GENES THAT INFLUENCE MENOPAUSE AGE

Genome-Wide Association Studies (GWAS) are based on common SNP variants. However, recent papers have highlighted some limitations, for example, the exclusion of tandem repeat variants, which are a significant source of phenotypic variation, from arrays (1, 2). Another inherent bias in GWAS is the absence of rare variants on the genotyping arrays.

GWAS have identified genes involved in age at menopause, but these have explained only a small portion of the large variation observed in the general population of women. In contrast, two recent studies (3, 4) have focused on rare variants and genes that account for much larger variations. For example, women homozygous for a stop-gain variant in *CCDC201* experience menopause 9 years earlier than other women (4). Another key gene is *ZNF518A*, which is involved in DNA repair. Unsurprisingly children of mothers with these variants have a higher mutation load, and the gene is also implicated in tumorigenesis.

Summaries or News & Views commentaries on the two papers are available. (5).


1. https://www.cell.com/trends/genetics/abstract/S0168-9525(24)00175-6?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0168952524001756%3Fshowall%3Dtrue
2. https://www.nature.com/articles/s41576-024-00736-8
3. https://www.nature.com/articles/s41586-024-07931-x
4. https://www.nature.com/articles/s41588-024-01885-6
5. Nature | Vol 633 | 19 September 2024