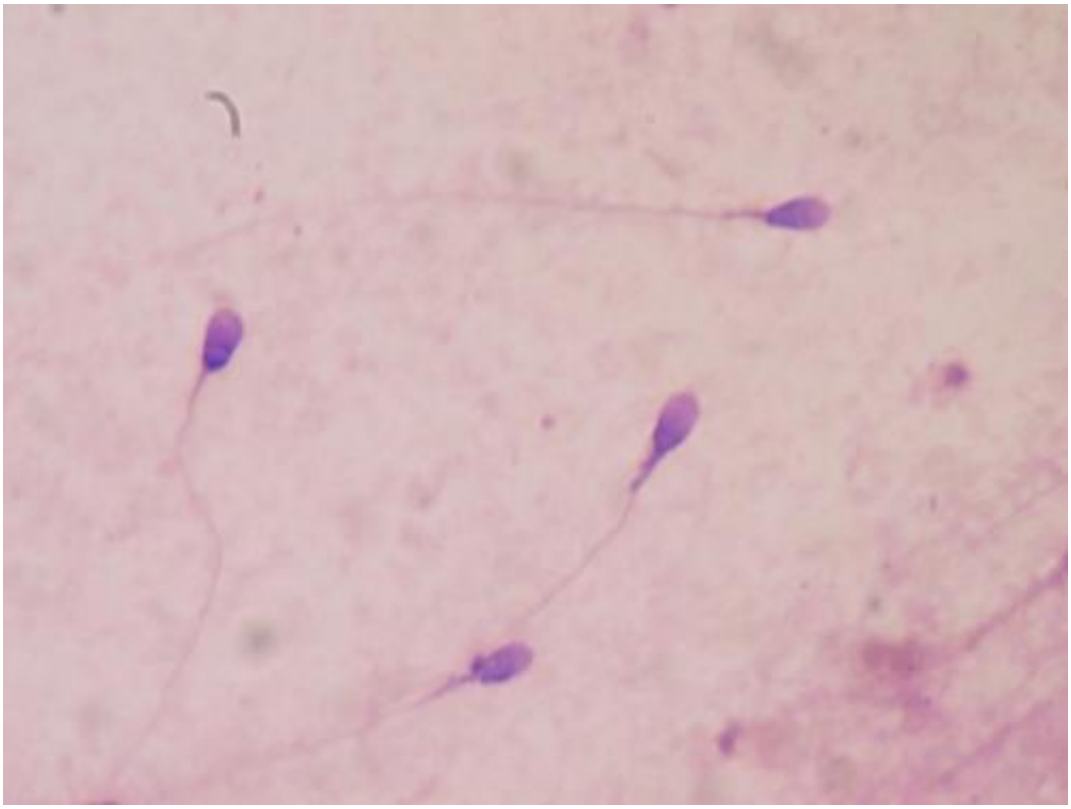
Changes to small RNA in sperm may help fertilization

July 26 2018



Human sperm stained for semen quality testing in the clinical laboratory. Credit: Bobjgalindo/Wikipedia

Two papers by UMass Medical School Professor Oliver J. Rando, MD, Ph.D., shed new light on the processes of fertilization and epigenetic inheritance in mammals. Together, the research provides important insight into how epigenetics—the study of inheritable traits that are

carried outside the genome—work from father to offspring. The studies appear in the journal *Developmental Cell* and provide new information about the epigenetic contribution of males to their offspring.

Studies over the past decade in the field of epigenetics have provided unexpected support to the notion that conditions experienced by a parent can affect disease risk and other traits in future generations. Contributions of mammalian females to their offspring are apparent—both nuclear and mitochondrial DNA, for example, as well as exposure to various factors during gestation—but less is known about male contributions beyond the DNA found in sperm.

"The study of paternal contributions to development, including environmental contributions to the health of sperm, is a burgeoning field of research," said Dr. Rando, professor of biochemistry and molecular pharmacology at UMMS. "In addition, because of the rise in the use of assisted reproduction, it's also vital to look at the differences between sperm removed directly from the testicles and ejaculated sperm, to investigate whether these differences may have an impact on the long-term health of the offspring."

Both studies looked at small RNAs to determine how these molecules contribute to epigenetic changes in sperm in mice.

In the first study, led by Upasna Sharma, Ph.D., postdoctoral fellow at UMMS, the investigators looked at what happens to small RNAs when sperm leave the testes and travel through the epididymis toward the vas deferens, a process that takes about two weeks. Researchers found that the sperm underwent dramatic changes to its their RNA "payload—small RNAs carrying information -during this time. They also confirmed that some of the RNA found in sperm originates in the paternal epididymis and is later transferred to sperm cells.

The second study looked at the functional implications of small RNAs in sperm and whether these small RNAs have any effect on sperm or the fertilized egg. The team, led by UMMS Postdoctoral Associate Colin C. Conine, Ph.D., found that small RNAs in sperm are essential for normal pre-implantation development. Specifically, they showed that embryos fertilized using sperm from early in the epididymis—where sperm have not yet gained a full payload of regulatory RNAs—exhibit gene misregulation early in development and then fail to implant in the uterus efficiently. The researchers could correct these defects by injecting small RNAs from the end of the epidydimal pathway into the newly formed embryo.

Earlier studies from Rando and others suggested that paternal environmental conditions can affect the health of their offspring and that a man's lifestyle and exposure to potentially hazardous elements—such as stress and toxins—can affect the levels and types of small RNA in the sperm. The researchers plan to continue studying the role of small RNAs in reproduction and development.

"A substantial subset of embryos are created using fertilization with testicular sperm, which have subtly different RNA contents from ejaculated sperm," said Rando. "Since we now show that even relatively subtle RNA differences between sperm from the beginning versus the end of the epididymis can impact offspring it will be interesting to explore these effects of sperm used in assisted reproduction."

More information: *Developmental Cell*, Sharma et al.: "Small RNAs are trafficked from the epididymis to developing mammalian sperm." www.cell.com/developmental-cel … 1534-5807(18)30540-9 , DOI: 10.1016/j.devcel.2018.06.023

Developmental Cell, Conine et al.: "Small RNAs gained during epididymal transit of sperm are essential for embryonic development in

mice." www.cell.com/developmental-cel … 1534-5807(18)30541-0 , DOI: 10.1016/j.devcel.2018.06.024

Provided by University of Massachusetts Medical School