SOUTHWESTERN NEWS

Media Contact: Donna Steph Hansard
214-648-3404
donna.hansard@utsouthwestern.edu

UT SOUTHWESTERN RESEARCHERS' DISCOVERY MAY LEAD TO GENE TARGETS FOR NEW FORM OF CONTRACEPTIVE

DALLAS – Dec. 3, 2003 – Deleting a particular ion channel from sperm cells causes those cells to lose the power needed for fertilization, researchers at UT Southwestern Medical Center at Dallas found while expanding studies into male infertility.

These findings, which could eventually lead to more effective forms of contraception, are currently available online and will appear in the Dec. 9 issue of the *Proceedings of the National Academy of Sciences*.

In studies on mice, disrupting a gene that contains a putative calcium-permeable ion channel – identified in earlier research as CatSper2 – did not change normal sperm cell production or basic sperm motility, or movement. It did, however, prevent the appearance of a stimulated form of sperm motility, called hyperactivation, normally seen near the time of fertilization. Sperm cells were, thus, incapable of generating the power needed to penetrate an egg cell's extracellular matrix, or outer shell, which is necessary for fertilization.

"Basically this protein or ion channel plays a critical role in sperm cell hyperactivation, which is essential for fertilization," said Dr. Timothy Quill, first author of the study and an instructor of pharmacology and a researcher in the Cecil H. and Ida Green Center for Reproductive Biology Sciences. "The same protein exists in human sperm cells, so it is likely that disruption of CatSper2 would result in infertility in men as well. If a contraceptive drug could be designed that would bind to the protein and block its function, then those sperm cells would be rendered ineffective or infertile."

Such an ion channel-blocking contraceptive would likely be fast acting, Dr. Quill said. It also could have fewer side effects than other available contraceptives, as it would target a protein found only in sperm cells.

"Blocking the protein's activity would not cause defects in the development of the sperm cell, but only prevent hyperactivation," he said. "This discovery could serve as one of the next

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steps in the process of creating a new type of contraceptive that would offer less risk and perform faster."

UT Southwestern researchers recently identified more than 350 genes that appear to be active in maturing sperm cells in mice. In a study published in the *PNAS* earlier this fall, researchers showed that, so far, 17 of those genes are necessary for normal male fertility. Because these genes appear to be active only in developing sperm, creating contraceptive drugs targeting these genes also could be a possibility.

Dr. David Garbers, director of the Green Center, a Howard Hughes Medical Institute investigator and senior author of both *PNAS* studies, is well-known for his investigations into how the egg and sperm communicate, research that led to his election to the National Academy of Sciences.

Other contributors to the most recent study, all from UT Southwestern, include Dr. Robert Hammer, professor of biochemistry and in the Green Center; Lynda Doolittle, research specialist for HHMI, and Sarah Sugden, research assistant in the Green Center.

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