

USC researchers explore genetic causes for male infertility

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Researchers at the University of Southern California (USC) suggest epigenetics, or the way DNA is processed and expressed, may be the underlying cause for male infertility. The study will be published in the Dec. 12 issue of *Public Library of Science One*.

“This is the first report based on our knowledge that a broad epigenetic defect is associated with abnormal semen development,” says Rebecca Sokol, M.D., MPH, professor of obstetrics and gynecology at the Keck School of Medicine of USC. “From our data, it is plausible to speculate that male infertility may be added to the growing list of adulthood diseases that have resulted from fetal origins.”

In the United States, about 4 million married couples of child-bearing age are infertile and in approximately 40 percent of the cases, the infertile partner is the man. In most cases, the cause of the male infertility is not known. However, preliminary data suggest that genetics play a role in infertility. Changes in chromosomes and the genetic code have been well documented. Attention is now focused on epigenetic changes. Epigenetic change, which is defined as in addition to changes in genetic sequence, includes any process that alters gene activity without changing the DNA sequence. Some of these epigenetic changes are inherited from one generation to the next.

The researchers studied semen samples from male members of couples attending an infertility clinic. Using highly specialized molecular biology techniques, the researchers studied the epigenetic state of DNA from

each man's sperm. They found that sperm DNA from men with low sperm counts or abnormal sperm had high levels of methylation, which is one of the ways the body regulates gene expression. However, DNA from normal sperm samples showed no abnormalities of methylation.

DNA methylation results from well known biochemical alterations that occur during epigenetic reprogramming, which is a normal physiologic process that occurs during embryonic development.

“Disturbance of epigenetic programming can result in abnormal gene activity or function, even if there is no change in DNA sequence,” continues Sokol.

The epigenetic irregularity found in these abnormal sperm samples was present in a high proportion of genes that were studied. The results suggest that the underlying mechanism for these epigenetic changes may be improper erasure of DNA methylation during epigenetic reprogramming of the male germ line.

“If we can identify what causes these changes to the sperm DNA, then we might be able to prevent certain types of male infertility,” concludes Sokol. “This is particularly important because recent animal studies have suggested that epigenetics may have broader implications. Exposures to chemicals as a fetus may lead to adult diseases. Perhaps such exposures may be causing the changes in the sperm DNA that we have identified. Studies to uncover a relationship between chemical exposures and alterations in sperm DNA should shed light on this.”

Source: University of Southern California

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