Scientist discover rare genotype causing early menopause

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Credit: Nadezhda Moryak from Pexels

Scientists have identified a sequence variant in the CCDC201 gene that, when inherited from both parents homozygous, causes menopause on average nine years earlier.

deCODE genetics and collaborators from Iceland, Denmark, the UK, and Norway published a study in *Nature Genetics* today revealing a rare genotype with a significant impact on women's health.

Age at menopause significantly affects fertility and disease risk. This research focused on recessive models, or on individuals with two copies of a sequence variant called homozygotes, which are less commonly studied than the additive model, which mainly relies on individuals carrying one copy of a sequence variant, especially when this one is rare.

By analyzing data from over 174,000 women across Iceland, Denmark, the UK, and Norway, the researchers discovered a stop gain variant leading to a change from and Arginine at position 162 to Termination in the CCDC201 gene, that dramatically impacts AOM.

The CCDC201 gene, only identified in humans as a protein coding gene in 2022 and has since then been shown to be highly expressed in egg cells, and this study demonstrates that its complete loss-of-function significantly impacts female reproductive health.

Women carrying two copies of this variant, referred to as homozygotes, experience menopause an average of nine years earlier than non-carriers. This homozygous genotype is found in roughly 1 in 10,000 women of Northern European descent, leading to primary ovarian insufficiency, defined as age at menopause before the age of 40, in nearly half of carriers. Consequently, women with this genotype have fewer children and have children very rarely after the age of 30.

This discovery highlights the importance of considering various genetic models in understanding diseases such as primary ovarian insufficiency.

The study underscores the potential benefits of genetic counseling for women with this specific genotype. Early diagnosis allows for informed

reproductive choices and management of symptoms associated with early menopause.

More information: Homozygosity for a stop-gain variant in CCDC201 causes primary ovarian insufficiency, *Nature Genetics* (2024). DOI: 10.1038/s41588-024-01885-6

Provided by deCODE genetics