

## POFUT1 gene

protein O-fucosyltransferase 1

### Normal Function

The *POFUT1* gene provides instructions for making a protein called protein O-fucosyltransferase 1. This protein is located in a cell structure called the endoplasmic reticulum, which helps with protein processing and transport. Protein O-fucosyltransferase 1 adds sugar molecules, specifically a sugar called fucose, to other proteins called Notch receptors. Notch receptors are a family of proteins that are involved in a signaling pathway that guides normal development of many tissues throughout the body, both before birth and throughout life. Receptor proteins have specific sites into which certain other proteins, called ligands, fit like keys into locks. Attachment of a ligand into a Notch receptor triggers signaling in the pathway.

The addition of fucose molecules alters the shape of the Notch receptor. The receptor is then able to attach (bind) to its ligand and trigger signaling. Through its integral role in Notch receptor function, protein O-fucosyltransferase 1 allows the Notch pathway to proceed. The Notch pathway regulates a variety of processes including the specialization of cells into certain cell types that perform particular functions in the body (cell fate determination). It also plays a role in cell growth and division (proliferation), maturation (differentiation), and self-destruction (apoptosis).

In skin cells, Notch signaling likely plays a role in the maintenance of precursor cells that mature into pigment-producing skin cells called melanocytes and may regulate interactions between melanocytes and other skin cells called keratinocytes.

### Health Conditions Related to Genetic Changes

#### Dowling-Degos disease

At least 13 mutations in the *POFUT1* gene have been found to cause Dowling-Degos disease. This condition results in various skin abnormalities, including a characteristic lacy pattern of abnormally dark skin coloring (hyperpigmentation) that occurs most often in the body's folds and creases.

The *POFUT1* gene mutations that cause Dowling-Degos disease either lead to an abnormally short protein with no function or change single protein building blocks (amino acids), resulting in a partial loss of protein function. As a result, protein O-

fucosyltransferase 1 is less able or unable to add fucose molecules to Notch receptors. Without these sugar molecules, Notch receptors cannot bind to their ligands and the Notch pathway is halted. Because the varied functions of the Notch pathway affect many body systems and Dowling-Degos disease affects only the skin, it is unclear whether the signs and symptoms of this condition are due to impaired Notch signaling or disruption of an unknown function of protein O-fucosyltransferase 1 in melanocytes or other skin cells.

### **Other Names for This Gene**

- FUT12
- KIAA0180
- O-Fuc-T
- o-fucosyltransferase protein
- O-FucT-1
- O-FUT
- OFUCT1
- peptide-O-fucosyltransferase 1

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of POFUT1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23509\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23509[geneid]))

#### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28POFUT1%5BTIAB%5D%29+OR+%28O-fucosyltransferase+1%5BTIAB%5D%29%29+AND+%28%28Gene+5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D%29%29%29>)

#### Catalog of Genes and Diseases from OMIM

- PROTEIN O-FUCOSYLTRANSFERASE 1; POFUT1 (<https://omim.org/entry/607491>)

#### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/23509>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=POFUT1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=POFUT1[gene]))

## References

- Buket Basmanav F, Fritz G, Lestringant GG, Pachat D, Hoffjan S, Fischer J, Wehner M, Wolf S, Thiele H, Altmüller J, Pulimood SA, Rutten A, Kruse R, Hanneken S, Frank J, Danda S, Bygum A, Betz RC. Pathogenicity of POFUT1 in Dowling-Degos disease: additional mutations and clinical overlap with reticulate acropigmentation of kitamura. *J Invest Dermatol*. 2015 Feb;135(2):615-618. doi:10.1038/jid.2014.406. Epub 2014 Sep 17. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25229252>)
- Li M, Cheng R, Liang J, Yan H, Zhang H, Yang L, Li C, Jiao Q, Lu Z, He J, Ji J, Shen Z, Li C, Hao F, Yu H, Yao Z. Mutations in POFUT1, encoding protein O-fucosyltransferase 1, cause generalized Dowling-Degos disease. *Am J Hum Genet*. 2013 Jun 6;92(6):895-903. doi: 10.1016/j.ajhg.2013.04.022. Epub 2013 May 16. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23684010>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3675235/>)
- McMillan BJ, Zimmerman B, Egan ED, Lofgren M, Xu X, Hesser A, Blacklow SC. Structure of human POFUT1, its requirement in ligand-independent oncogenic Notch signaling, and functional effects of Dowling-Degos mutations. *Glycobiology*. 2017 Aug 1;27(8):777-786. doi: 10.1093/glycob/cwx020. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/28334865>)

## Genomic Location

The *POFUT1* gene is found on chromosome 20 (<https://medlineplus.gov/genetics/chromosome/20/>).

**Last updated August 1, 2017**