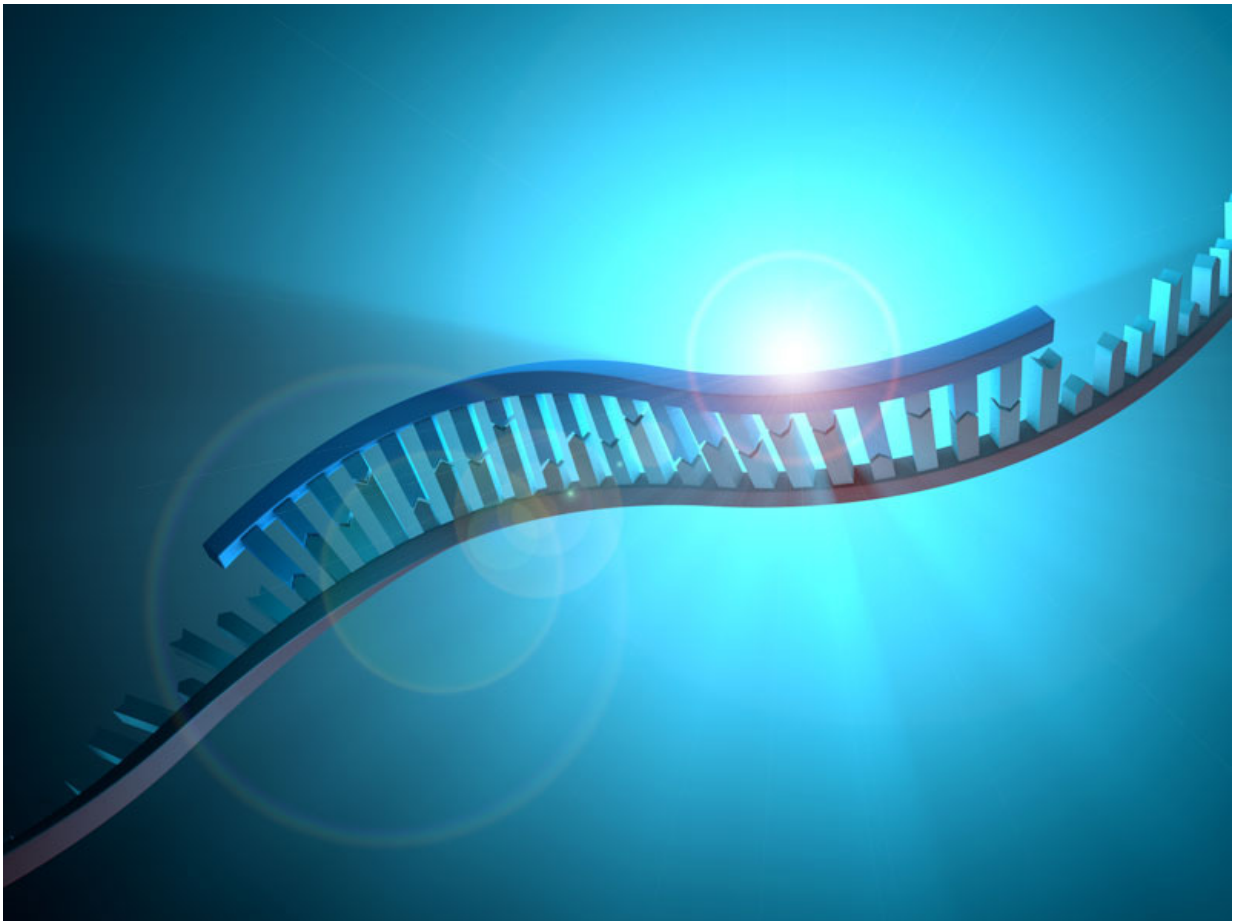


Genetic test may help spot male fertility problems

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Sperm harbors a rich population of RNA, molecules that direct protein production and regulate gene expression. Researchers have identified a set of sperm RNA elements that may be critical to male fertility. Credit: C. Bickel / Science Translational Medicine

A new genetic test for sperm could help determine whether a couple should resort to in vitro fertilization to conceive a child, researchers say.

Men whose [sperm](#) lack critical RNA [elements](#) tend to have lower chances of naturally conceiving a child, according to study findings published July 8 in the journal *Science Translational Medicine*.

An RNA analysis of a potential father's sperm can tell fertility doctors whether a couple should skip less-invasive treatments and go straight to assisted reproductive technology (ART), in which eggs are combined with sperm in the laboratory to achieve fertilization, the study's authors said.

"The absence of one or more of these RNA elements was indicative of those who would be successful by ART, which is a more invasive technique, versus those who would be successful by timed intercourse or intrauterine insemination, which is less invasive," said study lead author Stephen Krawetz. He is a professor of fetal therapy and diagnosis and associate director of the C.S. Mott Center for Human Growth and Development at Wayne State University School of Medicine in Detroit.

About 13 percent of couples face problems with infertility, the study authors said in background notes. There are a wide battery of diagnostic tests available to women who are struggling to conceive. But, fertility testing for men currently is limited to a physical examination of their sperm's movement, volume and concentration, Krawetz said.

"If you think about it, it's how good do the sperm look. That really doesn't tell you much about the quality," Krawetz said. "A sperm may look fantastic, but yet could not be up to the job of fertilization."

To study [sperm quality](#) in more depth, Krawetz and his team first studied couples who had been able to naturally conceive by having sex on days

when the woman was most fertile.

Genetic analysis of the men's sperm revealed a set of 648 RNA elements that are vital to male fertility. Many of these elements correspond to genes involved in sperm development, the ability to move, energy production, fertilization and embryo formation, the researchers said.

RNA, or ribonucleic acid, is a molecule used by the body to help code, decode and produce genetic information. Recent research has shown that sperm cells harbor a surprisingly rich amount of RNA, which appears to play a distinct role in fertilization and early development of the embryo, the study authors said.

The researchers then turned to 96 couples who seemed completely healthy but had been unable to conceive. The investigators performed an RNA analysis of the men's sperm, and then provided a series of increasingly invasive fertility treatments for the couple.

Most infertile men did not carry a complete set of sperm RNA elements, the researchers found, and lacking some RNA elements reduced the success rate of natural pregnancy from 73 percent to 27 percent. The greater the number of RNA elements missing from the [sperm cell](#), the lower the likelihood of conception, the researchers said.

However, that didn't mean these couples could not conceive, Krawetz said—just that they would need more medical assistance.

"When we took those same individuals and went to assisted reproductive technologies, their rate of fertilization and live birth approached that of the group that was successful by the relatively non-invasive techniques," he said.

Dr. Rebecca Sokol, president of the American Society for Reproductive

Medicine, praised the researchers' efforts to figure out a man's contribution to conception.

"As a specialist in male reproduction, I think I can say the field of male infertility is in desperate need of a biomarker like this," said Sokol, a professor of obstetrics and gynecology at the University of Southern California Keck School of Medicine. "As far as the field of infertility is concerned, not enough focus is put on the male."

But the results of this preliminary research need to be reproduced, Sokol said. The trial was small, involved a select group of patients, and did not include a truly random control group, she said.

"It's not perfect," she said. "Nothing's perfect. But it's a good first step."

Krawetz hopes that RNA analysis ultimately will prove a useful early test in fertility treatment. Sokol noted that such analysis is time-consuming and potentially expensive, but she could not put a price tag on the procedure.

"For this to be truly used as a screening test, it will have to be made more facile and less expensive," she said.

A similar genetic test for women likely is not possible, Krawetz said, and it's all down to numbers. A single male ejaculation contains sperm in the hundreds of millions, providing a great deal of genetic material for analysis, while a woman carries just one egg, which gives doctors much less material with which to work, he explained.

More information: Absence of sperm RNA elements correlates with idiopathic male infertility, [stm.sciencemag.org/lookup/doi/...
scitranslmed.aab1287](http://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aab1287)

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