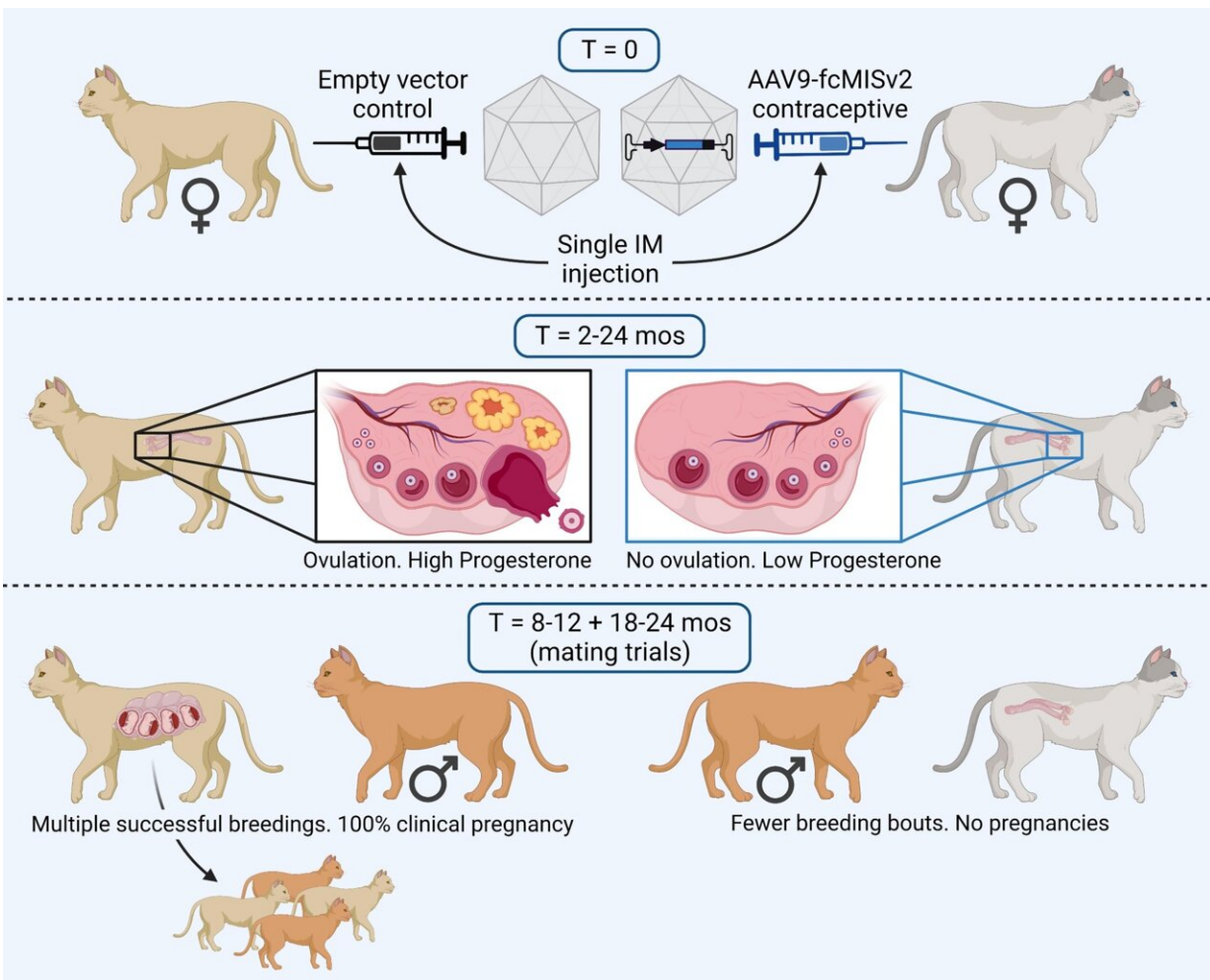


# Gene therapy produces long-term contraception in female domestic cats

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None of the six adult female cats that received the contraceptive (right) conceived during the two four-months long mating trials while the three control females (left) all delivered kittens. Treated females did not ovulate and presented lower levels of progesterone than controls. Credit: Philippe Godin and Marie-Charlotte Meinsohn. Created with BioRender.com

Currently there are no contraceptives capable of producing permanent sterilization in companion animals. Spaying, the surgical removal of the ovaries and uterus, is the most widely used strategy to control unwanted reproduction in female cats.

For the first time, researchers at Massachusetts General Hospital (MGH), a founding member of Mass General Brigham (MGB), and their collaborators have demonstrated that a single dose of anti-müllerian hormone (AMH) gene [therapy](#) can induce long-term contraception in the [domestic cat](#), potentially providing a safe and effective alternative to surgical spaying. The research is published in *Nature Communications*.

During previous research to evaluate AMH (also known as müllerian inhibiting substance, or MIS) as a method to protect [ovarian reserve](#) in women undergoing chemotherapy, senior author David Pépin, Ph.D., Associate Director of the Pediatric Surgical Research Laboratories at Massachusetts General Hospital, and an Associate Professor at Harvard Medical School discovered that raising the level of AMH beyond a certain threshold suppressed the growth of ovarian follicles, effectively preventing ovulation and conception.

"AMH is a naturally occurring non-steroidal hormone produced by the ovaries in human females and other mammals, and in the testes in males," says Patricia K. Donahoe, MD, a co-author of this study and the Director of Pediatric Surgical Research Laboratories and Chief Emerita of Pediatric Surgical Services at Massachusetts General Hospital.

In 2017, Pépin and his collaborators were the first to publish the contraceptive potential of AMH in rodents.

The team then turned their attention to felines. To raise AMH levels in

female domestic cats, the researchers created an adeno-associated viral (AAV) gene therapy vector with a slightly altered version of the feline AMH gene. Human therapies using similar AAV vectors to deliver various therapeutic genes have proven to be safe and effective and have been approved by the FDA.

"A single injection of the gene therapy vector causes the cat's muscles to produce AMH, which is normally only produced in the ovaries, and raises the overall level of AMH about 100 times higher than normal," says Pépin.

The researchers treated six female cats with the gene therapy at two different doses, and three cats served as controls. A male cat was brought into the female colony for two, four-month-long mating trials. The researchers followed the female cats for more than two years, assessing the effect of the treatment on reproductive hormones, ovarian cycles, and fertility.

All the control cats produced kittens, but none of the cats treated with the gene therapy got pregnant. Suppressing ovarian follicle development and ovulation did not affect important hormones such as estrogen. There were no adverse effects observed in any of the treated [female cats](#), demonstrating that at the doses tested, the gene therapy was safe and well tolerated.

"The treatment maintained high AMH levels for over two years, and we're confident that those contraceptive levels will be sustained in the animals for much longer," says veterinarian Philippe Godin, DVM, Ph.D., co-author and research fellow at MGH. Additional studies in a larger number of cats are needed to confirm these promising findings, he adds.

"A non-surgical sterilant for community and [companion animals](#) is long

overdue and will transform [animal welfare](#)," said Gary K. Michelson, MD, founder and co-chair of Michelson Philanthropies and the Michelson Found Animals Foundation. "This breakthrough discovery is a major milestone in our quest to provide pet owners with an alternative to surgical spay and neuter."

"This technology may be a little ahead of its time," acknowledges Pépin, noting that the infrastructure needed to produce enough doses to sterilize millions of cats via gene therapy does not yet exist. "Our goal is to show that safe and effective permanent contraception in companion animals can be achieved using gene therapy. And we hope that as the manufacturing capability of producing viral vectors increases with the rise of [gene therapy](#) in humans, delivering this contraceptive in the field to control unowned outdoor cat populations will become feasible."

Co-authors include Lindsey M. Vansandt, Marie-Charlotte Meinsohn, Guangping Gao, Dan Wang, and William F. Swanson.

**More information:** William Swanson, Durable contraception in the female domestic cat using viral-vectored delivery of a feline anti-Müllerian hormone transgene, *Nature Communications* (2023). [DOI: 10.1038/s41467-023-38721-0](#).  
[www.nature.com/articles/s41467-023-38721-0](http://www.nature.com/articles/s41467-023-38721-0)

Provided by Massachusetts General Hospital

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