

# SRD5A2 Gene

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Steroid 5 alpha-reductase 2: The SRD5A2 gene provides instructions for making an enzyme called steroid 5-alpha reductase 2.

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## 1. 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.

## 2. Health Conditions Related to Genetic Changes

### 2.1. 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 predominantly female, or that are not clearly male or clearly female (sometimes called ambiguous genitalia). Other affected infants have external genitalia that appear predominantly male, 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.

### 2.2. 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.

## 2.3. Cancers

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.

## 3. 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

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