UNC13D gene

unc-13 homolog D

Normal Function

The *UNC13D* gene provides instructions for making a protein that is involved in the process of cell destruction (cytolysis) and the regulation of the immune system.

The UNC13D protein is involved in the release of substances from cells (exocytosis). In particular, it is important for the exocytosis of structures called cytolytic granules from immune cells called T cells and NK cells. T cells and NK cells destroy other cells by secreting these cytolytic granules, which contain cell-killing proteins, onto the membranes of the target cells. The UNC13D protein helps transport these granules to the membrane of the target cell, allowing cytolytic proteins to enter the cell and trigger it to self-destruct.

This cytolytic mechanism also helps regulate the immune system by destroying unneeded T cells. Controlling the number of T cells prevents the overproduction of immune proteins called cytokines that lead to inflammation and which, in excess, cause tissue damage.

Health Conditions Related to Genetic Changes

Familial hemophagocytic lymphohistiocytosis

More than 50 *UNC13D* gene mutations have been identified in people with familial hemophagocytic lymphohistiocytosis. Most of these mutations alter the way the gene's instructions are pieced together to produce the UNC13D protein, leading to a dysfunctional protein. The resulting shortage of functional UNC13D protein interferes with its role in cell destruction and immune system regulation, leading to the exaggerated immune response characteristic of familial hemophagocytic lymphohistiocytosis.

Other disorders

A variant (polymorphism) of the *UNC13D* gene has been associated with a higher risk of a complication called macrophage activation syndrome in people with systemic juvenile idiopathic arthritis (SJIA). SJIA is an autoimmune disorder that causes persistent joint inflammation beginning in childhood. Autoimmune disorders occur when

the immune system malfunctions and attacks the body's own tissues and organs. Macrophage activation syndrome is a life-threatening complication of SJIA with symptoms similar to those of familial hemophagocytic lymphohistiocytosis, including fever, an enlarged liver and spleen, liver damage, and low numbers of blood cells.

The *UNC13D* gene variant associated with macrophage activation syndrome in people with SJIA consists of a specific combination of individual changes in 12 DNA building blocks (nucleotides). It is unknown how this genetic change results in an increased risk of this complication in affected individuals.

Other Names for This Gene

- FHL3
- HLH3
- HPLH3
- Munc13-4
- UN13D_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of UNC13D (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=201294[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28UNC13D%5BTIAB%5D%29+OR+%28Munc13-4%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+1080+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- RHEUMATOID ARTHRITIS, SYSTEMIC JUVENILE (https://omim.org/entry/604302)
- UNC13 HOMOLOG D; UNC13D (https://omim.org/entry/608897)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/201294)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=UNC13D[gene])

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Genomic Location

The *UNC13D* gene is found on chromosome 17 (https://medlineplus.gov/genetics/chromosome/17/).

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