Scientists record electrical currents that control male fertility

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Performance anxiety? Not for this human sperm.

He doesn't know the bright lights and cameras are for him. He doesn't know he's swimming on a glass stage with no egg. And he's clueless that researchers are watching his every move at high magnification - viewing his inner workings.

Biologists Yuriy Kirichok and Polina Lishko of the University of California, San Francisco, have made a name for themselves recording the electrical currents that course through, yes, sperm cells. Their work is not only offering new hope to infertile couples, but also may lead one day to an effective male birth control pill.

In a pivotal study, the husband-and-wife team has uncovered how progesterone - a hormone involved in menstruation and embryo development - switches on a sperm's internal electricity. The electric current kicks sperm tails into overdrive, powering the final push toward the egg. Sperm that fail to heed progesterone's "get-up-and-go" signal could help explain some couples' struggles to conceive, say Kirichok and Lishko, both Ukrainian immigrants.

The pair also studies mitochondria, the vital energy-generating components of cells. But Kirichok said sperm cells tend to steal the show. "People are kind of fascinated," he said. "The first question is always, 'Where do you get the sperm cells from?' The second question is, 'What do you do with them?'"

Sperm donated by healthy dads - guaranteeing no fertility problems - goes under the microscope, where the scientists carefully break the cells' outer membranes to measure the electrical currents within. The goal is eventually to understand sperm biology as well as we understand the female reproductive system.

About 15 percent of U.S. couples are infertile, and roughly half of those cases can be linked to male infertility, according to reproductive biologist Harvey Florman of the University of Massachusetts. Yet 80 percent of male infertility cases cannot be explained, says Lishko. When it comes to women, researchers have already discovered what's behind about 80 percent of infertility cases.

Last year, Lishko began using a technique called "whole-cell recording" to perform some of the world's first electrical recordings from human sperm - a breakthrough that allowed the researchers to map out a key process in fertilization.

Two recent articles in the scientific journal Nature - one by Lishko and Kirichok, another by researchers in Germany - provide the first evidence that progesterone activates sperm tails by binding to a protein on the sperm's surface, called CatSper.

Scientists have long suspected that progesterone from around the egg triggers sperm tails to pump harder in the final stages of fertilization. The tail's normal undulations switch to a one-sided flicking motion, like a whip being cracked against the ground.

Called "hyperactivation," the whipping motion is thought to give sperm a last-minute boost to the egg and help one lucky winner to poke through the egg's protective vestments. In fact, in vitro experiments show that fertilization cannot happen without hyperactivation. But until now, researchers couldn't explain how progesterone transmits its signal.

Contact with CatSper starts a rush of electrically charged calcium ions into the cell, the new research found. While the sperm tail contains no real muscle, it is constructed of some of the same molecules. So just as muscles contract in response to calcium currents, the sperm tail reacts with a forceful twitch.

"In terms of how we understand fertilization, this is a large step," said Florman, who was not associated with the studies. "In terms of contraception, this is highly significant."

If activating the CatSper molecule excites sperm tails, he explained, then blocking the receptor - with some drug that elbows progesterone out of its docking spot - could keep sperm in check.

Ultimately, CatSper is only part of a complex system that controls male fertility, said Lishko, and many molecules remain to be identified. Eventually, she hopes doctors will be able to screen the genes of infertile men for defects in CatSper and other sperm proteins.

These crucial molecules have been tough to identify so far. But the advent of electrical recordings in human sperm could be a game-changer, said Kirichok.

"For the first time, we have a reliable method to record, in a very direct fashion, the molecules that control male fertility," he said. "Now I believe the field will move faster."