids) in the CFTR protein or delete a small amount of DNA from the *CFTR* gene. The most common mutation, called delta F508, is a deletion of one amino acid at position 508 in the CFTR protein. The resulting abnormal channel breaks down shortly after it is made, so it never reaches the cell membrane to transport chloride ions.

Disease-causing mutations in the *CFTR* gene alter the production, structure, or stability of the chloride channel. All of these changes prevent the channel from functioning properly, which impairs the transport of chloride ions and the movement of water into and out of cells. As a result, cells that line the passageways of the lungs, pancreas, and other organs produce mucus that is abnormally thick and sticky. The abnormal mucus obstructs the airways and glands, leading to the characteristic signs and symptoms of cystic fibrosis.

2.3. Hereditary pancreatitis

2.4. Other disorders

A few mutations in the *CFTR* gene have been identified in people with isolated problems affecting the digestive or respiratory system. For example, *CFTR* mutations have been found in some cases of idiopathic pancreatitis, an inflammation of the pancreas that causes abdominal pain, nausea, vomiting, and fever. Although *CFTR* mutations may be a risk factor, the cause of idiopathic pancreatitis is unknown.

Changes in the *CFTR* gene also have been associated with rhinosinusitis, which is a chronic inflammation of the tissues that line the sinuses. This condition causes sinus pain and pressure, headache, fever, and nasal congestion or drainage. Other respiratory problems, including several conditions that partially block the airways and interfere with breathing, are also associated with *CFTR* mutations. These conditions include bronchiectasis, which damages the passages leading from the windpipe to the lungs (the bronchi), and allergic bronchopulmonary aspergillosis, which results from hypersensitivity to a certain type of fungal infection. Additional genetic and environmental factors likely play a part in determining the risk of these complex conditions.

3. Other Names for This Gene

- ABC35
- ABCC7
- cAMP-dependent chloride channel
- CF
- CFTR_HUMAN
- cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7)
- cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7)

- MRP7

References

1. Cohn JA. Reduced CFTR function and the pathobiology of idiopathicpancreatitis. J Clin Gastroenterol. 2005 Apr;39(4 Suppl 2):S70-7. Review. Citation on PubMed
2. Cuppens H, Cassiman JJ. CFTR mutations and polymorphisms in male infertility. Int J Androl. 2004 Oct;27(5):251-6. Review. Citation on PubMed
3. Deignan JL, Astbury C, Cutting GR, Del Gaudio D, Gregg AR, Grody WW, Monaghan KG, Richards S; ACMG Laboratory Quality Assurance Committee. CFTR varianttesting: a technical standard of the American College of Medical Genetics andGenomics (ACMG). Genet Med. 2020 Aug;22(8):1288-1295. doi:10.1038/s41436-020-0822-5. Epub 2020 May 14. Citation on PubMed
4. Gadsby DC, Vergani P, Csanády L. The ABC protein turned chloride channel whosefailure causes cystic fibrosis. Nature. 2006 Mar 23;440(7083):477-83. Review. Citation on PubMed or Free article on PubMed Central
5. Kulczycki LL, Kostuch M, Bellanti JA. A clinical perspective of cysticfibrosis and new genetic findings: relationship of CFTR mutations togenotype-phenotype manifestations. Am J Med Genet A. 2003 Jan 30;116A(3):262-7.Review. Citation on PubMed
6. Nick JA, Rodman DM. Manifestations of cystic fibrosis diagnosed in adulthood. Curr Opin Pulm Med. 2005 Nov;11(6):513-8. Review. Citation on PubMed
7. Noone PG, Knowles MR. 'CFTR-opathies': disease phenotypes associated withcystic fibrosis transmembrane regulator gene mutations. Respir Res.2001;2(6):328-32. Epub 2001 Aug 9. Review. Citation on PubMed or Free article on PubMed Central
8. Ong T, Marshall SG, Karczeski BA, Sternen DL, Cheng E, Cutting GR. CysticFibrosis and Congenital Absence of the Vas Deferens. 2001 Mar 26 [updated 2017Feb 2]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K,Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1250/ Citation on PubMed
9. Ratbi I, Legendre M, Niel F, Martin J, Soufir JC, Izard V, Costes B, Costa C, Goossens M, Girodon E. Detection of cystic fibrosis transmembrane conductanceregulator (CFTR) gene rearrangements enriches the mutation spectrum in congenitalbilateral absence of the vas deferens and impacts on genetic counselling. HumReprod. 2007 May;22(5):1285-91. Epub 2007 Feb 28. Citation on PubMed
10. Rowe SM, Miller S, Sorscher EJ. Cystic fibrosis. N Engl J Med. 2005 May12;352(19):1992-2001. Citation on PubMed

11. Taulan M, Girardet A, Guittard C, Altieri JP, Templin C, Beroud C, des GeorgesM, Claustres M. Large genomic rearrangements in the CFTR gene contribute toCBAVD. BMC Med Genet. 2007 Apr 20;8:22. Citation on PubMed or Free article on PubMed Central
12. Vankeerberghen A, Cuppens H, Cassiman JJ. The cystic fibrosis transmembraneconductance regulator: an intriguing protein with pleiotropic functions. J CystFibros. 2002 Mar;1(1):13-29. Review. Citation on PubMed