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.

**Chromosomal Location**

Cytogenetic Location: 4q31.23, which is the long (q) arm of chromosome 4 at position 31.23

Molecular Location: base pairs 148,078,764 to 148,444,698 on chromosome 4 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

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

Educational Resources
• Endocrinology: An Integrated Approach (2001): Aldosterone Actions in the Kidney

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28NR3C2%5BTIAB%5D%29+OR+%28%28aldosterone+receptor%5BTIAB%5D%29+OR+%28mineralocorticoid+receptor%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• HYPERTENSION, EARLY-ONSET, AUTOSOMAL DOMINANT, WITH SEVERE EXACERBATION IN PREGNANCY
  http://omim.org/entry/605115
• NUCLEAR RECEPTOR SUBFAMILY 3, GROUP C, MEMBER 2
  http://omim.org/entry/600983

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/NR3C2ID44262ch4q31.html
• ClinVar
• HGNC Gene Symbol Report
• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4306
• NCBI Gene
• UniProt
  https://www.uniprot.org/uniprot/P08235
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10051674  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC268161/  

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10884226  

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10718622  

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• OMIM: NUCLEAR RECEPTOR SUBFAMILY 3, GROUP C, MEMBER 2  
  http://omim.org/entry/600983  

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16972228  

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12538613  

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