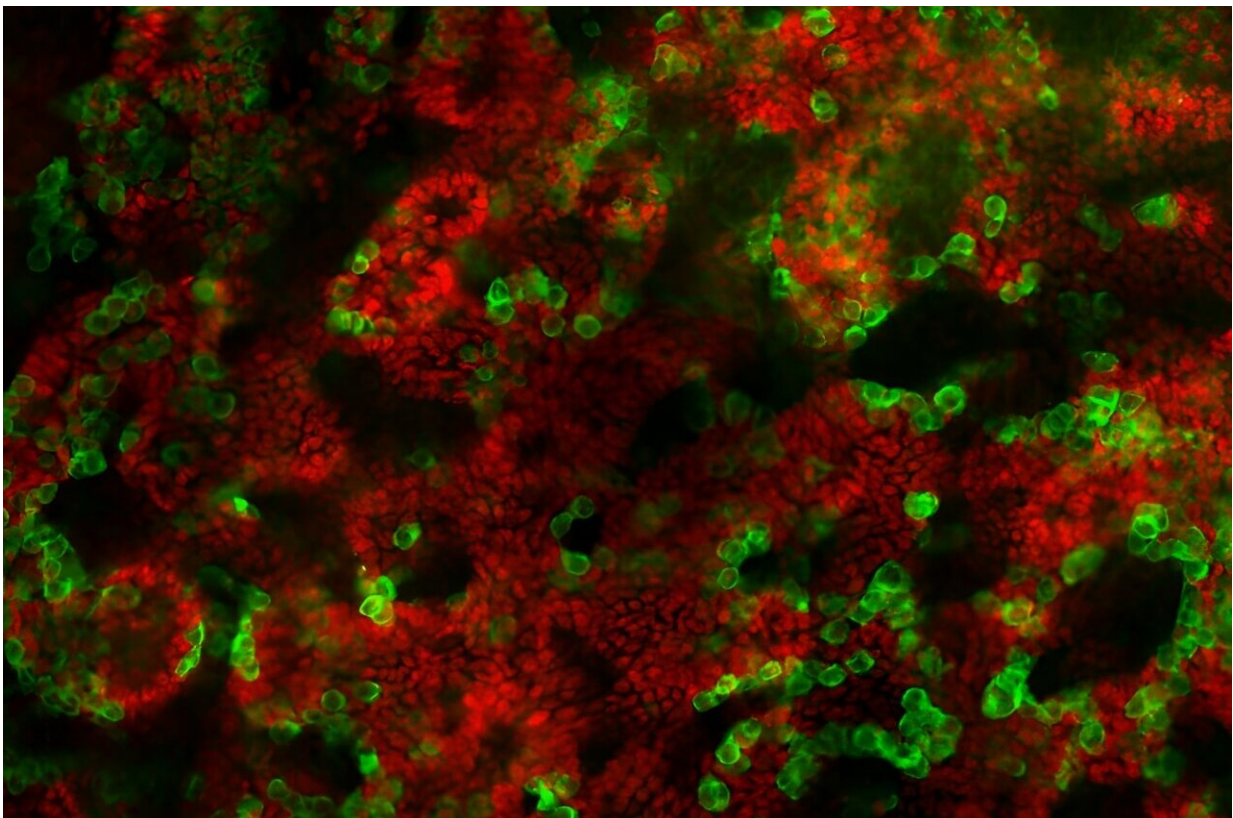


Researchers create 'laboratory testicles,' organoids that could advance male infertility research

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Testicular organoids generated from mice pups and incubated in a dish for 21 days. Sertoli cells, which are the cells responsible for the formation of the tubules in the testicle, appear in red and germ cells, which will produce the sperm cells, appear in green. Germ cells always stay close proximity to Sertoli cells as they support them during the formation of sperm cells. Credit: Aviya Stopel

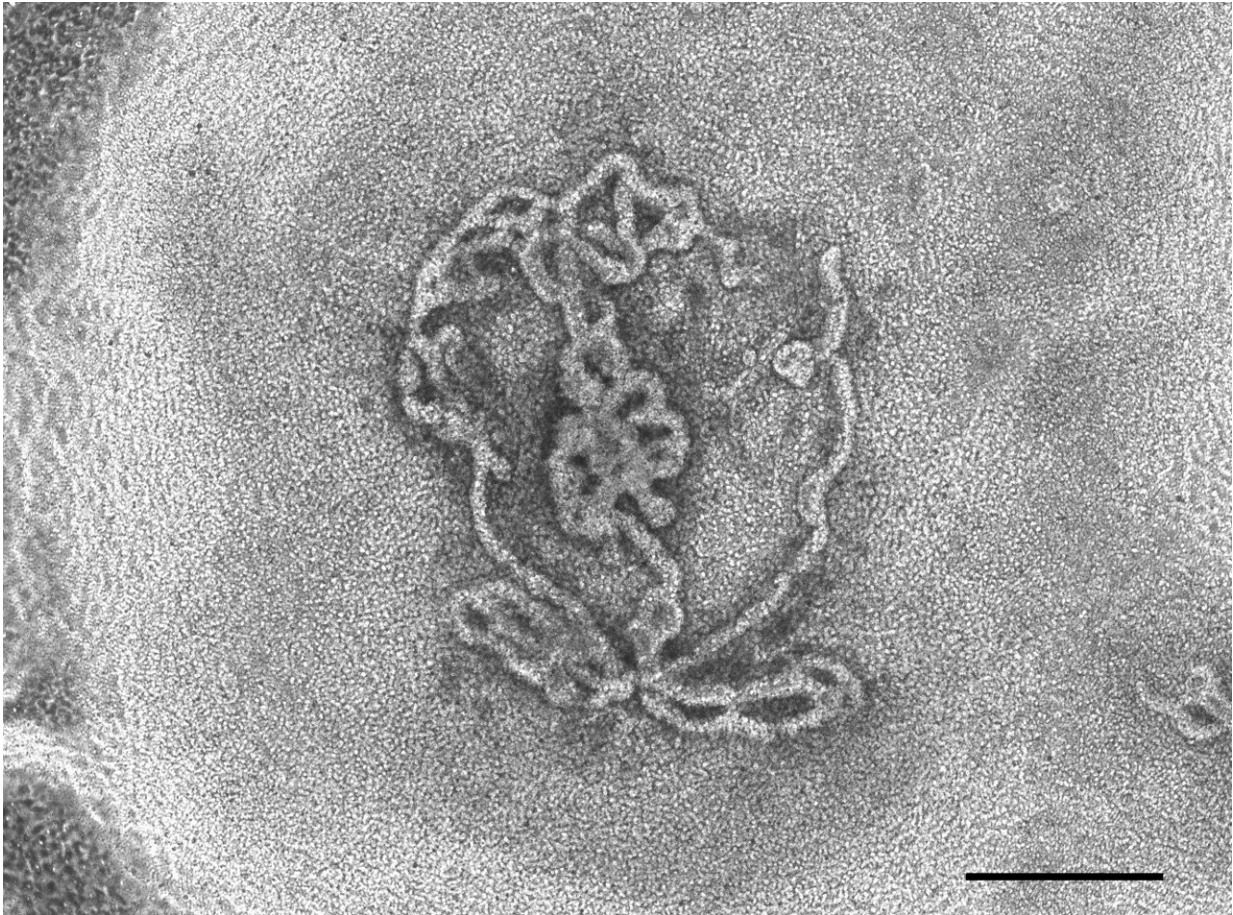
The testis is responsible for sperm production and testosterone synthesis. Abnormalities in testis development and function lead to disorders of sex development (DSD) and male infertility. Currently, no in vitro system exists for modeling the testis.

Dr. Nitzan Gonen, a researcher specializing in the process of fetal sex determination, together with research students Aviya Stopel, Cheli Lev, and Stav Dahari, has succeeded in creating "laboratory testicles" that may significantly advance understanding of the mechanisms involved in sex determination and provide solutions for male infertility, which affects 1 in 12 men worldwide.

The artificial testicles produced in Dr. Gonen's lab at the Goodman Faculty of Life Sciences and the Institute of Nanotechnology and Advanced Materials at Bar-Ilan University are testis organoids—tiny, [artificial organs](#) produced from real mouse testis. The development of organoids has greatly advanced in the last decade with the realization that two-dimensional cellular samples in vitro cannot mimic the behavior of an entire organ.

Today, organoids of the brain, kidneys, intestines, and other organs have already been produced. The testicular organoids created by Gonen's group closely simulate a natural testicle.

The artificial testicles were cultured from immature testicular cells sampled from neonatal mice. The research team realized the procedure was a success when they identified tubule-like structures and cellular organization highly resembling that of the in vivo testis. These tubular structures parallel the multiple seminiferous tubules present in the natural testicle, where the sperm is produced.



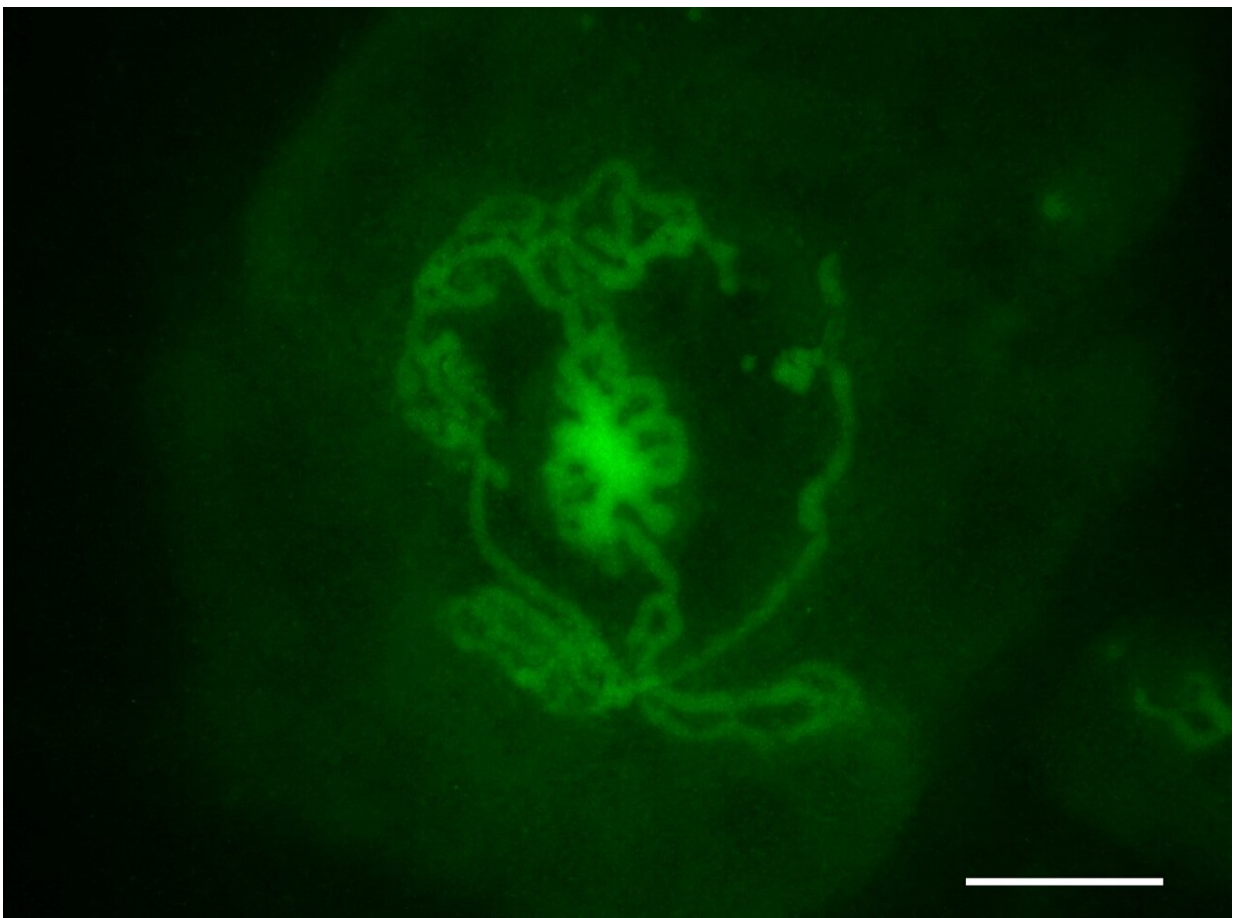
A bright field image of a testicular organoid created from mouse embryos and incubated in a dish for 14 days. The tubular structures formed in the dish are clearly visible. Credit: Cheli Lev

The organoids were successfully cultured in vitro for nine weeks. This is considered a long period of time and can, theoretically, be enough time to complete the process of [sperm production](#) and hormone secretion. In mice, this takes 34 days, so the relatively long lifespan of the organoids may allow these processes to occur in vitro.

Dr. Gonen doesn't yet know if the existing model will actually produce

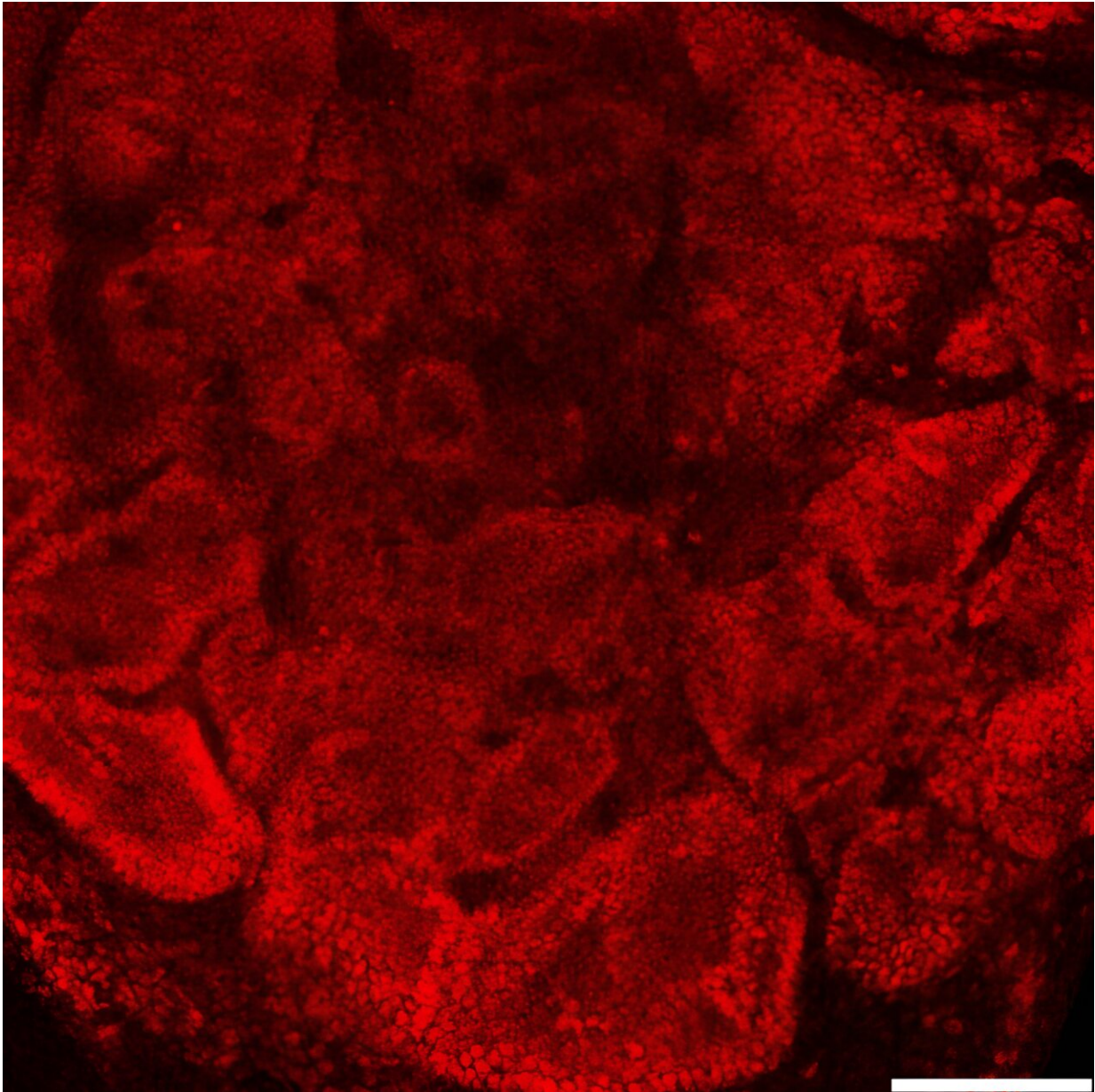
[sperm cells](#), but the laboratory team has already noticed signs of the beginning of meiosis, a process in which gametes are produced. Gametes are reproductive cells, in this case, sperm cells with half the number of chromosomes as in a normal cell, that "await" the completion of the other half from another gamete, in this case, an egg, upon fertilization.

Organoids usually resemble organs in the embryonic stage. In this case, the researchers created conditions that allowed the [organoid](#) to mature in the laboratory and showed that even testicles grown from embryonic cells can develop and grow clear sperm tubes. The team was unsuccessful in its attempt to grow organoids from adult mice testis.



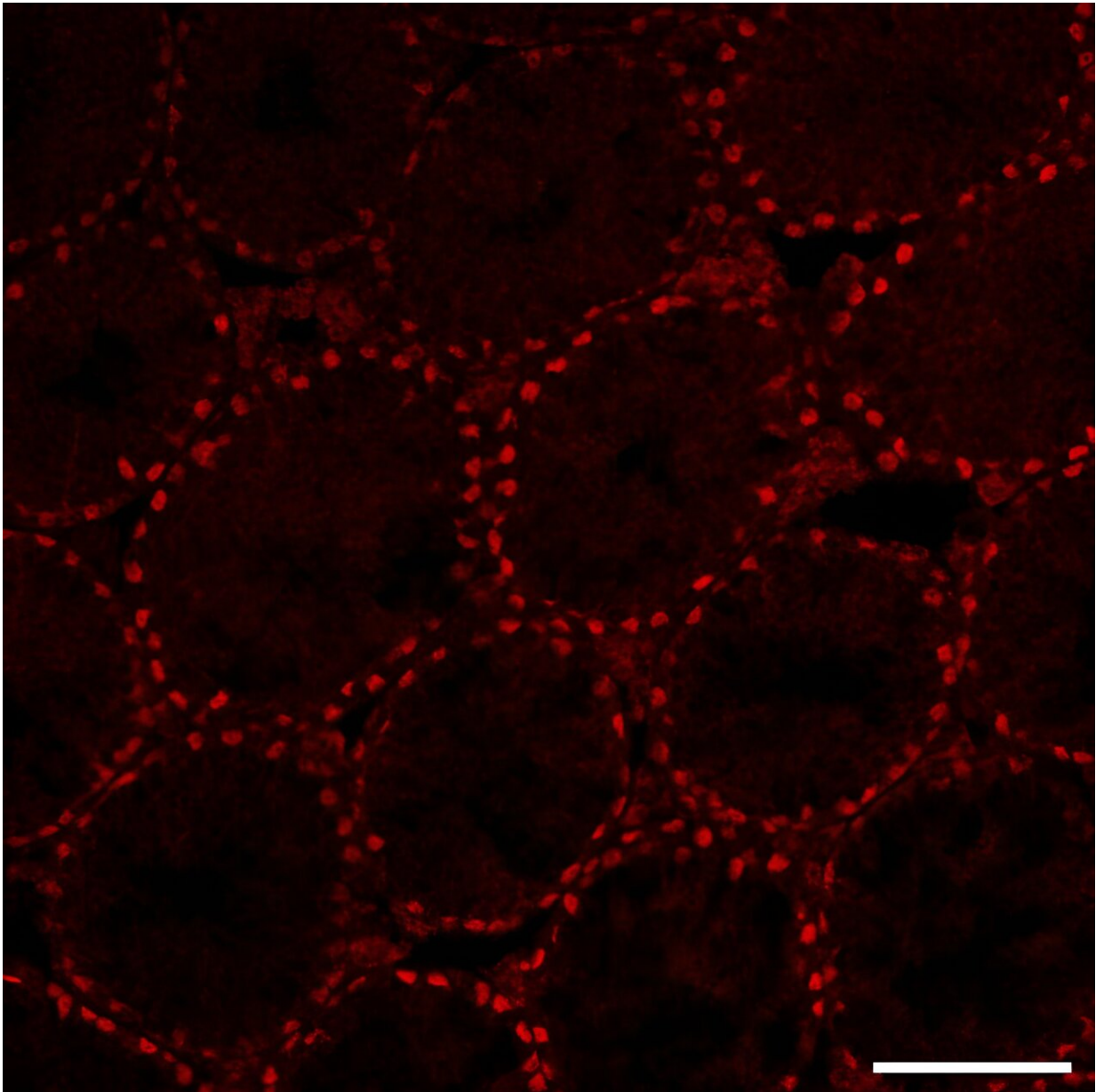
A fluorescent image of a testicular organoid created from mouse embryos and

incubated in a dish for 14 days. The tubular structures formed in the dish are clearly visible. Marked in green are Sertoli cells, which are the cells responsible for the formation of the tubules in the testicle and, indeed, create the tubules in the dish. Credit: Cheli Lev



Testicular organoids generated from mice pups and incubated in a dish for 21

days. Labeled in red are Sertoli cells, which are the cells responsible for the formation of the tubules in the testicle and, indeed, create the tubules inside the organoid—as in a real testicle. Credit: Aviya Stopel



Real testes of 28-day-old mice. The Sertoli cells, which are the cells responsible for the formation of the tubules in the testicle, are marked in red, and the

unmarked tubules of the testicle in which the sperm cells are produced are clearly seen. Credit: Aviya Stopel

"Artificial testicles are a promising model for basic research on [testicle](#) development and function, which can be translated into therapeutic applications for disorders of sexual development and infertility," explains Dr. Gonen.

In the future, she plans to produce organoids using human samples. A testis produced from human cells, for example, could help children being treated for cancer, which may impair their ability to produce functional sperm. As children are too young to produce their own sperm, these samples can be frozen and used in the future to have children. Gonen's vision is to grow testes organoids from biopsies of children with cancer and hopefully grow fertile sperm in vitro.

The findings of this study were recently published in the [International Journal of Biological Sciences](#).

More information: Aviya Stopel et al, Towards a "Testis in a Dish": Generation of Mouse Testicular Organoids that Recapitulate Testis Structure and Expression Profiles, *International Journal of Biological Sciences* (2024). [DOI: 10.7150/ijbs.89480](https://doi.org/10.7150/ijbs.89480)

Provided by Bar-Ilan University

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