

SRD5A2 gene

steroid 5 alpha-reductase 2

Normal Function

The *SRD5A2* gene provides instructions for making an enzyme called steroid 5-alpha reductase 2. This enzyme is involved in processing androgens, which are hormones that direct male sexual development. Specifically, the enzyme is responsible for a chemical reaction that converts the hormone testosterone to a more potent androgen, dihydrotestosterone (DHT), in male reproductive tissues.

Testosterone and DHT are essential for the normal development of male sex characteristics. Before birth, testosterone is responsible for the formation of internal male genitalia, including the tubes that collect sperm and carry it out of the testes (the epididymis and vas deferens) and glands that help produce semen (the seminal vesicles). DHT directs the development of the external genitalia, including the penis and scrotum, and the prostate gland. During puberty, these two hormones also play an important role in the development of male secondary sex characteristics such as the growth of facial and body hair, increased muscle mass, and deepening of the voice.

Health Conditions Related to Genetic Changes

5-alpha reductase deficiency

About 50 mutations in the *SRD5A2* gene have been identified in people with 5-alpha reductase deficiency. Most of these mutations change single protein building blocks (amino acids) in steroid 5-alpha reductase 2. Some of these genetic changes render the enzyme completely inactive. Other mutations reduce but do not eliminate the enzyme's function.

As a result of *SRD5A2* mutations, the body cannot effectively convert testosterone to DHT in reproductive tissues. A shortage of DHT disrupts the formation of external genitalia before birth. People with 5-alpha reductase deficiency are genetically male, with one X and one Y chromosome in each cell, but they may be born with external genitalia that look female-typical, or that are not clearly male or clearly female. Other affected infants have external genitalia that appear male-typical, but they often have an unusually small penis (micropenis) and the urethra opening on the underside of the penis (hypospadias).

During puberty, the testes produce more testosterone. Researchers believe that people with 5-alpha reductase deficiency develop secondary male sex characteristics in response to higher levels of this hormone. Some affected people also retain a small amount of 5-alpha reductase 2 activity, which may produce DHT and contribute to the development of secondary sex characteristics during puberty.

Prostate cancer

Certain normal variations (polymorphisms) in the *SRD5A2* gene may be associated with prostate cancer. Two of these polymorphisms have been studied extensively. The most common variation replaces the amino acid valine with the amino acid leucine at position 89 in steroid 5-alpha reductase 2 (written as Val89Leu or V89L). The other variation replaces the amino acid alanine with the amino acid threonine at position 49 in the enzyme (written as Ala49Thr or A49T). Some studies have suggested that these variations are associated with an increased risk of developing prostate cancer or having a more aggressive form of the disease. Other studies, however, have not shown these associations. It remains unclear what role *SRD5A2* polymorphisms play in prostate cancer risk.

Some gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes, which are called somatic mutations, are not inherited. Studies have shown that somatic *SRD5A2* mutations in prostate cancer cells may be associated with the progression of prostate cancer. These mutations may increase the activity of steroid 5-alpha reductase 2, which would raise the levels of DHT in prostate tissue. Research has shown that androgens such as DHT can stimulate prostate cancer growth.

Other disorders

In women, certain polymorphisms in the *SRD5A2* gene may affect the risk of developing a condition called polycystic ovary syndrome (PCOS). PCOS is characterized by a hormonal imbalance that can lead to irregular menstruation, acne, excess body hair (hirsutism), and weight gain. Some genetic variations increase the activity of steroid 5-alpha reductase 2 in the ovaries, which could contribute to the signs and symptoms of this condition. Other variations, including the common polymorphism Val89Leu, reduce the activity of steroid 5-alpha reductase 2 and are associated with a reduced risk of developing PCOS.

Other Names for This Gene

- 3-oxo-5 alpha-steroid 4-dehydrogenase 2
- 5 alpha-SR2
- MGC138457
- S5A2_HUMAN
- SR type 2
- steroid 5-alpha-reductase 2

- steroid-5-alpha-reductase, alpha polypeptide 2 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 2)
- Type II 5-alpha reductase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SRD5A2 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6716\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6716[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SRD5A2%5BTIAB%5D%29+OR+%28steroid-5-alpha+reductase%5BTIAB%5D%29+OR+%285-alpha+reductase%5BTIAB%5D%29%29+OR+%28%28steroid+5alpha+reductase%5BTIAB%5D%29+OR+%28testosterone+5-alpha-reductase%5BTIAB%5D%29+OR+%28delta+4-reductase%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

- POLYCYSTIC OVARY SYNDROME 1; PCOS1 (<https://omim.org/entry/184700>)
- PROSTATE CANCER (<https://omim.org/entry/176807>)
- STEROID 5-ALPHA-REDUCTASE 2; SRD5A2 (<https://omim.org/entry/607306>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/6716>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=SRD5A2\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=SRD5A2[gene]))

References

- Cicek MS, Conti DV, Curran A, Neville PJ, Paris PL, Casey G, Witte JS. Association of prostate cancer risk and aggressiveness to androgen pathway genes: SRD5A2, CYP17, and the AR. *Prostate*. 2004 Apr 1;59(1):69-76. doi:10.1002/pros.10358. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/14991867>)
- Goodarzi MO, Shah NA, Antoine HJ, Pall M, Guo X, Azziz R. Variants in the 5alpha-reductase type 1 and type 2 genes are associated with polycystic ovary syndrome and the severity of hirsutism in affected women. *J Clin Endocrinol Metab*. 2006 Oct; 91(10):4085-91. doi: 10.1210/jc.2006-0227. Epub 2006 Jul 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16849416>)

- Kim KS, Liu W, Cunha GR, Russell DW, Huang H, Shapiro E, Baskin LS. Expression of the androgen receptor and 5 alpha-reductase type 2 in the developing human fetal penis and urethra. *Cell Tissue Res.* 2002 Feb;307(2):145-53. doi:10.1007/s004410100464. Epub 2001 Nov 27. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11845321>)
- Makridakis N, Akalu A, Reichardt JK. Identification and characterization of somatic steroid 5alpha-reductase (SRD5A2) mutations in human prostate cancer tissue. *Oncogene.* 2004 Sep 23;23(44):7399-405. doi: 10.1038/sj.onc.1207922. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15326487>)
- Ntais C, Polycarpou A, Ioannidis JP. SRD5A2 gene polymorphisms and the risk of prostate cancer: a meta-analysis. *Cancer Epidemiol Biomarkers Prev.* 2003 Jul;12(7):618-24. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12869400>)
- Russell DW, Wilson JD. Steroid 5 alpha-reductase: two genes/two enzymes. *Annu Rev Biochem.* 1994;63:25-61. doi: 10.1146/annurev.bi.63.070194.000325. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/7979239>)
- Salam MT, Ursin G, Skinner EC, Dessissa T, Reichardt JK. Associations between polymorphisms in the steroid 5-alpha reductase type II (SRD5A2) gene and benign prostatic hyperplasia and prostate cancer. *Urol Oncol.* 2005 Jul-Aug;23(4):246-53. doi: 10.1016/j.urolonc.2004.12.014. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16018939>)
- Sasaki G, Ogata T, Ishii T, Kosaki K, Sato S, Homma K, Takahashi T, Hasegawa T, Matsuo N. Micropenis and the 5alpha-reductase-2 (SRD5A2) gene: mutation and V89L polymorphism analysis in 81 Japanese patients. *J Clin Endocrinol Metab.* 2003 Jul;88(7):3431-6. doi: 10.1210/jc.2002-021415. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12843198>)
- Wang Y, Li Q, Xu J, Liu Q, Wang W, Lin Y, Ma F, Chen T, Li S, Shen Y. Mutation analysis of five candidate genes in Chinese patients with hypospadias. *Eur J Hum Genet.* 2004 Sep;12(9):706-12. doi: 10.1038/sj.ejhg.5201232. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15266301>)
- Wilson JD, Griffin JE, Russell DW. Steroid 5 alpha-reductase 2 deficiency. *Endocr Rev.* 1993 Oct;14(5):577-93. doi: 10.1210/edrv-14-5-577. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/8262007>)

Genomic Location

The *SRD5A2* gene is found on chromosome 2 (<https://medlineplus.gov/genetics/chromosome/2/>).

Last updated April 1, 2008