

## TREM2 gene

triggering receptor expressed on myeloid cells 2

### Normal Function

The *TREM2* gene provides instructions for making a protein called triggering receptor expressed on myeloid cells 2 (TREM2). As its name suggests, this protein is made in myeloid cells, which are cells produced in bone marrow. The TREM2 protein is found on the cell surface, where it interacts with the protein produced from the *TYROBP* gene. The TREM2 and TYROBP proteins form a complex that transmits chemical signals to activate the cell.

The TYROBP-TREM2 complex was first identified in the immune system. This complex is involved in the growth and development of several types of immune cells, particularly dendritic cells. The TYROBP-TREM2 complex activates these cells, triggering an inflammatory response to injury or disease.

The TYROBP-TREM2 complex also activates cells in the skeletal system and in the brain and spinal cord (central nervous system). In the skeletal system, the complex is found in osteoclasts, which are specialized cells that break down and remove (resorb) bone tissue that is no longer needed. These cells are involved in bone remodeling, which is a normal process that replaces old bone tissue with new bone.

In the central nervous system, the TYROBP-TREM2 complex appears to play an important role in immune cells called microglia. These cells protect the brain and spinal cord from foreign invaders and remove dead nerve cells and other debris. Although the TYROBP-TREM2 complex plays a critical role in osteoclasts and microglia, its exact function in these cells is unclear.

### Health Conditions Related to Genetic Changes

#### Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy

Variants (also called mutations) in the *TREM2* gene have been identified in people with polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy (commonly known as PLOSL). Some variants prevent the cell from making any TREM2 proteins, while others result in the production of an abnormally short, nonfunctional version of the protein. Other variants change the structure of the TREM2 protein, preventing it from reaching the cell surface.

Researchers believe that the signs and symptoms of PLOSL are related to defective TYROBP-TREM2 signaling in osteoclasts and microglia. The bone abnormalities seen in people with this disorder are probably related to malfunctioning osteoclasts, which are less able to resorb bone tissue during bone remodeling. In the central nervous system, defective signaling through the TYROBP-TREM2 complex causes widespread abnormalities of microglia. Researchers are working to determine how these abnormalities lead to the neurological problems associated with PLOSL.

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

- TREM-2
- TREM2\_HUMAN
- Trem2a
- Trem2b
- Trem2c
- triggering receptor expressed on monocytes 2
- triggering receptor expressed on myeloid cells 2a

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of TREM2 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=54209\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=54209[geneid]))

#### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28TREM2%5BTIAB%5D%29+OR+%28TREM-2%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

#### Catalog of Genes and Diseases from OMIM

- TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS 2; TREM2 (<https://omim.org/entry/605086>)

#### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/54209>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=TREM2\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=TREM2[gene]))

## References

- Bouchon A, Hernandez-Munain C, Cella M, Colonna M. A DAP12-mediated pathway regulates expression of CC chemokine receptor 7 and maturation of human dendritic cells. *J Exp Med*. 2001 Oct 15;194(8):1111-22. doi: 10.1084/jem.194.8.1111. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11602640>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2193511/>)
- Cella M, Buonsanti C, Strader C, Kondo T, Salmaggi A, Colonna M. Impaired differentiation of osteoclasts in TREM-2-deficient individuals. *J Exp Med*. 2003 Aug 18;198(4):645-51. doi: 10.1084/jem.20022220. Epub 2003 Aug 11. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12913093>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2194167/>)
- Colonna M, Turnbull I, Klesney-Tait J. The enigmatic function of TREM-2 in osteoclastogenesis. *Adv Exp Med Biol*. 2007;602:97-105. doi:10.1007/978-0-387-72009-8\_13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17966394>)
- Colonna M. TREMs in the immune system and beyond. *Nat Rev Immunol*. 2003 Jun; 3(6):445-53. doi: 10.1038/nri1106. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12776204>)
- Humphrey MB, Daws MR, Spusta SC, Niemi EC, Torchia JA, Lanier LL, Seaman WE, Nakamura MC. TREM2, a DAP12-associated receptor, regulates osteoclast differentiation and function. *J Bone Miner Res*. 2006 Feb;21(2):237-45. doi: 10.1359/JBMR.051016. Epub 2005 Oct 20. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16418779>)
- Kiialainen A, Hovanec K, Paloneva J, Kopra O, Peltonen L. Dap12 and Trem2, molecules involved in innate immunity and neurodegeneration, are co-expressed in the CNS. *Neurobiol Dis*. 2005 Mar;18(2):314-22. doi: 10.1016/j.nbd.2004.09.007. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15686960>)
- Kiialainen A, Veckman V, Saharinen J, Paloneva J, Gentile M, Hakola P, Hemelsoet D, Ridha B, Kopra O, Julkunen I, Peltonen L. Transcript profiles of dendritic cells of PLOSL patients link demyelinating CNS disorders with abnormalities in pathways of actin bundling and immune response. *J Mol Med (Berl)*. 2007 Sep;85(9):971-83. doi: 10.1007/s00109-007-0191-4. Epub 2007 May 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17530208>)
- Klunemann HH, Ridha BH, Magy L, Wherrett JR, Hemelsoet DM, Keen RW, DeBleecker JL, Rossor MN, Marienhagen J, Klein HE, Peltonen L, Paloneva J. The genetic causes of basal ganglia calcification, dementia, and bone cysts: DAP12 and TREM2. *Neurology*. 2005 May 10;64(9):1502-7. doi:10.1212/01.WNL.0000160304.00003.CA. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15883308>)
- Neumann H, Takahashi K. Essential role of the microglial triggering receptor expressed on myeloid cells-2 (TREM2) for central nervous tissue immune homeostasis. *J Neuroimmunol*. 2007 Mar;184(1-2):92-9. doi:10.1016/j.jneuroim.2006.11.032. Epub 2007 Jan 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17239445>)
- Paloneva J, Mandelin J, Kiialainen A, Bohling T, Prudlo J, Hakola P, Haltia M,

Konttinen YT, Peltonen L. DAP12/TREM2 deficiency results in impaired osteoclast differentiation and osteoporotic features. *J Exp Med*. 2003 Aug 18;198(4):669-75. doi: 10.1084/jem.20030027. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12925681>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2194176/>)

- Paloneva J, Manninen T, Christman G, Hovanes K, Mandelin J, Adolfsson R, Bianchin M, Bird T, Miranda R, Salmaggi A, Tranebjaerg L, Konttinen Y, Peltonen L. Mutations in two genes encoding different subunits of a receptor signaling complex result in an identical disease phenotype. *Am J Hum Genet*. 2002 Sep;71(3):656-62. doi: 10.1086/342259. Epub 2002 Jun 21. Erratum In: *Am J Hum Genet*. 2003 Jan;72(1):225. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12080485>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC379202/>)

## Genomic Location

The *TREM2* gene is found on chromosome 6 (<https://medlineplus.gov/genetics/chromosome/6/>).

**Last updated October 17, 2023**