‘Here, CRISPR critter’: How to gene edit a hypo-allergenic cat

I pity the 15 percent of the human population that cannot live with a cat, due to allergy. I’ve seen it happen, a guest’s face blowing up. My best friend Wendy can visit here, where cats outnumber people two-to-one, only by megadosing on antihistamines and heading to the porch to breathe periodically. Even with that she’s good for only a day or two.

But CRISPR gene editing may come to the rescue, someday.

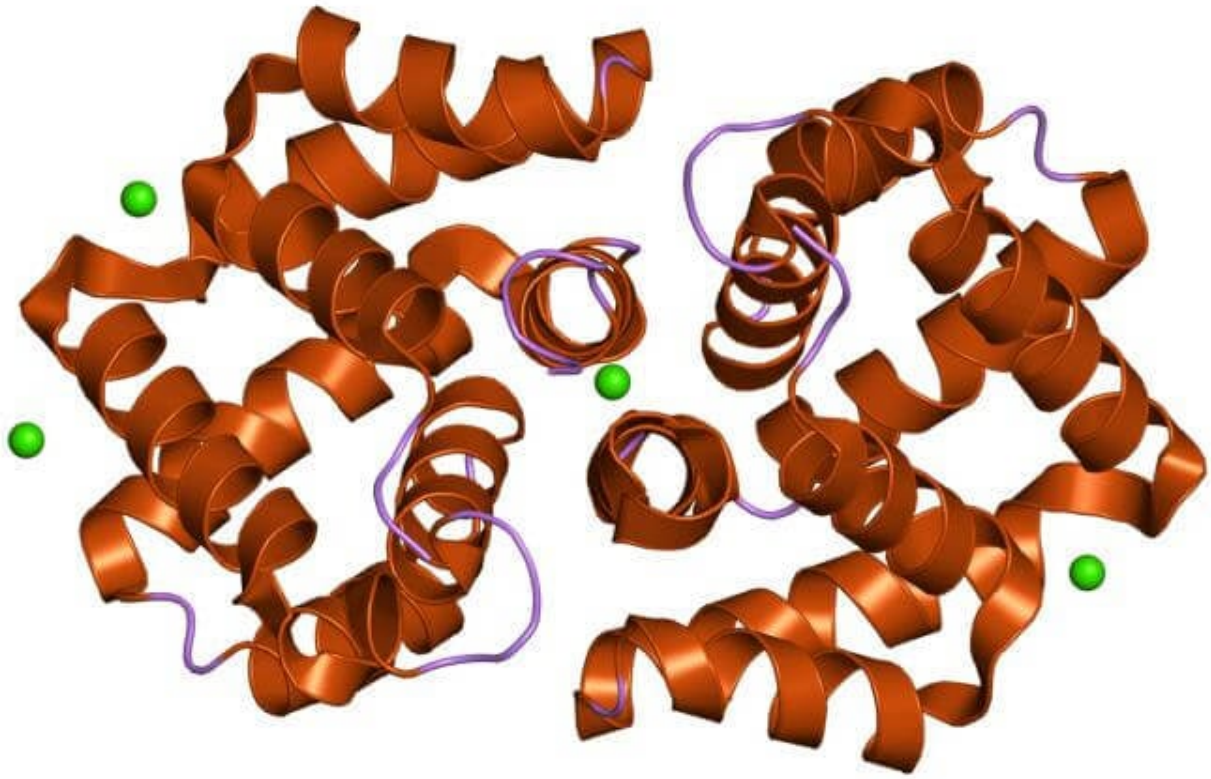
Snip out the gene that encodes a protein called Fel d 1, and the kitty can no longer make a hapless human’s eyes and nose run and bronchioles constrict in an asthma attack. That’s what Nicole F. Brackett and a team from InBio have done in cat cells. Their work was just published in The CRISPR Journal. (If googling makes this news seems recycled, it’s because an abstract appeared just before the world shut down in early 2020.)

CRISPR is a tool that can remove, replace, or add a selected bit of DNA to a chromosome. To counter cat allergy, CRISPR would delete the genes that encode the offending allergen.

Targeting Fel d 1

Fel d 1 is a protein consisting of two copies each of two types of chains, which two genes, *CH1* and *CH2*, encode. Because the genes are within 10,000 DNA building blocks of each other on cat chromosome E2, which is pretty close, CRISPR could snip them out, like deleting from “blocks” to “chromosome” in this sentence.

With its four-part structure, Fel d 1 resembles hemoglobin, the protein that carries oxygen in blood. But its function in cats isn’t known. It might play a role in chemical communication, immune regulation, or keeping the skin infection-free.



Fel d 1 protein structure. Credit: HandWiki

The protein is a “secretoglobin,” and it pours out from glands in the animal’s skin, mouth, eyes, and anus. A feline doing her toilette smears the offending proteins throughout the fur, dispersing them along with dander (dried skin cells). “Natural levels of the allergen vary significantly between cats (>100-fold) and even within the same cat,” the researchers write.

In the new study, they collected discarded testes, ovaries, and uteri from 50 cats from spay and neuter clinics. Comparing the DNA sequence of the two allergen genes to their counterparts in several “wild felids” led to some intriguing evolutionary inferences. The other felines included the cougar, Chinese mountain cat, the wildcat *Felis silvestris* (the inspiration for the eponymous cartoon character?), the black-footed cat, leopard cat, fishing cat, Iberian lynx, African lion, and bengal tiger. Oh my!

Similar proteins are also found in rabbits, mice, and notably the treacherous slow loris. This southeast

Asian primate secretes the protein from its elbow, licks it to mix it with saliva into a venom, and when the animal bites, sends the unfortunate victim into anaphylactic shock.

The DNA sequences of the genes were very varied among the felids, which means, in genetics lingo, a lack of evolutionary conservation. That is, whatever the gene does, it isn't terribly important, or natural selection would have retained very similar DNA sequences across species. So deleting the gene shouldn't present a problem to an edited cat.

Using CRISPR to knock out the genes worked with an efficiency of up to 55% – not bad – and didn't insert DNA willy nilly into other parts of the genome, a major concern. "Our data indicate that Fel d 1 is both a rational and viable candidate for gene deletion, which may profoundly benefit cat allergy sufferers by removing the major allergen at the source," the researchers conclude.

The change would need to be made at the fertilized ovum stage so that all an animal's cells would lack the two genes. But create a few engineered cats, breed them, and presto, a non-allergy-inducing feline line should emerge. Then people can volunteer to breathe around the gene-edited felines to test it, like people in the COVID vaccine trials venturing into their communities to test protection against the virus.

Other ways to combat cat allergies (other than removing the cat)

Researchers have tried to disable the cat allergen before. Investigators from Nestlé Purina PetCare Global Resources described in a paper in Frontiers in Veterinary Science in 2020 coating dry cat food with desiccated chicken egg yolk that naturally contains antibodies against the cat protein. As kitty chews, the antibodies latch onto the allergen in their spit, rendering it unable to induce an attack in a human. The study followed 42 cats for 26 weeks, and analyzed anything that could be analyzed, and the treated animals fared as well as the controls, who got regular chow. And the product may have already been commercialized – this ad for LiveClear sounds like the chicken cure.

Another solution is to buy something from Amazon, such as this allergen spray. It is, of course, "all natural." The main ingredient is "sodium sesquicarbonate," which is a combo of sodium bicarbonate and sodium carbonate, with a sprinkling of phosphate salts. And it's good on doggie dander too. The product is to be sprayed on clothing and other surfaces, not cats.

Or, try the mysterious elixir Curex. *"Love your cat, but not your allergies? Say goodbye to cat allergies for good with Curex"* reads the ad, complete with testimonials. This immunotherapy is taken under the tongue, and supplies can be delivered four times a year, costing less than the monthly $95. But what, exactly, is Curex? According to the company website it is based on clinical studies "not reviewed by FDA" and is apparently useful for a variety of conditions. The photos of pretty trees suggest that Curex is pollen of some sort, which means that they might have named it Lorax after the Dr. Seuss character that "speaks for the trees." "Healthcare entrepreneurs and allergy clinicians" run the company. A three-dollar-a-day dose of pollen is making someone money.

Until CRISPR cat breeds are available and if you don’t want to splurge on products, here is some basic advice from second nature, a company that makes air filters:

Clean the house
Groom the cat
Change the air filters
Make sure the cat is healthy

Diabetes and obesity cause the cat to shed more dander. And don't forget stress. Ever notice that your cat suddenly springs white flakes when visiting the vet?

I'm signing Wendy up for the first clinical trial so I can give her a GMC – a genetically modified cat.

Ricki Lewis has a PhD in genetics and is a science writer and author of several human genetics books. She is an adjunct professor for the Alden March Bioethics Institute at Albany Medical College. Follow her at her website or Twitter @rickilewis

A version of this article was originally posted at PLOS and has been reposted here with permission. PLOS can be found on Twitter @PLOS