



In addition, targets outside the gut and brain are also being studied as potential obesity treatments. For example, Flier noted, multiple companies are exploring antagonists to 11 β -hydroxysteroid dehydrogenase, an enzyme found in fat tissue which, when overactive, promotes obesity and diabetes.

A MULTIPRONGED APPROACH

While it is tempting to hope for a miracle pill that will cure obesity, history has proved that a simple solution is unlikely. For example, many hoped that leptin, a hormone secreted by adipose tissue and thought to inhibit appetite, might provide a cure to obesity. Studies on mice showed promise, but it was later discovered that the hormone can only cure obesity in individuals with a rare genetic mutation that prevents them from producing the hormone, Flier said.

But most obese individuals actually produce a lot of leptin and appear to be insensitive to it. More recent research suggests that rather than inhibit eating, leptin may act as a signal that reassures the brain that adequate fat stores are available in the body to perform reproduction and other normal functions, Bloom said.

The complexity and redundancy of the systems regulating appetite, metabolism, and body weight indicate that successful treatment of obesity will require a multipronged approach, said Wyatt, who also directs the Denver-based Centers for Obesity Research and Education, a consortium of eight medical centers that conducts workshops on obesity management for health care workers. This approach may be similar to the approach used to treat diabetes with drugs, exercise, and nutritional components. Addressing environmental and behavioral factors that lead to obesity is also important, she said.

In the meantime, even though available treatments for obesity are far from ideal, physicians should not ignore obesity, said Wyatt, noting that even a modest weight loss of 5% to 7% of body weight and increased activity levels can have a positive effect on a patient's health. □

Therapy Takes Wheeze Out of Cat Allergies

Bridget M. Kuehn

THE ROUGHLY 10 MILLION INDIVIDUALS in the US who are allergic to cats—a condition that can trigger asthma or rhinitis—may one day find relief from a therapy that couples the cat allergy-causing protein with a human protein.

The experimental therapy reduced the allergic response to cat allergens in cells taken from humans who are allergic to cats as well as in two distinct sets of mice with cat allergies, a team of researchers reported in *Nature Medicine* (Zhu et al. *Nat Med.* 2005;11:446-449). In addition to offering new hope for sniffing and sneezing cat lovers, the new technique provides proof of concept that such an approach might be used to treat food allergies, which cause 150 deaths annually, and other allergic reactions that cannot be treated with conventional therapies, said Andrew Saxon, MD, the chief of the Division of Clinical Immunology and Allergy in the School of Medicine at the University of California, Los Angeles.

Conventional allergy treatments aim to desensitize individuals by exposing them to the offending allergens in small doses that are gradually increased. This protracted process takes 3 to 5 years, said Saxon. But this technique cannot be used to treat serious food allergies because the treatment itself can cause life-threatening reactions.

The new approach uses a fused protein that consists of the cat allergen protein Fel d 1 and human protein Fc γ , which is part of human immunoglobulin. In an individual who is allergic to cats, the Fel d 1 protein binds to antibodies that trigger the allergic response and unleash histamines, which cause allergy symptoms. Saxon explained that with the fused protein, as the Fel d 1 end of the fused protein



Geil Barrett

A new approach to treating allergies may one day help people who are allergic to cats.

binds to the antibodies, the Fc γ end binds to an Fc receptor on the cell, which inhibits the release of mediators of the allergic response.

Saxon and colleagues tested the therapy in blood donated by individuals allergic to cats and found that the therapy reduced the production of histamines by 90%. Subsequently, the researchers tested the therapy in one set of mice genetically engineered to have human cat allergy cell receptors, which developed an allergic response after exposure to human antibodies and the Fel d 1, and a second set of mice that were made allergic to cats by injections with Fel d 1 and an immune system booster. In both models, the therapy blocked the allergic reaction.

Such a treatment could provide relief to individuals who are allergic to cats in as little as 3 to 5 months, said Saxon, but further safety testing will be required before the treatment can be tested in humans. In the meantime, the investigators will test whether a similar approach could be used to treat peanut allergy, which affects 0.6% of individuals and causes the most severe food-induced allergic reactions, according to the National Institute of Allergy and Infectious Diseases. □