CYP19A1 gene
cytochrome P450 family 19 subfamily A member 1

Normal Function

The *CYP19A1* gene provides instructions for making an enzyme called aromatase. This enzyme converts a class of hormones called androgens, which are involved in male sexual development, to different forms of the female sex hormone estrogen.

In cells, aromatase is found in a structure called the endoplasmic reticulum, which is involved in protein production, processing, and transport. The activity (expression) of aromatase varies among different cell types depending on the cells' need for estrogen. In females, aromatase is most active in the ovaries, where it guides sexual development. In males, aromatase is most active in fat (adipose) tissue. In both males and females, estrogen plays a role in regulating bone growth and blood sugar levels. During fetal development, aromatase converts androgens to estrogens in the placenta, which is the link between the mother's blood supply and the fetus. This conversion in the placenta prevents androgens from directing sexual development in female fetuses. After birth, the conversion of androgens to estrogens takes place in multiple tissues.

Health Conditions Related to Genetic Changes

Aromatase deficiency

More than 20 mutations in the *CYP19A1* gene have been found to cause aromatase deficiency. This condition is characterized by reduced levels of estrogen and increased levels of androgens. These abnormal hormone levels lead to impaired sexual development in affected females and unusual bone growth, insulin resistance, and other signs and symptoms in both males and females with the condition. *CYP19A1* gene mutations that cause aromatase deficiency decrease or eliminate aromatase activity. A lack of aromatase function results in an inability to convert androgens to estrogens before birth and throughout life. As a result, there is a decrease in estrogen production and an increase in the levels of androgens, including testosterone. In women who are pregnant with an affected fetus, excess androgens in the placenta pass into the woman's bloodstream, and may cause her to have temporary signs and symptoms of aromatase deficiency.

Aromatase excess syndrome

More than 10 rearrangements of genetic material involving the *CYP19A1* gene have been found to cause aromatase excess syndrome. This condition is characterized by the increased conversion of androgens to estrogen. As a result, affected males have enlarged breasts (gynecomastia) and short stature; affected females can have irregular menstrual periods and short stature.
Several types of genetic rearrangement involving the CYP19A1 gene can cause aromatase excess syndrome. Some genetic rearrangements that cause aromatase excess syndrome duplicate parts of the CYP19A1 gene, doubling some of the instructions used for making the enzyme. As a result, more enzyme than normal is produced. Other genetic rearrangements, called deletions, remove (delete) parts of the CYP19A1 gene and a nearby gene. The remaining DNA is then fused together, creating a fusion gene composed of parts of two different genes. These fusion genes always contain part of the CYP19A1 gene, but can involve a piece of one of several other genes. As a result of these fusion genes, the CYP19A1 gene is active (expressed) in tissues where it is not normally expressed so more aromatase than normal is produced. Another type of rearrangement, called an inversion, occurs when DNA is broken in two places and the resulting piece of DNA is reversed and reinserted into the chromosome. Inversions involving the CYP19A1 gene and a nearby gene also result in the production of a fusion gene. These fusion genes lead to increased aromatase production.

The increase in aromatase production caused by CYP19A1 gene rearrangements leads to increased estrogen production, which results in the signs and symptoms of aromatase excess syndrome.

Breast cancer

Chromosomal Location

Cytogenetic Location: 15q21.2, which is the long (q) arm of chromosome 15 at position 21.2

Molecular Location: base pairs 51,208,057 to 51,338,596 on chromosome 15 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)
• CP19A_HUMAN
• CPV1
• CYAR
• CYP19
• CYPXIX
• cytochrome P-450AROM
• cytochrome P450 19A1
• cytochrome P450, family 19, subfamily A, polypeptide 1
• cytochrome P450, subfamily XIX (aromatization of androgens)
• estrogen synthase
• estrogen synthetase
• flavoprotein-linked monooxygenase
• microsomal monooxygenase
• P-450AROM

Additional Information & Resources

Educational Resources
• Basic Neurochemistry (sixth edition, 1999): Some Steroid Hormones are Converted in the Brain to More or Less Active Products that Interact with Receptors
  https://www.ncbi.nlm.nih.gov/books/NBK28144/#A3518
  https://www.ncbi.nlm.nih.gov/books/NBK9967/#A4124

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CYP19A1%5BTI%5D%29+OR+%28aromatase%5BTI%5D%29+NOT+%28inhibitor%5BTI%5D%29+AND+%28%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
• CYTOCHROME P450, FAMILY 19, SUBFAMILY A, POLYPEPTIDE 1
  http://omim.org/entry/107910
Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
- ClinVar
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:1588
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P11511

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19844120
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14623514
- OMIM: CYTOCHROME P450, FAMILY 19, SUBFAMILY A, POLYPEPTIDE 1
  http://omim.org/entry/107910
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20205115
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24064691

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