



PRPS1 gene

phosphoribosyl pyrophosphate synthetase 1

Normal Function

The *PRPS1* gene provides instructions for making an enzyme called phosphoribosyl pyrophosphate synthetase 1, or PRPP synthetase 1. This enzyme helps produce a molecule called phosphoribosyl pyrophosphate (PRPP). PRPP is involved in making purine and pyrimidine nucleotides. These nucleotides are building blocks of DNA, its chemical cousin RNA, and molecules such as ATP and GTP that serve as energy sources in the cell.

Purines and pyrimidines may be manufactured from smaller molecules, or they can be recycled from the breakdown of DNA and RNA in a series of reactions called the salvage pathway. Manufacturing purines and pyrimidines uses much more energy and takes more time than recycling them, which makes recycling these molecules more efficient. The salvage pathway ensures that cells have a plentiful supply of purines and pyrimidines.

PRPP synthetase 1 and PRPP are involved in the manufacture of new purines and pyrimidines, and are also essential for the purine salvage pathway.

Health Conditions Related to Genetic Changes

Arts syndrome

At least three *PRPS1* gene mutations have been identified in people with Arts syndrome, a disorder that causes serious neurological problems in males. Females can also be affected by this condition, but they typically have much milder symptoms.

The *PRPS1* gene mutations that cause Arts syndrome change single protein building blocks (amino acids) in the PRPP synthetase 1 enzyme. The mutations are believed to result in the production of an unstable enzyme with little or no activity. The lack of functional PRPP synthetase 1 enzyme disrupts both the manufacture and recycling of purines. The manufacture of pyrimidines is also affected, but not the pyrimidine salvage pathway. The disruption of purine production, and to a lesser extent pyrimidine production, may impair energy storage and transport in cells. Impairment of these processes may have a particularly severe effect on tissues that require a large amount of energy, such as the nervous system, resulting in the neurological problems characteristic of Arts syndrome.

Charcot-Marie-Tooth disease

Phosphoribosylpyrophosphate synthetase superactivity

At least seven mutations in the *PRPS1* gene that cause a severe form of phosphoribosylpyrophosphate synthetase superactivity (PRS superactivity) have been identified. These mutations change single amino acids in the PRPP synthetase 1 enzyme, resulting in a poorly regulated, overactive enzyme. In a milder form of PRS superactivity, the *PRPS1* gene is overactive for reasons that are not well understood. *PRPS1* gene overactivity increases the production of normal PRPP synthetase 1 enzyme, which increases the availability of PRPP. In both forms of the disorder, excessive amounts of purines are generated.

Under these conditions, uric acid, a waste product of purine breakdown, accumulates in the body. A buildup of uric acid can cause gout, which is a form of arthritis resulting from uric acid crystals in the joints. Affected individuals may also develop kidney or bladder stones formed from uric acid crystals.

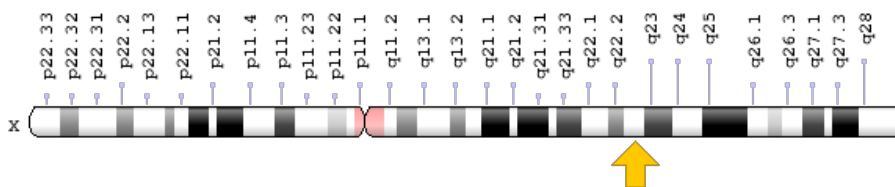
People with the severe form of PRS superactivity have additional symptoms including loss of hearing caused by changes in the inner ear (sensorineural hearing loss), weak muscle tone (hypotonia), impaired muscle coordination (ataxia), and developmental delay. It is unclear how the *PRPS1* gene mutations that cause the severe form of PRS superactivity are related to these neurological problems.

Nonsyndromic hearing loss

Chromosomal Location

Cytogenetic Location: Xq22.3, which is the long (q) arm of the X chromosome at position 22.3

Molecular Location: base pairs 107,628,424 to 107,651,026 on the X chromosome (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ARTS
- CMTX5
- dJ1070B1.2 (phosphoribosyl pyrophosphate synthetase 1)

- KIAA0967
- PPRibP
- PRPS1_HUMAN
- PRSI

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Purine Bases Can Be Synthesized de Novo or Recycled by Salvage Pathways
<https://www.ncbi.nlm.nih.gov/books/NBK22520/#A3532>

Clinical Information from GeneReviews

- Arts Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK2591>
- Charcot-Marie-Tooth Neuropathy X Type 5
<https://www.ncbi.nlm.nih.gov/books/NBK1876>
- Phosphoribosylpyrophosphate Synthetase Superactivity
<https://www.ncbi.nlm.nih.gov/books/NBK1973>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28PRPS1%5BTIAB%5D%29+OR+%28phosphoribosyl+pyrophosphate+synthetase+1%5BTIAB%5D%29%29+OR+%28%28PRSI%5BTIAB%5D%29+OR+%28CMTX5%5BTIAB%5D%29+OR+%28PPRibP%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+1440+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- PHOSPHORIBOSYLPYROPHOSPHATE SYNTHETASE I
<http://omim.org/entry/311850>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_PRPS1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=PRPS1%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:9462

- Inherited Peripheral Neuropathies Mutation Database
<http://www.molgen.ua.ac.be/CMTMutations/Mutations/Mutations.cfm?Context=43>
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:5631>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/5631>
- UniProt
<https://www.uniprot.org/uniprot/P60891>

Sources for This Summary

- Ahmed M, Taylor W, Smith PR, Becker MA. Accelerated transcription of PRPS1 in X-linked overactivity of normal human phosphoribosylpyrophosphate synthetase. *J Biol Chem.* 1999 Mar 12; 274(11):7482-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10066814>
- Becker MA, Smith PR, Taylor W, Mustafi R, Switzer RL. The genetic and functional basis of purine nucleotide feedback-resistant phosphoribosylpyrophosphate synthetase superactivity. *J Clin Invest.* 1995 Nov;96(5):2133-41.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/7593598>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC185862/>
- Becker MA, Taylor W, Smith PR, Ahmed M. Overexpression of the normal phosphoribosylpyrophosphate synthetase 1 isoform underlies catalytic superactivity of human phosphoribosylpyrophosphate synthetase. *J Biol Chem.* 1996 Aug 16;271(33):19894-9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/8702702>
- Kim HJ, Sohn KM, Shy ME, Krajewski KM, Hwang M, Park JH, Jang SY, Won HH, Choi BO, Hong SH, Kim BJ, Suh YL, Ki CS, Lee SY, Kim SH, Kim JW. Mutations in PRPS1, which encodes the phosphoribosyl pyrophosphate synthetase enzyme critical for nucleotide biosynthesis, cause hereditary peripheral neuropathy with hearing loss and optic neuropathy (cmtx5). *Am J Hum Genet.* 2007 Sep;81(3):552-8. Epub 2007 Jun 29.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17701900>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1950833/>
- Kim JW, Kim HJ. Charcot-Marie-Tooth Neuropathy X Type 5. 2008 Aug 26 [updated 2013 Jun 6]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1876/>
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20301731>
- Liu XZ, Xie D, Yuan HJ, de Brouwer AP, Christodoulou J, Yan D. Hearing loss and PRPS1 mutations: Wide spectrum of phenotypes and potential therapy. *Int J Audiol.* 2013 Jan;52(1):23-8. doi: 10.3109/14992027.2012.736032. Epub 2012 Nov 28. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23190330>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4511087/>
- Mittal R, Patel K, Mittal J, Chan B, Yan D, Grati M, Liu XZ. Association of PRPS1 Mutations with Disease Phenotypes. *Dis Markers.* 2015;2015:127013. doi: 10.1155/2015/127013. Epub 2015 May 24. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/26089585>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4458296/>

- Nyhan WL. Disorders of purine and pyrimidine metabolism. *Mol Genet Metab.* 2005 Sep-Oct; 86(1-2):25-33. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16176880>
- OMIM: PHOSPHORIBOSYLPYROPHOSPHATE SYNTHETASE I
<http://omim.org/entry/311850>
- Zheng M, Ma JW. Research progress in the genetics of hyperuricaemia and gout. *Yi Chuan.* 2016 Apr;38(4):300-13. doi: 10.16288/j.ycz.15-385. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/27103454>
- de Brouwer AP, Williams KL, Duley JA, van Kuilenburg AB, Nabuurs SB, Egmont-Petersen M, Lugtenberg D, Zoetekouw L, Banning MJ, Roeffen M, Hamel BC, Weaving L, Ouvrier RA, Donald JA, Wevers RA, Christodoulou J, van Bokhoven H. Arts syndrome is caused by loss-of-function mutations in PRPS1. *Am J Hum Genet.* 2007 Sep;81(3):507-18. Epub 2007 Aug 3.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17701896>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1950830/>
- de Brouwer AP, van Bokhoven H, Nabuurs SB, Arts WF, Christodoulou J, Duley J. PRPS1 mutations: four distinct syndromes and potential treatment. *Am J Hum Genet.* 2010 Apr 9;86(4): 506-18. doi: 10.1016/j.ajhg.2010.02.024. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20380929>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2850427/>
- de Brouwer APM, Duley JA, Christodoulou J. Arts Syndrome. 2008 Oct 21 [updated 2011 Mar 29]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from <http://www.ncbi.nlm.nih.gov/books/NBK2591/>
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20301738>
- de Brouwer APM, Duley JA, Christodoulou J. Phosphoribosylpyrophosphate Synthetase Superactivity. 2008 Sep 23 [updated 2015 Dec 17]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1973/>
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20301734>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/PRPS1>

Reviewed: September 2009
Published: June 11, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services