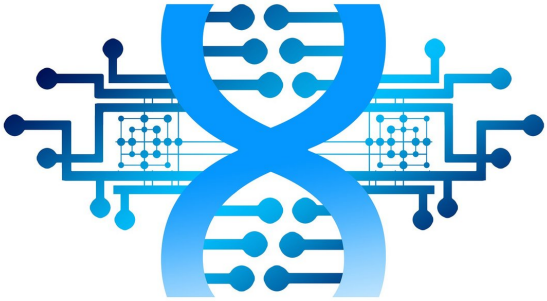
Genetic determinants of fertility and ongoing natural selection in humans

29 October 2020



Credit: CC0 Public Domain

An international team of researchers who identified genetic variants associated with reproductive success say their findings could highlight mechanisms underlying fertility and infertility. In addition, their analyses detected genetic alleles under present-day selection, providing an insight into the nature of ongoing natural selection in humans. Iain Mathieson, Ph.D., a population geneticist at the University of Pennsylvania, presented the results of the study at the American Society of Human Genetics 2020 Virtual Meeting.

"This study is of interest in relation to our findings on reproductive biology and potential links to infertility," says co-author of the study Melinda Mills, Ph.D., director of the Leverhulme Centre for Demographic Science at the University of Oxford.

"But it also empirically tests one of the most gripping and fundamental questions asked by scientists across many disciplines and decades: Is there evidence of ongoing natural selection in humans and, if so, what is it and how does it operate?"

The new study builds upon previous research on the genetic bases of reproductive behavior (timing and number of children) and reproductive development to identify individual genetic determinants of number of children ever born or childlessness.

The researchers performed genome-wide association studies in up to 785,604 individuals of European ancestry and identified 43 genetic loci associated with either number of children ever born or childlessness. These loci span diverse aspects of reproductive biology across the lifespan, including puberty timing, age at first birth, sex hormone levels, sexuality, and age at menopause.

The findings demonstrate that diverse biological mechanisms contribute to reproductive success, implicating both neuroendocrine and behavioral influences. Ultimately, the researchers believe this might lead to a better understanding of the biology of reproduction and perhaps the genetic basis of infertility.

Furthermore, by integrating these findings with data from ancient selection scans, the researchers were able to identify a unique example of an allele—known as FADS1/2—that was under selection in our ancient past and remains under selection today.

"Independent research has shown that this allele has been under selection for many thousands of years, potentially linked to changes in diet around the time of the transition to agriculture," says Dr. Mathieson. "Therefore, it represents perhaps the only example of a genetic variant with evidence of both historical and ongoing selection."

Dr. Mathieson says the study raises a number of questions to look into in the future, such as why the FADS1/2 locus is under selection. Experiments in animal models might provide a clue: Knocking out the FADS1 gene in mice leads to both male and

female infertility.

Additionally, Dr. Mills points out this study, like nearly 90% of contemporary genetic research, is limited by its use of data from only individuals of European ancestry.

"This is problematic, as we and others have addressed," she says. "Future extensions of this work will examine diverse non-European populations."

More information: Mathieson, I., Day, F.R., Barban, N., Tropf, F.C., Brazel, D., eQTLGen Consortium, BIOS Consortium, Vaez, A., van Zuydam, N., Bitarello, B.D., Snieder, H., den Hoed, M., Ong, K.K., Mills, M., Perry, J.R., and Human Reproductive Behaviour Consortium. (Date). Abstract: Genome-wide analysis identifies genetic effects on reproductive success and ongoing natural selection at the FADS locus. Presented at the American Society of Human Genetics 2020 Virtual Meeting.

Provided by American Society of Human Genetics