

Human fertility gene found

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Researchers have for the first time identified a gene that boosts fertility in humans. A single amino acid substitution in a gene linked with cystic fibrosis may be responsible for the differential reproductive success of some men living in a religious community in the US prairies, according to data presented yesterday (Apr. 2) at the Sackler Colloquium on Evolution in Health and Medicine in Washington, DC.

Many genes have been identified that cause infertility in humans, but finding genes that enhance fertility is tougher because people often choose to limit their family size for various cultural, social, and economic reasons. The Hutterites, however, do the opposite. This isolated group of Anabaptists living in the great plains of North America eschews birth control. Families often have more than 10 children, and they generally wait less than two years between successive births. Hutterites also rarely marry outside the community and they share a similar communal lifestyle, which reduces both genetic and environmental noise that can confound studies of inheritance.

Carole Ober, a geneticist at the University of Chicago who has been studying fertility in a population of Hutterites in South Dakota for more than 20 years, showed two years ago that reproductive success had a heritable component in both males and females. At the time, the finding was somewhat controversial, Ober told *The Scientist*. "There is a resistance among human geneticists to recognize that fertility is genetic," she said, but it should be "obvious," as fertility-related genes have been found in many model organisms, and there's no reason to suppose humans should be different.

Now, Ober and her graduate student Gülüm Kosova have performed a genome-wide association study to identify fertility-related genes. The "biggest hit," Ober said, was the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which codes for a chloride ion channel and has a few known polymorphisms that have been implicated in both cystic fibrosis and male infertility.

One of these polymorphisms is a single amino acid difference -- either a valine or a methionine -- in exon 10. The researchers genotyped this polymorphism in 207 Hutterite men, none of which suffered from infertility. They found that a valine residue was significantly correlated with increased male birth rate, resulting in an average of two more children per male over the span of a 25-year breeding period. All told, the polymorphism explained 4.3% of the variation in male birth rate -- a large amount for any single gene, Ober said. (By comparison, the 50-odd genes found to affect human height together only account for around 5% of the total variability in stature.)

Ober also analyzed the time to conception in 216 pregnancies among the partners of 103 men and found that men who carried two copies of the valine allele were 2.6 times more likely to conceive than men with two copies of the methionine allele at the same locus.

The findings could help explain earlier results showing that the amino acid difference was under positive natural selection, Ober said. In 2006, an Italian team of researchers found that the valine substitution was widespread in Europe and Asia but only the ancestral methionine allele was present in Africa. The researchers had concluded that the genetic difference probably affected

lung function to protect people from cystic fibrosis, but Ober argued that fertility differences are probably a stronger selective pressure.

Ober said she is now analyzing the semen of around 100 men to understand how valine bestows its bearers with their procreation prowess. "Presumably there's something different but whether it's number or morphology or what, I don't know what to expect," Ober said. "I'm not sure that a standard semen analysis is going to be enough [to identify valine's effect], but if we do it will be amazing."