

## AR gene

androgen receptor

### Normal Function

The *AR* gene provides instructions for making a protein called an androgen receptor. Androgens are hormones (such as testosterone) that are important for normal male sexual development before birth and during puberty. Androgen receptors allow the body to respond appropriately to these hormones.

The receptors are present in many of the body's tissues, where they attach (bind) to androgens. The resulting androgen-receptor complex then binds to DNA and regulates the activity of androgen-responsive genes. By turning the genes on or off as necessary, the androgen receptor helps direct the development of male sexual characteristics. Androgens and androgen receptors also have other important functions in both males and females, such as regulating hair growth and sex drive.

In one region of the *AR* gene, a DNA segment known as CAG is repeated multiple times. This CAG segment is called a triplet or trinucleotide repeat. In most people, the number of CAG repeats in the *AR* gene ranges from fewer than 10 to about 36.

### Health Conditions Related to Genetic Changes

#### Androgen insensitivity syndrome

Hundreds of different variants (also called mutations) in the *AR* gene have been identified in people with androgen insensitivity syndrome, a condition that affects sexual development before birth and during puberty. Most of these variants are changes in single DNA building blocks (base pairs). Other variants insert or delete multiple base pairs in the gene or affect how the gene is processed into a protein. Some variants lead to an abnormally short version of the androgen receptor protein, while others result in the production of an abnormal receptor that cannot bind to androgens or to DNA.

As a result of these changes, cells that are normally sensitive to androgens become less responsive to these hormones or unable to use these hormones at all. People with this condition are genetically male, with one X chromosome and one Y chromosome in each cell. Because their bodies are unable to respond to androgens, they may have mostly female sex characteristics or signs of both male and female sexual development.

Variants that eliminate the function of the androgen receptor cause complete androgen

insensitivity syndrome. Genetic changes that significantly reduce but do not eliminate the receptor's activity cause partial androgen insensitivity syndrome. Variants that only slightly reduce the activity of the receptor cause mild androgen insensitivity syndrome.

### Spinal and bulbar muscular atrophy

Spinal and bulbar muscular atrophy, a disorder of specialized nerve cells that control muscle movement (motor neurons), results from an expansion of the CAG trinucleotide repeat in the *AR* gene. Instead of the typical 10 to 36 repeats, CAG is repeated from 38 to more than 60 times in people with this disorder. Although the extended CAG region changes the structure of the androgen receptor, it is unclear how the altered protein damages nerve cells. Researchers believe that a fragment of the androgen receptor protein containing the CAG repeats accumulates within these cells and interferes with normal cell functions. This buildup leads to the gradual loss of motor neurons, which results in muscle weakness and wasting (atrophy).

### Androgenetic alopecia

Changes in the *AR* gene are associated with an increased risk of androgenetic alopecia, a form of hair loss also known as male pattern baldness in men and female pattern hair loss in women. The variations change the number or order of DNA building blocks (base pairs) that make up the *AR* gene. These genetic changes appear to be most frequent in men with hair loss that begins at an early age. Researchers believe that *AR* gene variations may increase the activity of androgen receptors in the scalp. Although androgenetic alopecia is related to the effects of androgens on hair growth, it remains unclear how changes in the *AR* gene increase the risk of hair loss in people with this condition.

### Polycystic ovary syndrome

MedlinePlus Genetics provides information about Polycystic ovary syndrome

### Prostate cancer

MedlinePlus Genetics provides information about Prostate cancer

## **Other Names for This Gene**

- AIS
- ANDR\_HUMAN
- androgen receptor (dihydrotestosterone receptor; testicular feminization; spinal and bulbar muscular atrophy; Kennedy disease)
- DHTR
- HUMARA
- KD
- NR3C4

- SBMA
- SMAX1
- TFM

## **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

- Tests of AR ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=367\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=367[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28AR%5BTI%5D%29+OR+%28androgen+receptor%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D>)

### Catalog of Genes and Diseases from OMIM

- ANDROGEN RECEPTOR; AR (<https://omim.org/entry/313700>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/367>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=AR\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=AR[gene]))

## **References**

- Adachi H, Katsuno M, Minamiyama M, Waza M, Sang C, Nakagomi Y, Kobayashi Y, Tanaka F, Doyu M, Inukai A, Yoshida M, Hashizume Y, Sobue G. Widespread nuclear and cytoplasmic accumulation of mutant androgen receptor in SBMA patients. *Brain*. 2005 Mar;128(Pt 3):659-70. doi: 10.1093/brain/awh381. Epub 2005 Jan 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15659427>)
- Beitel LK, Scanlon T, Gottlieb B, Trifiro MA. Progress in Spinobulbar muscular atrophy research: insights into neuronal dysfunction caused by the polyglutamine-expanded androgen receptor. *Neurotox Res*. 2005;7(3):219-30. doi:10.1007/BF03036451. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15897156>)
- Bennett NC, Gardiner RA, Hooper JD, Johnson DW, Gobe GC. Molecular cell biology of androgen receptor signalling. *Int J Biochem Cell Biol*. 2010 Jun;42(6):813-27. doi: 10.1016/j.biocel.2009.11.013. Epub 2009 Nov 30. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19931639>)

- Gottlieb B, Beitel LK, Nadarajah A, Paliouras M, Trifiro M. The androgenreceptor gene mutations database: 2012 update. Hum Mutat. 2012 May;33(5):887-94.doi: 10.1002/humu.22046. Epub 2012 Mar 13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22334387>)
- Gottlieb B, Beitel LK, Wu J, Elhaji YA, Trifiro M. Nuclear receptors and disease: androgen receptor. Essays Biochem. 2004;40:121-36. doi:10.1042/bse0400121. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15242343>)
- Hillmer AM, Hanneken S, Ritzmann S, Becker T, Freudenberg J, Brockschmidt FF, Flaquer A, Freudenberg-Hua Y, Jamra RA, Metzen C, Heyn U, Schweiger N, Betz RC, Blaumeiser B, Hampe J, Schreiber S, Schulze TG, Hennies HC, Schumacher J, Propping P, Ruzicka T, Cichon S, Wienker TF, Kruse R, Nothen MM. Genetic variation in the human androgen receptor gene is the major determinant of common early-onset androgenetic alopecia. Am J Hum Genet. 2005 Jul;77(1):140-8. doi:10.1086/431425. Epub 2005 May 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15902657>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1226186/>)
- Katsuno M, Adachi H, Tanaka F, Sobue G. Spinal and bulbar muscular atrophy: ligand-dependent pathogenesis and therapeutic perspectives. J Mol Med (Berl). 2004 May;82(5):298-307. doi: 10.1007/s00109-004-0530-7. Epub 2004 Feb 27. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15133611>)
- Levy-Nissenbaum E, Bar-Natan M, Frydman M, Pras E. Confirmation of the association between male pattern baldness and the androgen receptor gene. Eur J Dermatol. 2005 Sep-Oct;15(5):339-40. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16172040>)
- Poletti A, Negri-Cesi P, Martini L. Reflections on the diseases linked to mutations of the androgen receptor. Endocrine. 2005 Dec;28(3):243-62. doi:10.1385/ENDO:28:3:243. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16388114>)
- Zajac JD, Fui MN. Kennedy's disease: clinical significance of tandem repeats in the androgen receptor. Adv Exp Med Biol. 2012;769:153-68. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23560310>)

## Genomic Location

The *AR* gene is found on the X chromosome (<https://medlineplus.gov/genetics/chromosome/x/>).

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