# TYROBP gene

transmembrane immune signaling adaptor TYROBP

## Normal Function

The *TYROBP* gene provides instructions for making the TYRO protein tyrosine kinase binding (TYROBP) protein. This protein is found in a variety of cells that are produced in bone marrow (myeloid cells) and other immune system cells (lymphoid cells). The protein is located on the cell surface, where it helps transmit chemical signals that activate the cell.

The TYROBP protein interacts with several other proteins on the surface of cells. For example, it forms a complex with the protein produced from the *TREM2* gene. The TYROBP protein and its partners were first identified in the immune system, where they activate certain cells (such as natural killer cells and dendritic cells) that trigger 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 *TYROBP* gene have been identified in people with polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy ( commonly known as PLOSL). One *TYROBP* gene variant has been found to cause PLOSL in all affected people of Finnish ancestry. This variant deletes a large portion of the *TYROBP* gene, which prevents the cell from producing any proteins from this gene. Variants in other populations often result in the production of an abnormally short,

nonfunctional version of the protein or prevent the protein 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

- DAP12
- DNAX-activation protein 12
- KAR-associated protein
- KARAP
- killer activating receptor associated protein
- TYOBP_HUMAN

## Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of TYROBP (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7305[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28TYROBP%5BTIAB%5D%29+OR+%28TYRO+protein+tyrosine+kinase+binding+protein%5BTIAB%5D%29%29+OR+%28DAP12%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2880+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- TYRO PROTEIN TYROSINE KINASE-BINDING PROTEIN; TYROBP (https://omim.org/entry/604142)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7305)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=TYROBP[gene])

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## Genomic Location

The *TYROBP* gene is found on chromosome 19 (https://medlineplus.gov/genetics/chromosome/19/).

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