PSMB8 gene

proteasome subunit beta 8

Normal Function

The *PSMB8* gene provides instructions for making one part (subunit) of cell structures called immunoproteasomes. Immunoproteasomes are specialized versions of proteasomes, which are large complexes that recognize and break down (degrade) unneeded, excess, or abnormal proteins within cells. This activity is necessary for many essential cell functions. While proteasomes are found in many types of cells, immunoproteasomes are located primarily in immune system cells. These structures play an important role in regulating the immune system's response to foreign invaders, such as viruses and bacteria. One of the primary functions of immunoproteasomes is to help the immune system distinguish the body's own proteins from proteins made by foreign invaders, so the immune system can respond appropriately to infection.

Immunoproteasomes may also have other functions in immune system cells and possibly in other types of cells. They appear to be involved in some of the same fundamental cell activities as regular proteasomes, such as regulating the amount of various proteins in cells (protein homeostasis), cell growth and division, the process by which cells mature to carry out specific functions (differentiation), chemical signaling within cells, and the activity of genes. Studies suggest that, through unknown mechanisms, the subunit produced from the *PSMB8* gene in particular may be involved in the maturation of fat cells (adipocytes).

Health Conditions Related to Genetic Changes

Nakajo-Nishimura syndrome

At least one mutation in the *PSMB8* gene has been found to cause Nakajo-Nishimura syndrome, a condition that has been described only in the Japanese population. The identified mutation changes a single protein building block (amino acid) in the protein produced from the *PSMB8* gene, replacing the amino acid glycine with the amino acid valine at protein position 201 (written as Gly201Val or G201V). This mutation greatly reduces the production of this protein, which impairs the normal assembly of immunoproteasomes and causes the immune system to malfunction. For unknown reasons, the malfunctioning immune system triggers abnormal inflammation that can damage tissues throughout the body.

Abnormal inflammation likely underlies many of the signs and symptoms of Nakajo-Nishimura syndrome, including the development of red, swollen lumps (nodular erythema) on the skin, recurrent fevers, joint problems, and an enlarged liver and spleen (hepatosplenomegaly). It is less clear how mutations in the *PSMB8* gene

lead to other characteristic features of the condition, including muscle weakness and wasting and a loss of fatty tissue (lipodystrophy), mainly in the upper body. Because the protein produced from the *PSMB8* gene may be involved in the maturation of adipocytes, studies suggest that a shortage of this protein may interfere with the normal development and function of these cells.

Other disorders

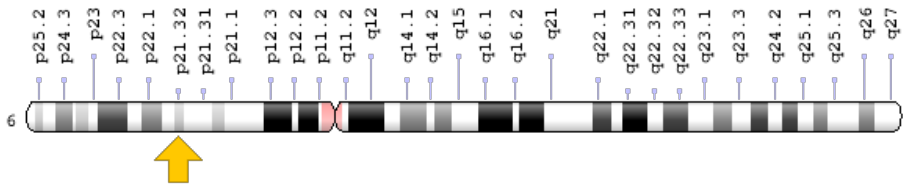
Mutations in the *PSMB8* gene have also been found in two conditions with signs and symptoms that overlap with those of Nakajo-Nishimura syndrome: one called joint contractures, muscular atrophy, microcytic anemia, and panniculitis-induced lipodystrophy (JMP) syndrome; and the other called chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome. All three conditions are characterized by skin abnormalities and lipodystrophy. Although they are often considered separate disorders, some researchers believe they may represent different forms of a single condition.

One *PSMB8* gene mutation has been identified in families with JMP syndrome and in families with CANDLE syndrome. This mutation replaces the amino acid threonine with the amino acid methionine at protein position 75 (written as Thr75Met or T75M). Another mutation has been found only in people with CANDLE syndrome; it replaces the amino acid cysteine with a signal to stop protein production prematurely (written as Cys135Ter or C135X). Each of these mutations greatly reduces protein production from the *PSMB8* gene. It is unclear how mutations in this gene lead to the overlapping but distinct patterns of signs and symptoms in Nakajo-Nishimura syndrome, JMP syndrome, and CANDLE syndrome. Researchers speculate that mutations in different areas of the gene may have different effects on protein function.

Chromosomal Location

Cytogenetic Location: 6p21.32, which is the short (p) arm of chromosome 6 at position 21.32

Molecular Location: base pairs 32,840,717 to 32,844,935 on chromosome 6 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ALDD
- beta5i
- D6S216
- D6S216E
- JMP
- large multifunctional peptidase 7
- LMP7
- low molecular mass protein 7
- low molecular weight protein 7
- macropain subunit C13
- multicatalytic endopeptidase complex subunit C13
- NKJO
- protease component C13
- proteasome (prosome, macropain) subunit, beta type, 8
- proteasome (prosome, macropain) subunit, beta type, 8 (large multifunctional peptidase 7)
- proteasome catalytic subunit 3i
- proteasome component C13
- proteasome-related gene 7
- proteasome subunit beta 5i
- proteasome subunit beta type-8
- proteasome subunit Y2
- PSB8_HUMAN
- PSMB5i
- really interesting new gene 10 protein
- RING10

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): The Proteasome Digests the Ubiquitin-Tagged Proteins
  https://www.ncbi.nlm.nih.gov/books/NBK22397/#A3205
- The Cell: A Molecular Approach (second edition, 2000): Protein Degradation
  https://www.ncbi.nlm.nih.gov/books/NBK9957/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PSMB8%5BTIAB%5D%29+OR+%28%28LMP7%5BTIAB%5D%29+OR+%28low+molecular+mass+protein+7%5BTIAB%5D%29+OR+%28low+molecular+weight+protein+7%5BTIAB%5D%29+OR+%28RING10%5BTIAB%5D%29%29+AND+%28%28Genes%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

Catalog of Genes and Diseases from OMIM

- PROTEASOME SUBUNIT, BETA-TYPE, 8
  http://omim.org/entry/177046

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PSMB8.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PSMB8%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:9545
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5696
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5696
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Reviewed: November 2013
Published: May 14, 2019

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