

Targeted vaccines against feline dander could be the cat's meow

A man and a woman walk into a doctor's office. She has a cat allergy; he has a cat. "They say, 'You've got to do something or we can't get married,'" says Michael Blaiss. It sounds like the beginning of a bad joke, but it's actually a typical day at Blaiss's private allergy practice in Memphis, Tennessee. People often face tough decisions when a loved one cannot cohabit with feline companions.

Cat dander—microscopic pieces of dry cat skin coated with Fel d 1, a protein responsible for most cat allergies that is secreted by cat glands onto the skin and transferred to fur from cat saliva through grooming—elicits a reaction in an estimated 17% of individuals in the US. Antihistamines and steroids can dull the symptoms, but the only disease-modifying therapy currently available is a series of injections made of cat dander extract, a soup of proteins literally washed from cat fur and bottled. Whole allergen treatment is time consuming, involving some 30–80 shots over three to five years, and risky, with the chance of rare life-threatening anaphylactic reactions to the injections.

An Oxford, UK-based company, Circassia, hopes to change all that with its new ToleroMune cat allergy vaccine, a molecular approach to the problem. The vaccine is made of seven synthetic peptides, each only 15–20 amino acids long and derived from Fel d 1. The carefully selected peptides quiet the immune system's aberrant T cell response but avoid activating mast cells, which cause allergic reactions and anaphylaxis. "We know exactly what is in every vial," says Steve Harris, Circassia's chief executive.

In a recently published phase 2 study, 21 people received four injections of the therapeutic vaccine over a three-month period in which they were exposed to cat dander. A year after starting the treatment, these individuals showed a significantly greater reduction in nose- and eye-related symptoms than 29 participants who received a placebo and the same allergen hazard (*J. Allergy Clin. Immunol.* doi:10.1016/j.jaci.2012.07.028, 2012).

In early October, Circassia announced the launch of a phase 3 study of the vaccine in approximately 110 centers across the US, Canada and Europe. The company expects to complete the trial by mid-2014.

"This is what people have been trying to do for the last 25 years in immunotherapy—increase immunogenicity and decrease the likelihood of the vaccine triggering an allergic reaction," says Blaiss, who also teaches at the University of Tennessee Health Sciences Center in Memphis and was not affiliated with



Felling Fel d 1: New vaccines target the protein responsible for most cat allergies.

the Circassia trial. "This is the most impressive peptide study that I've seen."

The cat's out of the bag

Circassia's vaccine may be one of the furthest along of its kind, but is it not the only allergy vaccine based on a molecular approach. Tunitas Therapeutics, a San Francisco-based biotechnology company, has genetically engineered a cat allergy vaccine by fusing a Fel d 1 peptide to a portion of a human immunoglobulin G protein that inhibits mast cell activation. "We block the allergy component by using this brake, but the [Fel d 1] protein is still available to drive tolerance," says Nolan Sigal, president and chief executive of Tunitas. The company initiated a phase 1 trial of their cat allergy vaccine in 2011 but halted the trial when the vaccine did not block local reactions to cat dander as expected. "We learned a lot, but it was not good enough to move forward into full-scale clinical development," he adds. The company is now making a second attempt at a cat allergy vaccine based on the same principle but testing different molecules to act as the brake.

Vienna-based Biomay has taken a similar tack, fusing parts of Fel d 1 to a noninfectious hepatitis B virus protein. The allergen peptides cause immunization without activating mast cells, whereas the hepatitis peptides subdue inflammatory T cells, which can cause late-stage side effects. "We wanted to add another layer of security," says Rudolf Valenta at the Medical University of Vienna, inventor of

the vaccine technology and a consultant for Biomay. Biomay's cat allergy vaccine is only in preclinical development, but the company has a grass pollen allergy vaccine based on the same concept that requires just three doses over two months and is in phase 2 trials.

Meanwhile, Thomas Kündig at the University of Zurich Hospital recently designed and tested a cat allergy vaccine that fuses Fel d 1 sequences to two additional peptides: an HIV-derived peptide that whisks the protein quickly into immune cells and a human peptide that targets the construct straight to the endoplasmic reticulum so that it is not degraded in the lysosome. In a clinical trial reported earlier this year, three injections of the vaccine into the lymph node over two months led to an increase in tolerance to cat dander in 12 allergy sufferers versus 8 who took placebo (*J. Allergy Clin. Immunol.* **129**, 1290–1206, 2012). Unfortunately, the project is currently stalled, says Kündig, as he has been unable to find a partner or additional funding to pursue the vaccine.

All in all, "if these things work, it would be game changing," says Robert Wood, director of the allergy and immunology division at the Johns Hopkins Children's Center in Baltimore. Cat lovers may rejoice, but Fido aficionados with allergies will have to wait a bit longer. Cat allergies are far more common than dog allergies and often lead to asthma attacks, which dog allergies rarely do. "Dog is on the list," says Circassia's Harris, "but it's some way down."

Megan Scudellari