New Therapy Tested in Mice Could Chase Away Cat Allergies

A hybrid protein designed to block cat allergies successfully prevented allergic reactions in laboratory mice, as well as in human cells in a test tube, reported a UCLA study in the April 2005 issue of *Nature Medicine*.

When an allergic person is exposed to allergens—pieces of protein found in cat saliva or dander—the immune cells spew out histamine, a chemical that provokes the itchy eyes, sneezing and runny nose associated with allergies.

UCLA scientists tethered the cat allergen to a human antibody and dubbed the hybrid protein GFD, or gamma *Feline domesticus*. The cat side attaches to antibodies on the surface of the immune cell, while the human end stops the cell from releasing histamines, preventing the allergic reaction.

Led by Dr. Andrew Saxon, chief of clinical immunology and allergy, researchers cultured GFD and cat allergen in blood donated by people allergic to cats, and measured the level of resulting histamine.

“The blood cultures mixed with GFD released 90 percent less histamine,” Saxon says. “This suggests that GFD prevented the immune cells from reacting to cat allergen.”

GFD also blocked the ability of human allergic antibodies to release histamine in mice genetically bred to react to human allergic antibodies.

Scientists also injected a second set of mice with cat allergen to produce an allergic response. After treating some of these mice with GFD, the team exposed the airways of all the mice to cat allergen.

The untreated animals developed asthma-like lung symptoms and generalized allergic reactions. The mice treated with GFD did not react to the cat allergen.

Saxon believes the molecule has the potential to prevent allergic reactions long after injections stop. He hopes the approach will lead to a new therapy for cat allergies in humans, as well as for deadly food allergies, such as to peanuts.
Study Shows Green-tea Extract’s Potential as Anti-cancer Weapon

A Jonsson Cancer Center study on bladder cancer cell lines in culture demonstrated green-tea extract’s ability to target tumor cells while leaving healthy cells alone. Clinical Cancer Research published the research on Feb. 15, 2005.

Led by Dr. JianYu Rao, associate professor of pathology and laboratory medicine, scientists demonstrated that green-tea extract interrupts a cellular process that enables bladder cancer cells to invade other parts of the body. Called actin remodeling, the process is regulated by several cell-signaling pathways, including one called Rho.

Green-tea extract switched on Rho signaling, reorganizing the cancer cells’ actin skeletal protein and making them adhere more tightly. Both results limited the cells’ ability to move.

“Green-tea extract may keep the cancer cells confined locally, where they are easier to treat with better prognosis,” Rao says. “Green-tea extract interrupts the invasive process of the cancer.”

The next phase of his research will analyze urine from bladder-cancer patients and look for specific biomarkers associated with actin remodeling and activation of the Rho signaling pathway.

“We’re hoping the results from these studies will tell us who will best benefit from the agent,” Rao says.

Bladder cancer is the fifth most common cancer in the U.S., with about 56,000 new cases diagnosed each year.

Green-tea extract promotes the formation of actin fibers (stained green) in cancer cells. The fibers promote increased cell attachment (red), which helps to prevent cancer cells from spreading.

Research Disputes Antidepressant/Suicide Link; Scientists Fear Rise in Deaths from Untreated Depression

Challenging claims linking antidepressant use to suicidal behavior, a UCLA study found that American suicide rates dropped steadily after the introduction of Prozac and other selective serotonin reuptake inhibitor (SSRI) drugs. The February 2005 edition of Nature Reviews Drug Discovery reported the research.

Dr. Julio Licinio, professor of psychiatry and endocrinology and a researcher at the Semel Institute for Neuroscience and Human Behavior, worked with fellow psychiatrist Dr. Ma-Li Wong to conduct an exhaustive database search of studies published between 1960 and 2004 on antidepressants and suicide.

The team reviewed each piece of research and created a timeline of key regulatory events related to antidepressants. Then they generated charts tracking antidepressant use and suicide rates in the United States. What they found surprised them.

“Suicide rates rose steadily from 1960 to 1988 when Prozac, the first SSRI drug, was introduced,” Licinio says. “Since then, suicide rates have dropped precipitously, sliding from the eighth to the 11th leading cause of death in the United States.”

Several large-scale studies in the United States and Europe also screened blood samples from suicide victims and found no association between antidepressant use and suicide.

“Researchers found blood antidepressant levels in less than 20 percent of suicide cases,” Licinio notes. “This implies that the vast majority of suicide victims never received treatment for depression.

“Our findings suggest that these individuals who committed suicide were not reacting to their SSRI medication,” he adds. “They killed themselves due to untreated depression. This was particularly true in men and in people under 30.”

The authors caution that regulatory actions to limit SSRI prescriptions may increase death rates from untreated depression, the leading cause of suicide.

Depression affects some 10 percent of men and 20 percent of women in the United States during their lifetime. Ten percent to 15 percent of depressed people commit suicide.
UCLA Study Links Changes in Brain Chemistry to Premenstrual Syndrome

UCLA neurologists have uncovered a biological basis for the behavior that often accompanies premenstrual syndrome. Reported May 15, 2005, by Nature Neuroscience, the team found visible changes in brain chemistry that may underlie behavioral fluctuations.

Dr. István Mody, Coelho Professor of Neurology, discovered female mice were more anxious when their hormone levels paralleled those of premenstrual women. He examined the rodents’ brains and found that the neurons held lower levels of delta GABA, a key receptor subunit that prevents nerves from firing too often and has been linked to epileptic seizures.

“We’ve known for a while that epileptic women are prone to seizures around menstruation, when progesterone levels are low,” he says.

Mody hypothesizes that premenstrual women’s seizures, irritability and anxiety are side effects of neurons firing unchecked. The discovery may also relate to postpartum depression and mood swings during pregnancy.

The team’s next step will be to identify the mechanisms behind these changes.

“We want to reveal the molecular identities of the players responsible for reducing the number of these receptors on the surface of nerve cells,” he notes.

New Dosing Approach Boosts Height 50 Percent More than Current Methods in Children with Short Stature

Challenging the current weight-based approach to growth hormone therapy, a new dosing model improved height outcomes in children with severe short stature due to a growth-hormone deficiency or unknown (idiopathic) cause. The UCLA findings were presented June 6 at the 2005 annual meeting of The Endocrine Society.

The new dosing approach involves the serum levels of insulin-like growth factor-1 (IGF-1), the hormone that mediates growth hormone’s effect on children’s development.

Led by Dr. Pinchas Cohen, chief of pediatric endocrinology at Mattel Children’s Hospital at UCLA, researchers randomly administered one of three types of growth-hormone therapies to prepubescent children diagnosed with severe short stature.

One group received a conventional growth-hormone dose according to weight. Two other groups received a dose adjusted to achieve either an IGF-1 level equivalent to the mean for their age and gender, or the upper limit of normal for IGF-1.

Cohen’s team found that the group of children whose dosage was increased to achieve a higher IGF-1 level grew 50 percent more than the other children. The higher IGF-1 approach also enhanced the growth of patients with growth-hormone deficiency or idiopathic short stature.

“Some of the growth hormone being produced by the pituitary gland is not reaching the body’s tissues, so we’re giving more growth hormone,” Cohen observes.

Researchers monitored female mice’s cycles and discovered that a rise in estrus and drop in diestrus correlated to increased anxiety before menstruation.
UCLA-pioneered Surgery to Treat Vocal-cord Spasms and Restore Voice Shows Long-term Success

The first large, long-term study of patients who had surgery to control vocal-cord spasms showed excellent results in the majority of cases, reported UCLA research presented May 14, 2005, at the 126th annual meeting of the American Laryngological Association.

“We are very encouraged by our results,” says Dr. Dinesh Chhetri, assistant professor of head and neck surgery, who presented the findings. “When spasmodic dysphonia symptoms do not return within one year, they generally will not come back. Our findings suggest that this surgical technique provides the first permanent solution to treating the condition.”

Spasmodic dysphonia is a neurological condition that disrupts nervous signals to the vocal cords, preventing them from vibrating properly. Reducing the voice to a strangled, choppy whisper, the disorder affects 50,000 people in the United States, and its cause remains unknown. Botox injections can provide temporary relief, but are not effective for everyone.

In 1993, Dr. Gerald Berke, UCLA chief of head and neck surgery, pioneered the first surgery to permanently treat spasmodic dysphonia symptoms. In this procedure, the surgeon severs the nerve that sends abnormal signals to the vocal cords, and then attaches a healthy nerve from the throat to maintain the vocal cords’ muscle tone.

Chhetri’s team surveyed 131 patients at an average of four years post-surgery. Of the 81 patients who completed the survey, 91 percent expressed greater satisfaction with their vocal quality post-surgery compared to post-Botox. Overall, 83 percent noted that the procedure significantly improved their physical, social and emotional well-being.

“The surgery continued to provide long-lasting relief of vocal cord spasms and voice breaks in a majority of patients,” Chhetri notes. “This suggests that the procedure will expand as an important therapeutic technique for the treatment of spasmodic dysphonia.”

Statin Therapy within 24 Hours After Heart Attack Cuts Patients’ In-hospital Deaths by More than Half

UCLA researchers discovered that treating cardiac patients with a statin drug within 24 hours after a heart attack cut in-hospital death rates by more than half. The American Journal of Cardiology reported the findings on Sept. 1, 2005.

“We knew that long-term statin therapy was beneficial, but this study offered the strongest clinical support to date of the early protective effects of statins immediately following a heart attack,” said Dr. Gregg Fonarow, professor of cardiology and Eliot Corday Chair in Cardiovascular Medicine and Science.

UCLA researchers studied data from more than 170,000 patients in the National Registry of Myocardial Infarction 4, a database of patients hospitalized due to heart attack.

They found that patients who received statin therapy before hospitalization and within 24 hours after heart attack were 54 percent less likely to die in the hospital compared to patients who did not receive statin therapy. That risk reduction rose to 58 percent in heart-attack patients who received the drugs after hospitalization but who had no previous statin use.

“We were surprised that statin therapy showed such a striking effect immediately after a heart attack,” says Fonarow, also director of the Ahmanson-UCLA Cardiomyopathy Center. “Statins provided protection from other heart-attack complications, as well.” They included a lower incidence of cardiac arrest, cardiac shock, cardiac rupture and ventricular fibrillation.

Statins work by increasing nitric oxide in the cardiovascular system. This result reduces inflammation, which may help limit cell damage from a heart attack.

The next step is to develop a randomized clinical trial to corroborate the UCLA team’s observations. Fonarow believes that early statin use may become a standard treatment for heart-attack victims upon their arrival to the emergency room.

Treating cardiac patients with a statin drug within 24 hours after a heart attack cuts in-hospital death rates by more than half.