

A company's shady past and questionable science raise doubts on their promises of a \$4,000 hypoallergenic cat.

By Kerry Grens

Felis Enigmaticus

On a brilliant fall morning in west Los Angeles, cars zoom down Olympic Avenue, west toward the posh boutiques of Santa Monica, and east toward the hills of Westwood. Nestled between two midrise buildings on the corner of Olympic and Purdue, a sleek tower of reflected glass rises above the traffic. Inside, Suite 200 is the registered home of Allerca.

Knowing the address gives little insight into the secretive company that claims to have bred the "world's first scientifically-proven hypoallergenic cats." There are no laboratories or scientists, no cats or kittens on the second floor of 11400 Olympic Avenue. Suite 200 is a shared office, leased to a number of companies to use for meetings and telephone answering services.

Then-Allerca spokesperson Steven May doesn't meet me at 11400 Olympic. Instead, I interview him at a café near the University of California, Los Angeles, in October. "There's a reason why you can't find the address," says May, now president of the company. May explains that the company's details are kept confiden-

tial to protect employees from people who "have very personal feelings about what is happening" when it comes to animal testing and science. The company claims it has found and bred cats that possess a gene for the major cat allergen - a protein called Fel d 1 - that is modified so that humans do not have an allergic response to the cats.

Allerca's confidentiality is selective, however. The company has been making the rounds of television, magazines, and newspapers advertising their low-allergen cats. *Time* magazine honored Allerca's discovery as one of the Best Inventions of 2006. May speaks excitedly about the debut of the first litter, "definitely in the spring of 2007." By then three or four kittens will be ready for adoption. They are a modest start to satisfying what May says is an "overwhelming" response by people with allergies seeking a cat - despite the one-year wait and \$4,000 price tag. "It's a little pricey," May says. "However, if you break it down over the years, over 15 years that someone's been deprived, it's priceless." ▶

Theoretically, there could be many "someones." Cat allergies are some of the most common; in a survey of 10,000 Americans, 17% reacted to a cat-allergen skin test.¹ Fel d 1, which is unique to cats, is responsible for most people's allergic reactions to cats.² Still, little is known about

GENETIC FEASIBILITY, CLINICAL CONCERNS

In June 2006 an Allerca press release announced that customers could begin reserving their hypoallergenic cats. Less than a year earlier Allerca's scientists (whose identities have been kept under

mented in the literature. "Every Allerca cat had those," Brooks says. He would not disclose the differences, saying that the information is proprietary. He did not sample the actual cats, nor did he do any work with Fel d 1 to see how changes in the sequence might affect the hypoal-

There's a lot of skepticism in the academic community about whether or not these cats are hypoallergenic.

—Martin Chapman

the protein and Allerca's findings could lend insight into the unknown function of Fel d 1 in cats, says Leslie Lyons, assistant professor at the UC-Davis School of Veterinary Medicine. "We're interested in pursuing this stuff a little farther," she says, but "they don't present enough data to say how they've done it."

Lyons isn't the only one scratching her head over the lack of peer review of Allerca's claims. "There's a lot of skepticism in the academic community about whether or not these cats are hypoallergenic," says Martin Chapman, a former professor of Medicine and Microbiology at the University of Virginia and the founder of Indoor Biotechnologies, a company that designs allergy tests. "We've not come across any documented scientific study that this is a real phenomenon."

Compounding the scientific skepticism are the many failed and sometimes-fraudulent business endeavors of Allerca's founder and chairman, a convicted criminal named Simon Brodie. Hot air balloons, glow-in-the-dark deer, the world's most powerful computer, and knockout, allergen-free cats have all collapsed despite Brodie's public optimism and legal issues often trail behind these entrepreneurial efforts.

wraps) stumbled upon a family of hypoallergenic cats while testing out the company's newly developed genetic assay, says Brodie. He explains that the researchers were screening cats randomly across the country for the initial project to develop allergen-free cats using RNAi. "The test was initially to look for the *fel d 1* gene," Brodie says, "and it was not found positive for the mutant cats. We did additional work ... and found the molecular weight of the protein was different in the mutant cats." Brodie declines to say more about how the assay was developed or precisely what it is designed to detect in the cats.

Allerca hired Microbac, a commercial laboratory in Tennessee, to compare the *fel d 1* sequences between Allerca's cats and control cats. Robert Brooks, then the biotechnology laboratory manager at Microbac, conducted the analysis in May, June, and July 2006. Allerca provided Brooks with cheek swabs from several parent cats, and later from several kittens. Brooks used the DNA to compare amino acid sequences between Allerca and control cats.

Fel d 1 comprises two subunits, each encoded by a different gene.³ In chain 2 Brooks found several amino-acid differences in Fel d 1 between Allerca cats and control cats, which have not been docu-

menting the literature. "I don't have anything to do with cats themselves," Brooks says. "There are definite differences [in their protein]; what they mean, I can't tell you."

Brodie says Allerca's researchers (not Microbac's) discovered that these differences translate into cats that don't elicit allergic responses in people. Allerca's team also found the trait was passed along to offspring, and began breeding the hypoallergenic cats in the fall of 2005 to "allow allergic consumers to enjoy the love and companionship of a pet without the cost, inconvenience, risk, and limited effectiveness of current feline allergy treatments."

Such a finding is feasible, says Lyons. There could be enough variation in the *fel d 1* gene in the domestic cat population (about 30 million in the United States) to allow for a hypoallergenic mutation to exist, she says. Others have shown it's feasible at the molecular level as well. Modifying a recombinant Fel d 1 to destabilize the protein can result in hypoallergenicity. Hans Grönlund at the Karolinska Institutet Hospital in Stockholm and his colleagues showed that modifying the three-dimensional structure of Fel d 1 could reduce its IgE antibody-binding capacity 400 to 900 times that of an unaltered Fel d 1.⁴ Grönlund writes in

an E-mail that it's impossible to speculate on what mutations might be responsible for the Allerca cats' hypoallergenicity, though "probably a deletion or several point mutations would be needed."

Lyons says that demonstrating a mutant *fel d 1* gene in certain cats would be easy, as several studies have described the gene and protein. Characterizing the way humans will respond to the animals, and showing that they really are hypoallergenic, would be more difficult. Lyons says she doesn't have many doubts as to whether Allerca could have found cats with a mutant *Fel d 1*. "For me, the question is, how are they proving it?"

That's where Sheldon Spector comes in. An allergist with the California Allergy and Asthma Group in Los Angeles, he conducted Allerca's human exposure trial earlier in the year. (Spector declined to be interviewed until after his second round of trials was complete, which an Allerca spokesperson estimated would be in late November. As of press time, Spector had not responded to further requests.) For his first trials Spector used three rooms, each randomly housing a hypoallergenic cat, a regular cat, or a stuffed animal. Volunteers who had been diagnosed with allergies entered the room blindfolded and reported their allergic responses.

Spector found the hypoallergenic cats did not elicit an allergic response, though he has not published the results in a peer-reviewed journal.

Using this experimental design is not always a reliable predictor for hypoallergenicity, says Andy Saxon at the UCLA Medical Center: "It's a mess using cat rooms; they're totally uncontrolled." Saxon says several problems exist with cat rooms: The amount of allergen a person is exposed to is not controlled, and a person's response (even to the same amount of allergen) can vary with each exposure. Even Spector told *The New York Times* in October that he would not recommend people buy an ▶

What the data say

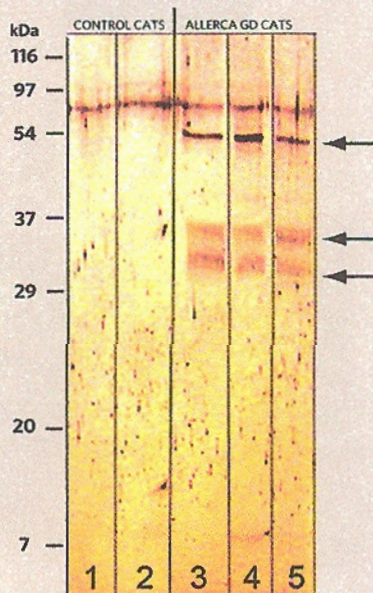
The only data Allerca has released to the public are pictures of a Western blot and a DNA gel, posted on its Web site, and a summary of a DNA analysis conducted by Microbac, a company Allerca contracted. Martin Chapman, founder of Indoor Biotechnologies, a Virginia company that develops environmental tests to measure the presence of household allergens, says some of the data published on the Web site don't seem to add up.

One image shows the results of gel electrophoresis of PCR products using primers for *fel d 1*. Arrows point to four lanes derived from control cats, each with a band at 1.7 kb, which the image describes as denoting *fel d 1*. Six other lanes, derived from Allerca's hypoallergenic cats, show no bands at 1.7 kb. Two genes encode the proteins of each subunit.³⁷ The gel does not indicate the subunit gene for which the primers were designed, although the gene for chain 1 of *Fel d 1* is 1.7 kb (GenBank accession number X62477). Chain 2 is 2.4 kb (GenBank accession number X62478). Microbac's genetic analysis concludes, however, that mutations found in chain 1 "are documented in the literature as naturally occurring" and that "chain 1 is not responsible for the hypoallergenic effects of the Allerca cats." The company found that mutations in chain 2 differed for Allerca and control cats, but the company does not show data about chain 2 on its website.

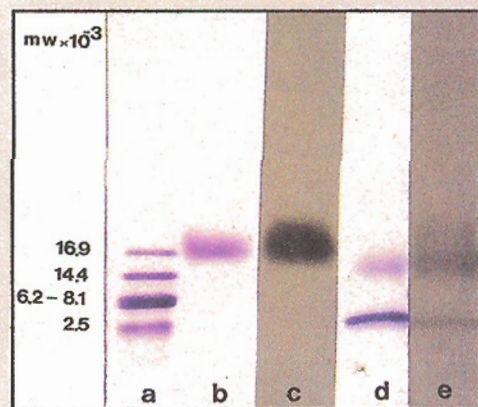
Chapman takes less issue with the DNA gel than with Allerca's Western blot. Chapman explains that when *Fel d 1* is run on gels, the molecular weight normally shows up at about 18 kDa, reflecting the two subunits of the molecule.⁸

Under reducing conditions two bands appear, one at 14 kDa and another at 4 kDa.^{8,9} However, control cats on Allerca's gel show no *Fel d 1* bands at 18, 14, or 4 kDa. Rather, the hypoallergenic cats show bands at around 35 and 33 kDa, which are closer to the molecular weight of the native protein.

"Even if it's a labeling issue," Chapman says, "the bands don't seem to match up." Why would control cats lack any bands for the protein and why do the hypoallergenic cats have *Fel d 1* bands at a higher molecular weight? "The quality of this blot is just awful," Chapman says. "If that's an example of their science, it's just not very well worked out."



Comparison between Allerca's Western blot and a typical Western blot for *Fel d 1*. Allerca's control cats (lanes 1 and 2) lack any bands for *Fel d 1*, which is 18 kDa under nonreducing conditions (lanes B and C), and two bands at 14 and 4 kDa under reducing conditions (lanes D and E).⁸



Allerca cat, because his study was not definitive and people can still react to other allergens that cats produce.

Sensitization also plays a role. "If you eliminate only part of the protein, you may develop sensitization to a different part," says Fernando Martinez, director of the Arizona Respiratory Center. Martinez says that the number of epitopes humans respond to on Fel d 1 is not well known, and sensitization to particular areas of the protein has not been explored exhaustively. "I would argue that there are essentially unlimited number of epitopes," writes Grönlund. As the oldest generation of Allerca cats is just three years old, there is no evidence that they will maintain their hypoallergenicity for pet owners over a lifetime. The lack of a published peer-

reviewed trial concerns a skeptical Martinez. "It's very worrisome that before there's any demonstration of a true effect, we start giving these [cats] to people," he says.

ALLERCA'S HISTORY

In 1992, Brodie was a young, Lamborghini-driving man of 29, working out of plush offices in London and renting a large home. He had launched a hot-air ballooning company called Cloudboppers, which, according to news reports in 1992 by British newspaper *The Argus*, grossed £1 million in its first year and had ambitions for expanding to a £50 million enterprise stateside. It was advertised as the largest ballooning company in the world, but after Brodie announced that the company was

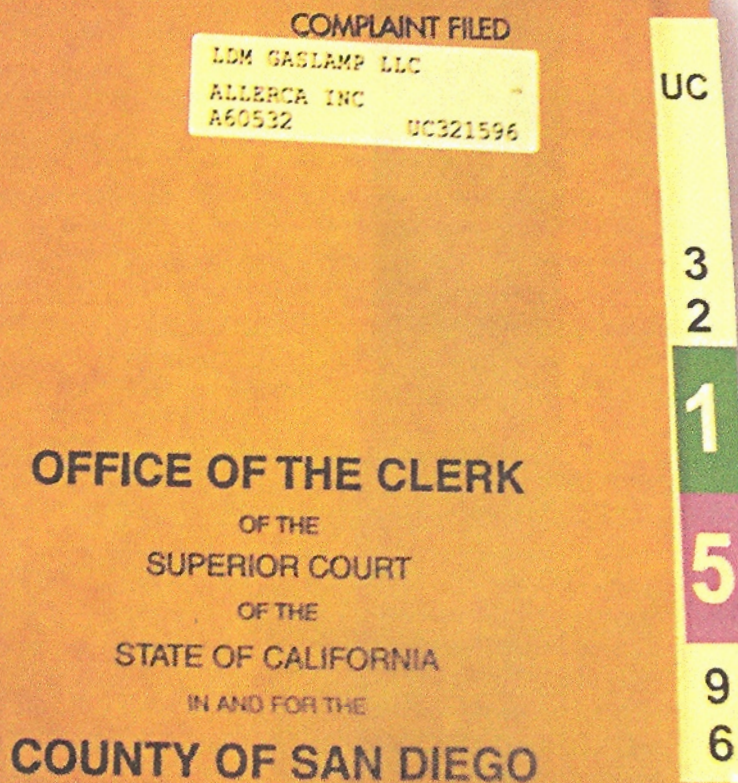
going to be bought for £4 million, his success collapsed.

Reporter Richard Fleury of *The Argus* conducted an investigation that exposed a number of lies and ultimately resulted in a jail sentence for Brodie. Not only did the £4 million deal never take place, "We discovered Cloudboppers owned just two balloons and had been running up sky-high debts for months," reported *The Argus* in 1994. "The firm was continuing to take bookings for expensive balloon flights even after the Civil Aviation Authority revoked its license to fly." The Lamborghini was repossessed, the offices abandoned, and employees were not paid. According to published reports, Brodie was sentenced to two-and-a-half years in jail after pleading guilty to multiple counts of false accounting.

Brodie's legal troubles followed him to the United States. Olympic Avenue, where Allerca had its official headquarters, dead-ends behind the Santa Monica County Building. Court records inside the low, white building reveal Brodie has been sued a number of times in the Los Angeles Superior Court for contractual fraud, eviction, and unpaid debt. A 2004 case shows Brodie was using an alias, Simon Campbell, and was connected with Cerentis Corporation and Integra Associates. Cerentis' goal in 1999 was to develop the world's largest supercomputer by linking together 10,000 PCs with a downloaded screen-saver called Terra One, according to a press release. The project never saw completion, or perhaps never even began.

Similarly, one of Brodie's former companies, Geneticas, claimed it would provide customers an allergy-free cat based on RNAi and had already accepted hundreds of nonrefundable \$250 deposits. Geneticas also predicted it could bring the cost of cloning a cat below \$10,000. The cats never came and Geneticas disappeared (see "Doubts About Allergy-Free Cats" and "Cloning for Profit," *The Scientist*, Jan. 31, 2005).

In July of last year, the *San Diego Union-Tribune* detailed more of Brodie's former undertakings, each leaving behind a stain of debt, broken contracts, and phantom products. Brodie says the report



A court file against Allerca for unpaid rent

The Hypoallergenic Cat: A timeline

is "full of inaccuracies" but wouldn't be specific. (May calls the report "grossly inaccurate.") "I can't say much more because there are some legal things going on," Brodie says. "I'm here to talk about the company. I'm not here to talk about me." But when asked about the company — where the offices, laboratory, and breeding facilities are located, who the scientists are that discovered the cats, and what precisely is the mutation responsible for the cats' hypoallergenicity — Brodie says "we don't want to divulge the process and our information."

To find out more about Allerca, one must follow the trail of legal breadcrumbs down from Los Angeles to San Diego, where Allerca claimed its headquarters from 2004 to 2006. Inside the records room of the Hall of Justice the clerk hands over another court file, this time against Allerca and not Simon Brodie. In February 2006 the company was sued in San Diego Superior Court for \$3,297 in back rent for a loft space just a few blocks from The Hall of Justice in the stylish Gas Lamp district. (A company Brodie founded in 2005, called Cyntegra, is still registered to the address, according to the California Secretary of State's Web site.)

Searching through the files of the San Diego Superior Court leads to yet another courthouse, situated among the strip malls of Clairemont Mesa Boulevard. On a hand-written note, a former Allerca employee asks for an extended date to serve Brodie a small-claims court suit for \$4,600 in unpaid fees, because "he seems to know that I am trying to serve him and he is avoiding me ... he must have done this before and is quite skilled at hiding." The case was ultimately dismissed. (My attempts to contact the plaintiff, Daniel McDonnell, were unsuccessful.)

Allerca has been successful at keeping company details secret. Six full-time employees run the company, but May says up to 2,000 people can be working for Allerca at any given time. Most of them maintain the breeding facility (which May has not visited) and conduct research. Aside from Microbac's participation, no other names and locations have been reported.



Feb. 4, 2004—The beginnings of the allergy-free cat. Simon Brodie and David Avner agree on a business plan for using RNAi to knock out the gene for the major cat allergen fel d 1.

Sept. 24, 2004—Brodie and Avner agree to form a company called Allerca.

Oct. 12, 2004—Brodie backs out of his partnership with Avner.

Oct. 26, 2004—Brodie incorporates Allerca without Avner.

Oct. 28, 2004—Brodie sends out press releases promising hypoallergenic cats based on RNAi by 2007. "For the first time, people who have been unable to own a cat because of their allergies will be able to have a pet of their own without the associated risks and costs of allergy treatments."

Dec. 14, 2004—Avner sues Brodie for stealing and publicizing his trade secrets, soliciting his customers, and usurping investors, "because it appears, from the public's perspective, that [Allerca has] already 'cornered the market' on this new technology."

Jan. 31, 2005—U.S. District court in Colorado orders an injunction on Allerca "not to reenter the market for genetically engineered allergen-free cats until after 5/31/06."

Jan. 31, 2005—*The Scientist* publishes "Doubts About Allergy-Free Cats."

Spring 2005—Allerca scientists begin screening cats randomly across the country and in the United Kingdom to try out a fel d 1 genetic test with the intention of developing fel d 1 knockout cats.

Fall 2005—Allerca scientists stumble upon cats with a mutant fel d 1 that renders them hypoallergenic; they determine that the trait is dominant and begin breeding (cat gestation takes 57-69 days; cats reach maturity in 6-10 months).

Spring 2006—Second generation of hypoallergenic cats is born.

May-July 2006—Hired by Allerca, Microbac conducts genetic analysis on samples of hypoallergenic cats and concludes Allerca's cats have mutations not seen in control cats.

May 31, 2006—Injunction is lifted, allowing Allerca to pursue development of allergy-free cats.

June 7, 2006—Allerca announces it has bred hypoallergenic cats and begins accepting deposits.

Sept. 14 2006—In a press release Allerca announces success in independent clinical trials. "This observation exposure shows the Allerca cat has hypoallergenicity."

Fall 2006—Third generation of hypoallergenic cats is born.

Spring 2007—Allerca's scheduled delivery of hypoallergenic cats to customers.

Information gathered from: court documents in the US District Court in Colorado; the California Secretary of State; interviews with Allerca executives; and press releases from Allerca.

Brodie's Other Pet Projects

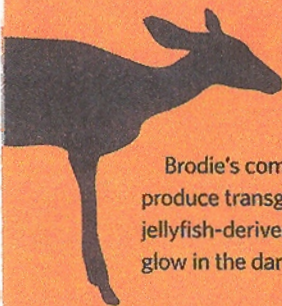
Geneticas: cloned cats—In

2004, Brodie claimed he would produce cloned cats based on RNAi by 2007 (see "Cloning for Profit," *The Scientist*, Jan. 31, 2005). The company also promised to reduce the cost of cloning a cat to less than \$10,000. Horse cloning was also part of Geneticas's plan, but that also dissolved. Geneticas had been registered with the Florida Secretary of State but is now inactive. The Web site has been dismantled.



Genetiate: glow-in-the-dark deer—To address the problem of hitting deer while driving in the dark,

Brodie's company Genetiate aimed to produce transgenic deer, whose imported jellyfish-derived gene would cause them to glow in the dark. The project never took off.

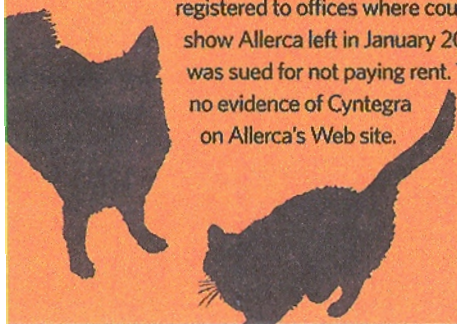


GeneSentinel: canine flu test—The Allerca subsidiary announced it had developed a rapid test that would detect canine influenza. A press release says the "diagnostic technology is similar to that used to detect the avian flu and SARS in humans." There is no evidence of GeneSentinel on Allerca's Web site.



Cyntegra: flu test for cats and dogs—Cyntegra's

Viogenix Duo, a diagnostic test based on the same technology as GeneSentinel's test, could detect two influenza viruses: H5N1 in cats and dogs and H3N8 in dogs, according to a press release. Cyntegra is still registered to offices where court records show Allerca left in January 2006 and was sued for not paying rent. There is no evidence of Cyntegra on Allerca's Web site.



The core of the company is hard to get a handle on as well. As of October, May was the spokesperson for the company, which then claimed its headquarters in San Diego though it was registered in Los Angeles. A press release on November 15 announced that May would become president of Allerca, Brodie would become chairman, and Robert Stephenson would become chief operations officer. The headquarters would move from San Diego to Los Angeles, and a satellite office was due to open in New York City. Shortly after the press release, Allerca moved its registered

worked in a lab at University of Virginia, trying to find a way to reduce the presence of Fel d 1. After testing over-the-counter products and bathing cats, he concluded that no effective method was available to get rid of the allergen. (Cats secrete Fel d 1 through their sebaceous glands and squamous epithelial cells and spread it through their fur during grooming.⁵ Cat allergen is one of the most common allergens, found in nearly all US homes.⁶)

"That's when I came up with the idea for genetic modifications to make an allergy-free cat," says Avner. "I said, why don't we just turn off the gene that makes the aller-

"It's very worrisome that before there's any demonstration of a true effect, we start giving these cats to people."

—*Fernando Martinez*

address from 11400 Olympic Avenue to another shared office down the road at 10940 Wilshire Boulevard. Brodie's name was replaced on the registration by that of Megan Young, Allerca's CEO.

Brodie wrote in an E-mail that the changes are part of Allerca's ongoing growth. But David Avner, a former partner of Brodie, says he's convinced that Brodie's secretive behavior is all part of a fraudulent pattern, and hypoallergenic cats are no exception.

FALSE STARTS

Brodie began promising cats for people with allergies long before the hypoallergenic cat was discovered. His first attempt was in 2004, and the plan was to design them allergen-free. Making an allergen-free cat has been on the mind of Avner, an emergency room physician at Sky Ridge Medical Center in Lone Tree, Colo., for over a decade. During the 1990s Avner

gen altogether?" But to launch his idea, Avner would need financial backing.

According to Avner, Simon Brodie approached him with a deal: Avner would set up a lab and Brodie would provide the capital. In 2004 the two men agreed to set up a company called Allerca and start working on knocking out a gene for Fel d 1. But before the first gene could be silenced, Brodie pulled out of the deal. "Within two weeks he basically took everything and claimed it was his own," says Avner. "He took all of our business plans, marketing, and filed his own papers to create his own company with the same name and everything."

On October 26, 2004, Brodie incorporated Allerca with the California Secretary of State, and shortly after that, Avner took Brodie to court. The judge ruled in Avner's favor, and enjoined Brodie from developing and marketing Fel d 1 knockout cats until May 31, 2006. But, Brodie claimed to have found an easier way to produce

hypoallergenic cats. One week after the injunction lifted, Allerca distributed a press release that the company was able to selectively breed, not clone, cats that don't stimulate the human immune system.

Avner says he thinks it's all a scam. "I don't believe they exist," says Avner, who is still seeking funding to launch his allergen-free cat research. "It's not a grudge. Their science is unsupported. Their claims are unsupported."

PROOF IS IN THE PETS

Brodie says not to expect any peer-reviewed papers or patents on Allerca's discoveries. His reasons are twofold. "Coca-Cola doesn't publish its secret recipe," he explains. With interested customers in 85 countries, Brodie says he wants to protect the international market and keep the information on the cats' mutation and their screening process proprietary. "We have something special here and we want to keep it confidential." Brodie's other reason stems from

the death threats Allerca says it receives each week from animal activists. "Our biggest concern is security. ... The more intelligent people out there realize it's dangerous [work]."

Brodie says he understands there are doubters, particularly in the scientific community. But with the first round of kittens planned for delivery in the next several months, Brodie says the truth about the cats will become apparent. "The proof is going to be that customers [with allergies] will have these cats and will be living with them. And that is the proof. We can provide every piece of scientific evidence and there will still be doubt."

UCLA's Saxon sees only one reason why Allerca should keep data from the public. "If they haven't published, why? Because it didn't work?" he asks. "I'm all for a hypoallergenic cat, but I'm not buying one yet." ■

Have a comment? Email us at mail@the-scientist.com

REFERENCES

1. S.J. Arbes, Jr. et al., "Prevalences of positive skin

test responses to 10 common allergens in the US population: results from the Third National Health and Nutrition Examination Survey," *J Allergy Clin Immunol*, 116:377-83, 2005.

2. M.C. Anderson, H. Baer, "Allergically active components of cat allergen extracts," *J Immunol*, 137:972-5, 1981.
3. I.J. Griffith et al., "Expression and genomic structure of the genes encoding Fd1, the major allergen from the domestic cat," *Gene*, 113:263-8, 1992.
4. T. Saarne et al., "Rational design of hypoallergens applied to the major cat allergen Fel d 1," *Clin Exp Allergy*, 35:657-63, 2005.
5. P. Mata et al., "Fel d 1 allergen—skin or saliva," *Annal Allergy*, 69:321-2, 1992.
6. S.J. Arbes et al., "Dog allergen (Can f 1) and cat allergen (Fel d 1) in US homes: results from the National Survey of Lead and Allergens in Housing," *J Allergy Clin Immunol*, 114:111, 2004.
7. J.P. Morgenstern et al., "Amino acid sequence of Fel d1, the major allergen of the domestic cat: protein sequence analysis and cDNA cloning," *Proc Natl Acad Sci*, 88:9690-4, 1991.
8. O.A. Duffort et al., "Studies on the biochemical structure of the major cat allergen Felis domesticus I," *Mol Immunol*, 28:301-9, 1991.
9. K. Leitermann, J.L. Ohman, "Cat allergen 1: biochemical, antigenic, and allergenic properties," *J Allergy Clin Immunol*, 74:147-53, 1984.