

## NR3C2 gene

nuclear receptor subfamily 3 group C member 2

### Normal Function

The *NR3C2* gene provides instructions for making a protein called the mineralocorticoid receptor. This protein is important in regulating the amount of sodium in the body. Sodium regulation plays a role in blood pressure control and fluid balance. Certain hormones called mineralocorticoids attach (bind) to and turn on (activate) the mineralocorticoid receptor. Aldosterone is one mineralocorticoid that activates the mineralocorticoid receptor. The activated mineralocorticoid receptor acts as a transcription factor, which is a protein that binds to specific regions of DNA and helps control the activity (transcription) of particular genes.

The mineralocorticoid receptor regulates specialized proteins in the cell membrane that control the transport of sodium or potassium into cells. In response to signals that sodium levels in the body are low, the mineralocorticoid receptor increases the number and activity of these proteins at the cell membrane, especially in certain kidney cells. One of these proteins transports sodium into the cell, while another protein simultaneously transports sodium out of the cell and potassium into the cell. These proteins help keep sodium in the body through a process called reabsorption and remove potassium from the body through a process called secretion.

### Health Conditions Related to Genetic Changes

#### Pseudohypoaldosteronism type 1

More than 50 mutations in the *NR3C2* gene have been identified in people with pseudohypoaldosteronism type 1 (PHA1), a condition that typically begins in infancy and is characterized by low levels of sodium (hyponatremia) and high levels of potassium (hyperkalemia) in the blood. In particular, *NR3C2* gene mutations are involved in autosomal dominant PHA1, a relatively mild form of the condition that can improve in childhood.

Mutations in the *NR3C2* gene lead to a nonfunctional or abnormally functioning mineralocorticoid receptor protein that cannot properly regulate the specialized proteins that transport sodium and potassium. As a result, sodium reabsorption and potassium secretion are both decreased, causing hyponatremia and hyperkalemia.

## Other disorders

One particular mutation in the *NR3C2* gene can cause early-onset hypertension with severe exacerbation in pregnancy. People with this condition develop high blood pressure (hypertension) at an early age. The condition can affect males or females, and hypertension worsens in pregnant females.

The mutation involved in this condition changes one protein building block (amino acid) in the mineralocorticoid receptor protein. The amino acid serine is replaced with the amino acid leucine at position 810 in the protein (written as Ser810Leu or S810L). This mutation changes the shape of the receptor, which allows the receptor to be abnormally activated by non-mineralocorticoid hormones such as progesterone and cortisol. The increased mineralocorticoid receptor activity causes excessive sodium reabsorption, which leads to hypertension. Progesterone levels are elevated during pregnancy, which is why the condition worsens in pregnant females.

## **Other Names for This Gene**

- aldosterone receptor
- FLJ41052
- MCR
- MCR\_HUMAN
- MGC133092
- mineralocorticoid receptor
- mineralocorticoid receptor 1
- mineralocorticoid receptor delta
- MLR
- MR
- NR3C2VIT
- nuclear receptor subfamily 3, group C, member 2

## **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

- Tests of NR3C2 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4306\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4306[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28NR3C2%5BTIAB%5D%29+OR+%28aldosterone+receptor%5BTIAB%5D%29+OR+%28mineralocorticoid+receptor%5BTIAB%5D%29%29+AND+%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5B>)

mh%5D+AND+%22last+720+days%22%5Bdp%5D)

### Catalog of Genes and Diseases from OMIM

- NUCLEAR RECEPTOR SUBFAMILY 3, GROUP C, MEMBER 2; NR3C2 (<https://omim.org/entry/600983>)
- HYPERTENSION, EARLY-ONSET, AUTOSOMAL DOMINANT, WITH SEVERE EXACERBATION IN PREGNANCY (<https://omim.org/entry/605115>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/4306>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=NR3C2\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=NR3C2[gene]))

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## Genomic Location

The *NR3C2* gene is found on chromosome 4 (<https://medlineplus.gov/genetics/chromosome/4/>).

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