TGFBR1 Gene

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transforming growth factor beta receptor 1

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1. Normal Function

The *TGFBR1* gene provides instructions for making a protein called transforming growth factor-beta (TGF-β) receptor type 1. 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, TGF-β receptor type 1 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 TGF-β receptor type 1, 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 1 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. Loeys-Dietz syndrome

More than 35 mutations in the *TGFBR1* gene have been found to cause Loeys-Dietz syndrome type I. 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. The *TGFBR1* gene mutations that cause Loeys-Dietz syndrome are present in one copy of the gene in each cell. Most of these mutations change single protein building blocks (amino acids) in TGF-β receptor type 1, 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 1 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 I.

2.2. Other cancers

More than 10 mutations in the *TGFBR1* gene have been found to increase the risk of developing a form of skin cancer called multiple self-healing squamous epithelioma (MSSE). This condition, also known as Ferguson-Smith disease, is characterized by the formation of multiple invasive skin tumors that grow uncontrollably for a few weeks, but then suddenly shrink and die off, leaving a noncancerous scar.

People with MSSE have a mutation in one copy of the *TGFBR1* gene in each cell. An additional mutation in the second copy of the *TGFBR1* gene is needed for tumors to form in MSSE. The second mutation, which is called a somatic mutation, is found only in the tumor cells and is not inherited. Unlike *TGFBR1* gene mutations that cause Loeys-Dietz

syndrome type I (described above), the mutations that cause MSSE prevent the production of any protein at all. A complete lack of functional receptor in certain cells results in a total loss of TGF-β pathway signaling and severely reduced tumor suppression, allowing the skin cancers to form. The mechanism responsible for the spontaneous healing of the multiple skin tumors in MSSE is unknown.

Familial thoracic aortic aneurysm and dissection

Prostate cancer

3. Other Names for This Gene

- serine/threonine-protein kinase receptor R4
- TBR-i
- TBRI
- TGF-beta receptor type I
- TGF-beta receptor type-1
- TGF-beta type I receptor
- TGFR-1
- TGFR1_HUMAN
- transforming growth factor beta receptor I
- transforming growth factor-beta receptor type I

References

1. Cardoso S, Robertson SP, Daniel PB. TGFBR1 mutations associated withLoeys-Dietz syndrome are inactivating. J Rec ept Signal Transduct Res. 2012Jun;32(3):150-5. doi: 10.3109/10799893.2012.664553.
2. Goudie DR, D'Alessandro M, Merriman B, Lee H, Szeverényi I, Avery S, O'Connor BD, Nelson SF, Coats SE, Stewart A, Christie L, Pichert G, Friedel J, Hayes I,Burrows N, Whittaker S, Gerdes AM, Broesby-Olsen S, Ferguson-Smith MA, Verma C,Lunny DP, Reversade B, Lane EB. Multiple self-healing squamous epithelioma iscaused by a disease-specific spectrum of mutations in TGFBR1. Nat Genet. 2011 Feb27;43(4):365-9. doi: 10.1038/ng.780.
3. Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, De Backer JF,Oswald GL, Symoens S, Manouv rier S, Roberts AE, Faravelli F, Greco MA, PyeritzRE, Milewicz DM, Coucke PJ, Cameron DE, Braverman AC, Byers P H, De Paepe AM,Dietz HC. Aneurysm syndromes caused by mutations in the TGF-beta receptor. N EnglJ Med. 2006 A ug 24;355(8):788-98.
4. 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.
5. Van Hemelrijk C, Renard M, Loeys B. The Loeys-Dietz syndrome: an update forthe clinician. Curr Opin Cardiol. 2010 N ov;25(6):546-51. doi:10.1097/HCO.0b013e32833f0220. Review.