

Male Contraceptive Disables Sperm

TDI-11861 temporarily disabled mouse and human sperm, and it prevented pregnancies in mice.

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Studies suggest that about half of all pregnancies worldwide are unintended. Most modern contraceptive methods are for women. Men generally have two options: condoms or vasectomies.

The challenge with creating new contraceptives for men is the high rate of sperm production. Men produce several million sperm per day—about 1,000 per second. To prevent pregnancy, all of these need to be stopped from reaching an egg.

Both hormonal and non-hormonal approaches to stop sperm have been in development. But many of these methods need about two months to become effective, and require continuous treatment to remain fully effective. Reversing their effects takes a similarly long time. Thus, there is an unfulfilled need for an on-demand, reversible approach.

Following ejaculation, sperm begin to vigorously beat their tails. This enables them to swim through the female reproductive tract and fertilize the egg. An enzyme called soluble adenylyl cyclase (sAC) is needed to trigger this behavior. Male mice engineered to lack sAC are infertile but have few other differences from normal mice. Men who have naturally occurring mutations that inactivate sAC are also infertile.

An NIH-funded team of researchers, led by Drs. Jochen Buck and Lonny Levin at Weill Cornell Medicine, developed a compound called TDI-11861 that binds and inhibits sAC. They tested its effects on sperm function and fertility. Their findings appeared in [Nature Communications](#) on February 14, 2023.

A variety of tests in mice didn't identify any potential safety issues with TDI-11861. The team then treated male mice with a single dose of TDI-11861 before allowing them to mate with females. The treated mice showed no differences in mating behavior from untreated mice. But the sperm from treated mice lost the ability to move on their own. Sperm remained immobile after being deposited in the female reproductive tract.

When male mice treated with TDI-11861 were paired with females, none of the females became pregnant. This contraceptive effect was observed for up to two and a half hours after treatment. In contrast, male mice treated with a control compound impregnated females 30% of the time. The effect of the treatment wore off with time, and by 24 hours after treatment, fertility had recovered.

completely.

These findings suggest that an sAC inhibitor could be developed into a safe, temporary contraceptive drug for men. “The team is already working on making sAC inhibitors better suited for use in humans,” Levin says.

However, more work is still needed before human clinical trials could begin. Several challenges remain before a drug could get approved for people to use.

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