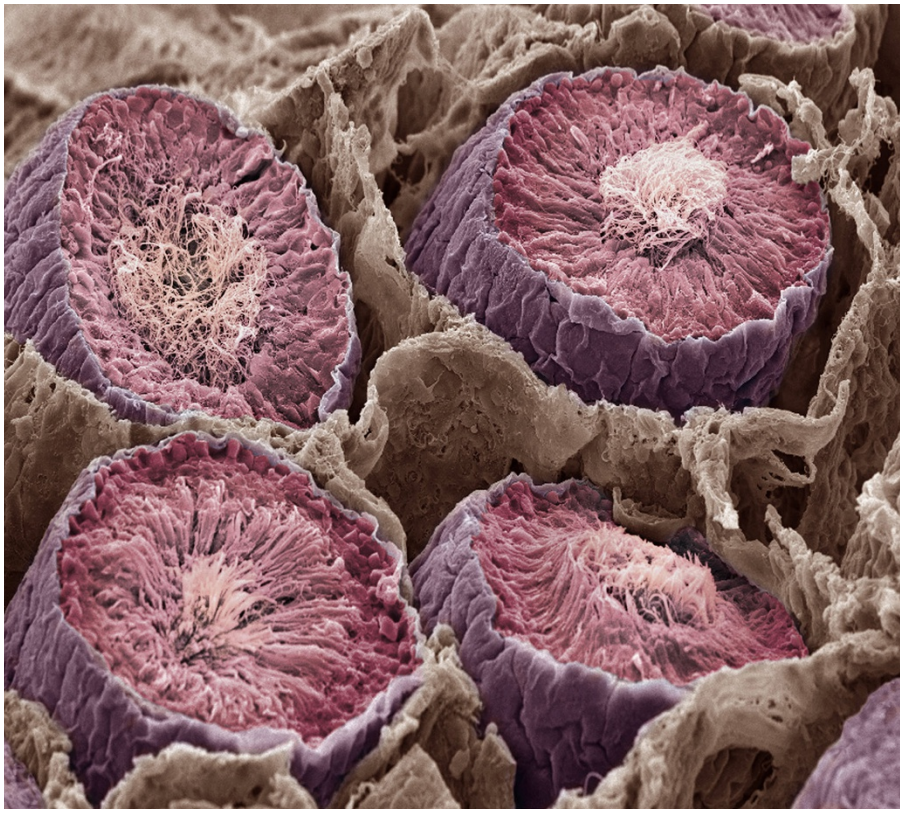

Steve Gschmeissner/Science Source

Tubular trappings: Seminiferous tubules with sperm tails clustered in the center and Sertoli cells on the outer edge of each tube.

interested in understanding immune privilege in the testes is also relatively small. But that may be changing, albeit slowly. A September 2016 workshop sponsored by the US National Institutes of Health (NIH) on immune privilege seems to indicate increased attention to the topic. Verma and Dufour, who were introduced to each other at the meeting, both say that this was the first such meeting they had attended.

As Routy indicated with his work on cancer, a major consideration that scientists are faced with is a practical dilemma: how can the benefit of immune privilege be maintained while also allowing the immune system to respond to infection in the testes? Except when viruses like Zika and HIV take refuge in the testes, immune privilege is a necessary benefit that protects sperm cells, and so targeting only the virus will be key. "What you don't want is for immune cells to break immune privilege," says Michael Diamond, an infectious disease researcher at Washington University in St. Louis. He adds that allowing the entrance of viruses into a testis is also not ideal because clearing virus in the absence of regular immune mechanisms is difficult.

A vaccine-based approach, in which the body is inoculated and gets rid of virus before it has a chance to enter the testes, may be a good solution. Diamond, for instance, is testing a Zika vaccine that was developed by collaborators at the University of Texas Medical Branch in Galveston, Texas. In September last year, his team reported that the live-attenuated vaccine was able to protect male mice from Zika-related damage to the testes[13]. Female mice that were vaccinated, mated with wild-type male mice, and then infected with Zika were monitored for Zika transmission to the fetus. A single dose of the vaccine reduced the viral load in 70% of the placenta and fetal brain samples to below detectable levels. Another group, based in Canada, has been testing a DNA-based vaccine for Zika and similarly found that mice were able to make antibodies in response to the vaccine, which prevented damage to mouse testes[14].

There may be room for pharmacological interventions, too. Nathan Cherrington, a pharmacologist at the University of Arizona, was also an attendee of the September NIH meeting, and in April last year, he was awarded a nearly $300,000 grant by the NIH to explore how drug molecules could circumvent the blood–testis barrier. His group has characterized how a family of drugs used against HIV and other viruses, the nucleoside analogs, cross the blood–testis barrier. The group has found several specific nucleoside transporter proteins that allow these compounds to go from the blood into epithelial cells lining the epididymis [15]. Beyond HIV, which can hide in the testes, Zika is "exactly the type of situation where our work could help," Cherrington says. "We know that sexual transmission happens," he says, so it's a matter of figuring out how to get compounds to infiltrate the testes.

No matter the route, researchers agree that an abundance of caution is necessary. "Messing with the immune system, especially when you don't understand it, is kind of a scary thing," Dufour says. The lack of constant headlines about Zika and Ebola have some scientists worrying that enthusiasm for conducting research into immune privilege could diminish. But the key to curing disease, whether Zika or HIV, will be to know how the testes preserve their unique position in the human body, according to Cherrington, adding, "If we can't understand the complexities of the testis, viruses and cancers that survive in that reservoir will continue to thwart our best efforts."

Shraddha Chakradhar is* Nature Medicine's *associate news editor in Boston.

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Correction

In the December 2017 issue, the article "Drugs that made headlines in 2017" (*Nat. Med.* **23**, 1392–1393, 2017) inaccurately described the mechanism of the RNAi drug fitusiran. The drug does not fix defective RNA code or a defective protein, but rather suppresses the production of a functional protein. The error has been corrected in the HTML and PDF versions of the article as of 9 January 2018.