NR0B1 gene

nuclear receptor subfamily 0 group B member 1

Normal Function

The *NR0B1* gene provides instructions for making a protein called DAX1. This protein plays an important role in the development and function of several hormone-producing (endocrine) tissues in the body. These tissues include the small glands located on top of each kidney (the adrenal glands), two hormone-secreting glands in the brain (the hypothalamus and pituitary), and the gonads (ovaries in females and testes in males). Before birth, the DAX1 protein helps regulate genes that direct the formation of these tissues. DAX1 also helps regulate hormone production in endocrine tissues after they have been formed.

Health Conditions Related to Genetic Changes

X-linked adrenal hypoplasia congenita

More than 110 *NR0B1* mutations that cause X-linked adrenal hypoplasia congenita have been identified. Some of these genetic changes are deletions of all or part of the *NR0B1* gene. Other mutations lead to the production of an abnormally short version of the DAX1 protein. Still other mutations change single protein building blocks (amino acids) in a critical region of DAX1.

Most of the mutations responsible for X-linked adrenal hypoplasia congenita prevent the *NR0B1* gene from producing any active DAX1 protein. A shortage of DAX1 disrupts the normal development and function of hormone-producing tissues in the body. The main characteristics of this condition result when endocrine glands such as the adrenals, hypothalamus, pituitary, and gonads do not produce the right amounts of specific hormones.

Swyer syndrome

Other disorders

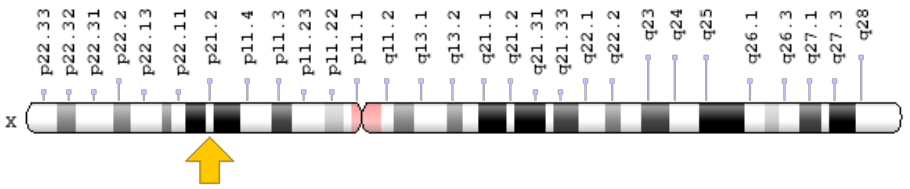
In some cases, genetic material is deleted from a region of the X chromosome that contains several genes, including *NR0B1*. This deletion results in a condition called adrenal hypoplasia congenita with complex glycerol kinase deficiency. In addition to the signs and symptoms of adrenal hypoplasia congenita, individuals with this condition may have delayed development and problems regulating their blood sugar levels. In rare cases, the deletion also includes the gene associated with Duchenne muscular dystrophy. People with this larger deletion have progressive

muscle weakness and wasting in addition to the other features of adrenal hypoplasia congenita with complex glycerol kinase deficiency.

Chromosomal Location

Cytogenetic Location: Xp21.2, which is the short (p) arm of the X chromosome at position 21.2

Molecular Location: base pairs 30,304,206 to 30,309,390 on the X chromosome (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- AHC
- AHCH
- AHX
- DAX-1
- DAX1
- DSS
- gonadotropin deficiency
- GTD
- HHG
- NR0B1_HUMAN
- nuclear hormone receptor
- nuclear receptor DAX-1
- nuclear receptor subfamily 0, group B, member 1

Additional Information & Resources

Educational Resources

- Developmental Biology (sixth edition, 2000): Phenotypic sex reversal in humans having two copies of the DAX1 locus
  https://www.ncbi.nlm.nih.gov/books/NBK9967/?rendertype=figure&id=A4121

Clinical Information from GeneReviews

- Nonsyndromic Disorders of Testicular Development
  https://www.ncbi.nlm.nih.gov/books/NBK1547
- NR0B1-Related Adrenal Hypoplasia Congenita
  https://www.ncbi.nlm.nih.gov/books/NBK1431

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28NR0B1%5BTIAB%5D%29+OR+%28DAX-1%5BTIAB%5D%29+OR+%28DAX1%5BTIAB%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

- 46,XY SEX REVERSAL 2
  http://omim.org/entry/300018
- GLYCEROL KINASE DEFICIENCY
  http://omim.org/entry/307030
- NUCLEAR RECEPTOR SUBFAMILY 0, GROUP B, MEMBER 1
  http://omim.org/entry/300473

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/NR0B1ID44131chXp21.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=NR0B1%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:7960
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:190

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/190
- UniProt
  https://www.uniprot.org/uniprot/P51843

Sources for This Summary

- Barbaro M, Oscarson M, Schoumans J, Staaf J, Ivarsson SA, Wedell A. Isolated 46,XY gonadal dysgenesis in two sisters caused by a Xp21.2 interstitial duplication containing the DAX1 gene. J Clin Endocrinol Metab. 2007 Aug;92(8):3305-13. Epub 2007 May 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17504899
- Clipsham R, McCabe ER. DAX1 and its network partners: exploring complexity in development. Mol Genet Metab. 2003 Sep-Oct;80(1-2):81-120. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14567960
- Iyer AK, McCabe ER. Molecular mechanisms of DAX1 action. Mol Genet Metab. 2004 Sep-Oct; 83(1-2):60-73. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15464421
- King TF, Conway GS. Swyer syndrome. Curr Opin Endocrinol Diabetes Obes. 2014 Dec;21(6): 504-10. doi: 10.1097/MED.0000000000000113. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25314337
- Lalli E, Sassone-Corsi P. DAX-1, an unusual orphan receptor at the crossroads of steroidogenic function and sexual differentiation. Mol Endocrinol. 2003 Aug;17(8):1445-53. Epub 2003 May 29. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12775766
- Lehmann SG, Lalli E, Sassone-Corsi P. X-linked adrenal hypoplasia congenita is caused by abnormal nuclear localization of the DAX-1 protein. Proc Natl Acad Sci U S A. 2002 Jun 11;99(12): 8225-30. Epub 2002 May 28.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12034880
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC123049/
- Lehmann SG, Wurtz JM, Renaud JP, Sassone-Corsi P, Lalli E. Structure-function analysis reveals the molecular determinants of the impaired biological function of DAX-1 mutants in AHC patients. Hum Mol Genet. 2003 May 1;12(9):1063-72.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12700175
- Ludbrook LM, Harley VR. Sex determination: a 'window' of DAX1 activity. Trends Endocrinol Metab. 2004 Apr;15(3):116-21. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15046740
- McCabe ER. DAX1: Increasing complexity in the roles of this novel nuclear receptor. Mol Cell Endocrinol. 2007 Feb;265-266:179-82. Epub 2007 Jan 8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17210221
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1847396/
- Niakan KK, McCabe ER. DAX1 origin, function, and novel role. Mol Genet Metab. 2005 Sep-Oct; 86(1-2):70-83. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16146703

- Sjarif DR, Ploos van Amstel JK, Duran M, Beemer FA, Poll-The BT. Isolated and contiguous glycerol kinase gene disorders: a review. J Inherit Metab Dis. 2000 Sep;23(6):529-47. Review. *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/11032329
- Smyk M, Berg JS, Pursley A, Curtis FK, Fernandez BA, Bien-Willner GA, Lupski JR, Cheung SW, Stankiewicz P. Male-to-female sex reversal associated with an approximately 250 kb deletion upstream of NR0B1 (DAX1). Hum Genet. 2007 Aug;122(1):63-70. Epub 2007 May 15. *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/17503084

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