Polycystic Ovarian Syndrome (Gene DENND1A)

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What is PCOS?

Polycystic ovarian syndrome is a hormonal disorder that is common in women of reproductive age. Women with PCOS usually struggle with symptoms such as infertility, irregular periods and fluid filled sacs on the ovaries, called cysts. Scientific studies suggest that gene DENND1A is associated with PCOS. DENND1A is located on the long arm of chromosome number 9. Research is being done to help us better understand the gene’s origins, and how it causes PCOS.

Where is DENND1A Located in The Human Genome?

- DENND1A is found on chromosome 9 in the human genome.
- It is located on the long arm of the chromosome, which is also known as the Q arm. The shorter end is the P arm.
- The band where DENND1A is found is 9q22.32

Genetic Study of PCOS:

- A combined approach of GWAS, candidate gene association, and family-based studies are required to fully explain the genetic contribution to the origins of PCOS.
- GWAS is genome-wide association study which associates specific genetic variations of particular diseases. In this process you scan genomes from many different people looking for genetic markers used to predict the presence of it.
- Family based studies and AIMS (Ancestry Informative Markers) help with tracking down inheritance patterns and understanding the impact of the genes in PCOS.
- Candidate gene association focuses on genetic variation within pre-specified genes of interest, and phenotypes or disease states.

Gene DENND1A

Alternative Splicing:

- The DENND1A gene consists of 22 exons extending over 500,000 bases, and encodes protein connecdenn 1 which is thought to facilitate endocytosis.
- Connecdenn 1 is a guanine nucleotide-exchange factor that interacts with members of the Rab family of small GTPases, which are involved in vesicular trafficking.
- DENND1A encodes two transcripts as a result of alternative splicing respectively: DENND1A.V1and DENND1A.V2
- In cultured human theca cells, immunofluorescence studies revealed that DENND1A.V2 is co-localized with the LH receptor and the small GTPase, RAB5B, which is involved in vesicular trafficking.

Actions of DENND1A:

- It is expressed in tissues all over the body.
- PCOS theca cells in culture show an increase in both the expression of the enzyme CYP17A1 and androgen secretion under basal conditions compared to theca cells from ovulatory women.
- Forced expression of DENND1A.V2 in normal theca cells increases the expression of genes involved in androgen biosynthesis and androgen secretion.

Signs/Symptoms and Treatment of PCOS:

Signs/Symptoms:

- PCOS symptoms can appear as early as the first menstrual cycle.
- Anovulation, irregular menstrual cycles, acne.
- Infertility.
- Obesity.
- Excessive hair growth on face, chest, abdomen, or upper thighs.
- Small fluid-filled sacs on the ovaries.

Treatment:

- Treatment depends on the individual’s concerns specifically such as infertility, excessive hair growth, acne or obesity.
- Lifestyle changes such as dieting and exercising.
- Medications like:
  - Birth control pills (helps with decreasing androgen production).
  - Progestin therapy (helps regulate endometrial cancer).
  - Medications to help with ovulation and excessive hair growth.

Conclusion

Polycystic ovarian syndrome is a relatively common disorder, and affects many women of reproductive age. Overexpression of DENND1A.V2 causes more androgen production than normal in women, causing PCOS. PCOS does not have a cure, but there are ways to treat the phenotypic characteristics. Varying person to person, doctors can treat patients with different medications or methods in order to suit the individual’s specific concerns.

References

1. www.mayoclinic.org/diseases-conditions/pcos/symptoms-causes/syc-20355849
2. en.wikipedia.org/wiki/DENND1A
13. https://doi.org/10.3390/ijms21041141
16. www.cumberland.edu/pmc/upcoming-conference/2022

Figure 1: polycystic ovary versus healthy ovary
Figure 2: Chromosome 9
Figure 3: Excessive facial hair

Polycystic ovary
Uterus
Healthy ovary

Figure 2: Chromium 9

Figure 3: Excessive facial hair