THE POTENTIAL OF GWAS IN UNDERSTANDING FEMALE INFERTILITY

In earlier posts on this forum, we have highlighted studies that demonstrate the value of exome sequencing in uncovering the genetic basis of infertility. A recent article in the *Am. J. Hum. Genet.* (1) takes an alternative approach, utilizing Genome-Wide Association Studies (GWAS) to investigate the genetic etiology of this condition.

Through GWAS, researchers identified a rare stop-gained mutation in the *TBPL2* gene using data from 22,849 women with infertility and 199,000 controls in the Finnish FinnGen cohort. This mutation disrupts a transcription factor crucial for oocyte development. Women with two mutated alleles exhibited reduced fertility, often requiring infertility treatment to conceive.

In addition to *TBPL2*, the study identified three age-specific genetic loci associated with infertility. Early-onset infertility (before age 30) was linked to variants in *CHEK2* and the major histocompatibility complex (MHC), while late-onset infertility was associated with a long non-coding RNA gene.

The study highlights the utility of GWAS as a cost-effective tool for uncovering the genetic basis of complex conditions like female infertility.

1. https://www.cell.com/ajhg/fulltext/S0002-9297(24)00387-2?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0002929724003872%3Fshowall%3Dtrue