CYP19A1 Gene

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Cytochrome P450 Family 19 Subfamily A Member 1

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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.

2. Health Conditions Related to Genetic Changes

2.1 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.

2.2 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.

3. Other Names for This Gene

- ARO
- ARO1
- aromatase
- 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

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