HSPB1 gene
heat shock protein family B (small) member 1

Normal Function

The *HSPB1* gene provides instructions for making a protein called heat shock protein beta-1 (also called heat shock protein 27). This protein is a member of the heat shock protein family, which helps protect cells under adverse conditions such as infection, inflammation, exposure to toxins, elevated temperature, injury, and disease. Heat shock proteins block signals that lead to programmed cell death. In addition, they appear to be involved in activities such as cell movement (motility), stabilizing the cell's structural framework (the cytoskeleton), folding and stabilizing newly produced proteins, and repairing damaged proteins. Heat shock proteins also appear to play a role in the tensing of muscle fibers (muscle contraction).

Heat shock protein beta-1 is found in cells throughout the body and is particularly abundant in nerve and muscle cells. In nerve cells, this protein helps to organize a network of molecular threads called neurofilaments that maintain the diameter of specialized extensions called axons. Maintaining proper axon diameter is essential for the efficient transmission of nerve impulses. Although it is thought to play a role in muscle contraction, the specific function of heat shock protein beta-1 in muscle cells is unclear.

Health Conditions Related to Genetic Changes

Charcot-Marie-Tooth disease

At least three *HSPB1* gene mutations have been reported in individuals with a form of Charcot-Marie-Tooth disease known as type 2F. Charcot-Marie-Tooth disease is a group of progressive disorders that affect the peripheral nerves. Peripheral nerves connect the brain and spinal cord to muscles and to sensory cells that detect sensations such as touch, pain, heat, and sound.

Each *HSPB1* gene mutation that causes Charcot-Marie-Tooth disease changes a single protein building block (amino acid) used to make heat shock protein beta-1. One mutation replaces the amino acid serine with the amino acid phenylalanine at protein position 135 (written as Ser135Phe or S135F). Other mutations replace the amino acid arginine with the amino acid tryptophan at position 127 (Arg127Trp or R127W) or position 136 (Arg136Trp or R136W). These mutations alter a region of the protein that is critical for heat shock protein beta-1 to function properly.

It is unclear how *HSPB1* gene mutations lead to the axon abnormalities that are characteristic of type 2F Charcot-Marie-Tooth disease. Researchers suggest that molecules of altered heat shock protein beta-1 cluster together (aggregate) and
interfere with the normal functions of nerve cells, particularly axon function. Another possibility is that the altered protein disrupts the assembly of neurofilaments, which affects axon diameter and impairs the transmission of nerve impulses.

**Distal hereditary motor neuropathy, type II**

Researchers have identified at least six *HSPB1* gene mutations that cause a condition called distal hereditary motor neuropathy, type II, which is similar to Charcot-Marie-Tooth disease. Distal hereditary motor neuropathy, type II affects peripheral nerves and is characterized by progressive weakness, primarily in the feet and legs. Unlike Charcot-Marie-Tooth disease, distal hereditary motor neuropathy, type II does not affect sensory cells.

*HSPB1* gene mutations that cause distal hereditary motor neuropathy, type II change single amino acids in heat shock protein beta-1. It is not well understood how these mutations lead to the signs and symptoms of this disorder. As with the *HSPB1* gene mutations that cause Charcot-Marie-Tooth disease, studies suggest that the altered protein may be more likely to form aggregates and block the transport of substances that are essential for the proper function of nerve axons. The disruption of other cell functions in which this protein is involved may also contribute to peripheral nerve disease.

**Chromosomal Location**

Cytogenetic Location: 7q11.23, which is the long (q) arm of chromosome 7 at position 11.23

Molecular Location: base pairs 76,302,558 to 76,304,301 on chromosome 7 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- CMT2F
- heat shock 27kDa protein 1
- heat shock protein beta-1
- HS.76067
• Hsp25
• HSP27
• HSP28
• HSPB1_HUMAN
• SRP27
• stress-responsive protein 27

Additional Information & Resources

Clinical Information from GeneReviews
• Charcot-Marie-Tooth Hereditary Neuropathy Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1358

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28HSPB1%5BTIAB%5D%29+OR+%28HSP27%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22+AND+5Bdp%5D

Catalog of Genes and Diseases from OMIM
• HEAT-SHOCK 27-KD PROTEIN 1
  http://omim.org/entry/602195

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/HSPB1ID40880ch7q11.html
• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HSPB1%5Bgene%5D
• HGNC Gene Family: Small heat shock proteins
  https://www.genenames.org/cgi-bin/genefamilies/set/585
• HGNC Gene Symbol Report
  https://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=5246
• Inherited Peripheral Neuropathies Mutation Database
  http://www.molgen.ua.ac.be/CMTMutations/Mutations/Mutations.cfm?Context=36
• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3315
Sources for This Summary


- OMIM: HEAT-SHOCK 27-KD PROTEIN 1
http://omim.org/entry/602195


Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/HSPB1

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