TGFBR2 Gene

Subjects: Genetics & Heredity
Contributor: Rui Liu

Transforming growth factor beta receptor 2: The TGFBR2 gene provides instructions for making a protein called transforming growth factor-beta (TGF-β) receptor type 2.

Keywords: genes

1. Normal Function

The *TGFBR2* gene provides instructions for making a protein called transforming growth factor-beta (TGF-β) receptor type 2. This receptor transmits signals from the cell surface into the cell through a process called signal transduction. Through this type of signaling, the environment outside the cell affects activities inside the cell such as stimulation of cell growth and division.

To carry out its signaling function, the TGF-β receptor type 2 spans the cell membrane, so that one end of the protein projects from the outer surface of the cell (the extracellular domain) and the other end remains inside the cell (the intracellular domain). A protein called TGF-β attaches (binds) to the extracellular domain of the TGF-β receptor type 2, which turns on (activates) the receptor and allows it to bind to another receptor on the cell surface. These three proteins form a complex, which triggers signal transduction by activating other proteins in a signaling pathway called the TGF-β pathway.

Signals transmitted by the TGF-β receptor complex trigger various responses by the cell, including the growth and division (proliferation) of cells, the maturation of cells to carry out specific functions (differentiation), cell movement (motility), and controlled cell death (apoptosis). Because TGF-β receptor type 2 helps prevent cells from growing and dividing too rapidly or in an uncontrolled way, it can suppress the formation of tumors.

2. Health Conditions Related to Genetic Changes

2.1. Familial thoracic aortic aneurysm and dissection

At least nine *TGFBR2* gene mutations have been identified in people with familial thoracic aortic aneurysm and dissection (familial TAAD). This disorder involves problems with the aorta, which is the large blood vessel that distributes blood from the heart to the rest of the body. The aorta can weaken and stretch, causing a bulge in the blood vessel wall (an aneurysm). Stretching of the aorta may also lead to a sudden tearing of the layers in the aorta wall (aortic dissection). Aortic aneurysm and dissection can cause life-threatening internal bleeding.

The *TGFBR2* gene mutations that cause familial TAAD disturb signal transduction. The disturbed signaling can impair cell growth and development. It is not known how these changes result in the specific aortic abnormalities associated with familial TAAD.

2.2. Loeys-Dietz syndrome

More than 100 mutations in the *TGFBR2* gene have been found to cause Loeys-Dietz syndrome type II. Loeys-Dietz syndrome affects connective tissue, which gives structure and support to blood vessels, the skeleton, and other parts of the body. This type of Loeys-Dietz syndrome is characterized by blood vessel abnormalities and skeletal deformities. Most *TGFBR2* gene mutations that cause Loeys-Dietz syndrome change single protein building blocks (amino acids) in TGF-β receptor type 2, resulting in a receptor with little or no function. Although the receptor has severely reduced function, TGF-β pathway signaling occurs at an even greater intensity than normal. Researchers speculate that the activity of other proteins in this signaling pathway is increased to compensate for the reduction in TGF-β receptor type 2 activity; however,

the exact mechanism responsible for the increase in signaling is unclear. The overactive signaling pathway disrupts development of connective tissue and various body systems and leads to the varied signs and symptoms of Loeys-Dietz syndrome type II.

Some *TGFBR2* gene mutations that cause Loeys-Dietz syndrome type II have also been found to cause familial TAAD (described above). Affected families can include some individuals with Loeys-Dietz syndrome and others with familial TAAD.

2.3. Cancers

Some *TGFBR2* gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes are called somatic mutations and are not inherited. People with somatic mutations in the *TGFBR2* gene appear to have an increased risk of developing various cancers. Somatic *TGFBR2* gene mutations probably disrupt the signaling process that helps regulate cell division. Unchecked cell division can lead to the formation of tumors, particularly when *TGFBR2* gene mutations occur in the colon, rectum, and esophagus. It is estimated that 30 percent of cancerous (malignant) colon tumors have *TGFBR2* gene mutations in their cells.

3. Other Names for This Gene

- HNPCC6
- MFS2
- RIIC
- TBR-ii
- TBRII
- TGF-beta receptor type IIB
- TGF-beta type II receptor
- TGFbeta-RII
- TGFR-2
- TGFR2_HUMAN
- transforming growth factor beta receptor II
- transforming growth factor, beta receptor II (70/80kDa)

References

1. Biswas S, Trobridge P, Romero-Gallo J, Billheimer D, Myeroff LL, Willson JK,Markowitz SD, Grady WM. Mutational inactivation of TGFBR2 in microsatelliteunstable colon cancer arises from the cooperation of genomic instability and the clonal outgrowth of transforming growth factor beta resistant cells. GenesChromosomes Cancer. 2008 Feb;47(2):95-106.
2. Frederic MY, Hamroun D, Faivre L, Boileau C, Jondeau G, Claustres M, Béroud C,Collod-Béroud G. A new locus-specific database (LSDB) for mutations in the TGFBR2gene: UMD-TGFBR2. Hum Mutat. 2008 Jan;29(1):33-8.
3. Jondeau G, Boileau C. Genetics of thoracic aortic aneurysms. Curr Atheroscler Rep. 2012 Jun;14(3):219-26. doi: 10.1007/s11883-012-0241-4. Review.
4. Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, Meyers J, LeitchCC, Katsanis N, Sharifi N, Xu FL, Myers LA, Spevak PJ, Cameron DE, De Backer J,Hellemans J, Chen Y, Davis EC, Webb CL, Kress W, Coucke P, Rifkin DB, De PaepeAM, Dietz HC. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. Nat Genet. 2005Mar;37(3):275-81.
5. Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, De Backer JF,Oswald GL, Symoens S, Manouvrier S, Roberts AE, Faravelli F, Greco MA, PyeritzRE, Milewicz DM, Coucke PJ, Cameron DE, Braverman AC, Byers PH, De Paepe AM,Dietz HC. Aneurysm syndromes caused by mutations in the TGF-beta receptor. N EnglJ Med. 2006 Aug 24;355(8):788-98.
6. Pannu H, Fadulu VT, Chang J, Lafont A, Hasham SN, Sparks E, Giampietro PF,Zaleski C, Estrera AL, Safi HJ, Shete S, Willing MC, Raman CS, Milewicz DM.Mutations in transforming growth factor-beta receptor type II cause familialthoracic aortic aneurysms and dissections. Circulation. 2005 Jul26;112(4):513-20.
7. Pezzini A, Del Zotto E, Giossi A, Volonghi I, Costa P, Padovani A.Transforming growth factor β signaling perturbation in the Loeys-Dietz syndrome. Curr Med Chem. 2012;19(3):454-60. Review.

8. Van Hemelrijk C, Renard M, Loeys B. The Loeys-Dietz syndrome: an update forthe clinician. Curr Opin Cardiol. 2010 Nov;25(6):546-51. doi:10.1097/HCO.0b013e32833f0220. Review.