plus one would not equal two, but market research seems to suggest that merging could in fact raise our profile," says Neil McDonald, a structural biologist at ICRF's headquarters in London. Indeed, predicts Steve Jackson, deputy director of the Wellcome-CRC Institute of Cancer and Developmental Biology at the University of Cambridge, Cancer Research UK should have more clout among both politicians and scientists. Coupled with a solid research program, that would amount to far more than a marriage of convenience.

–JOHN PICKRELL

John Pickrell is a science writer in Hertfordshire, U.K.

ASTHMA RESEARCH

Missing Gene Takes Mice's Breath Away

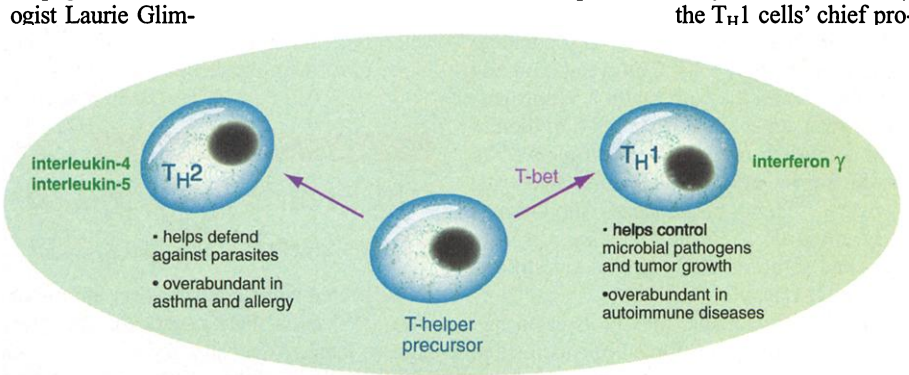
A strain of mice with a tendency to wheeze may help scientists get closer to the root of asthma in humans. Asthma constricts airways in patients' lungs and leaves them short of breath, sometimes fatally; it afflicts tens of millions of people worldwide and seems to be on the rise in many areas. Scientists are still struggling to decipher the cellular signals at the root of the attacks. Now, in reports on pages 336 and 338, immunologist Laurie Glimcher and her colleagues describe a mouse strain that mimics the human condition and might provide a better model system for studying the disease.

Researchers have created asthmatic mice before, but through a process involving injections of allergens and irritants. That scenario doesn't match the situation of many patients with chronic asthma, whose attacks are not triggered by known allergens. The new mice resemble those human asthmatics in several key ways, such as having characteristic chronic lung inflammation and thickened airway walls. What's more, the gene responsible for the mice's affliction appears to be misregulated in human asthmatics as well. "It's an exciting model," says immunologist William Paul of the National Institute for Allergy and Infectious Diseases in Bethesda, Maryland.

The engineered mice lack a gene called T-bet, which codes for a transcription factor, a protein that controls the expression of other genes. In previous experiments, Glimcher and her colleagues had shown that T-bet affects the development of immune system cells, encouraging the development of so-called T_H1 cells. These cells help organize attacks on unfamiliar cells such as invading microbes. They also make proteins that discourage overproduction of a sister cell type called T_H2 cells, whose main job is to help the body defend against parasites.

In most people, a complex set of feedback loops keeps the two cell types in balance. But many scientists suspect that in asthma patients something skews the balance, allowing T_H2 cells to predominate. The proteins those cells produce can lead to some of the changes seen in asthma patients' airways, including high numbers of trigger-happy immune cells that spark inflammation.

To find out more about T-bet's role in the immune system, the team created mice lacking the gene. As expected, the mice produced fewer T_H1 cells. Immature immune cells taken from the animals' lymph nodes produced very little interferon γ, the T_H1 cells' chief protein product, compared to their wild-type littermates. The cells also produced higher levels of interleukin-4 and interleukin-5, two products of T_H2 cells—and prime suspects in fueling asthma.



Proper balance. The T-bet gene prompts immature immune cells to become T_H1-type cells, keeping the number of T_H2 cells in check.

The animals' lungs resembled those of chronic asthma patients, with unusually thick layers of collagen and extensive networks of the musclelike cells that constrict airways. And even before exposure to an irritant, the animals' lungs showed signs of inflammation: They had significantly more immune system cells called eosinophils and lymphocytes than their littermates with functioning T-bet. Mice lacking T-bet were also extremely sensitive to the irritant methacholine; their airways narrowed and it took more effort to breathe. Although it is difficult to really hear a mouse wheeze, Glimcher says, "these mice have asthma."

T-bet might play a role in human asthma as well. The researchers found that asthma patients had significantly lower levels of T-bet expression in their lungs than people without asthma. Although the genetic causes of asthma are complex, the T-bet gene is in a region of the genome that has been implicated in asthma susceptibility.

The mice will be especially useful for fingering the proteins that interact with T-bet to encourage the development of T_H1 cells, says asthma specialist Jack Elias of Yale University School of Medicine. Such proteins might help scientists track down the still-mysterious cause of asthma. Although any treatments are years away, Glimcher says there may be ways to tweak the T-bet system in human lungs to discourage asthma attacks. Any such hints should help asthma patients breathe a little easier.

–GRETCHEN VOGEL

STEM CELL RESEARCH

Stem Cells May Shore Up Transplanted Hearts

Can a broken heart be mended? Perhaps, says a new report, which shows that after a heart transplant, cells migrate to the donated organ, possibly helping it recover. These migrants show signs of being stem cells, those multitalented cells that have the capacity to develop into a multitude of tissues.

Some parts of the body, such as the skin, regenerate readily when damaged. But "we all thought that once you lose a chunk of heart, it's gone," says cardiologist Roberto Bolli of the University of Louisville in Kentucky. One of the first indications that the heart can bounce back came in July 2001, when researchers reported that heart muscle cells can divide after a heart attack. Transplanted hearts are often similarly damaged: Many heart cells die during the hours the organ is out of the body.

Cardiovascular researchers Federico Quaini and Piero Anversa of New York Medical College in Valhalla and colleagues at the University of Udine, Italy, wanted to find out whether the transplant recipient's body pitches in to help heal the new organ. The team examined eight hearts transplanted from female donors into male patients. Up to 10% of cells in the transplanted hearts contained the male Y chromosome—a clear sign that cells from the recipient had taken up residence in the new heart, the group reports in the 3 January issue of *The New England Journal of Medicine*.

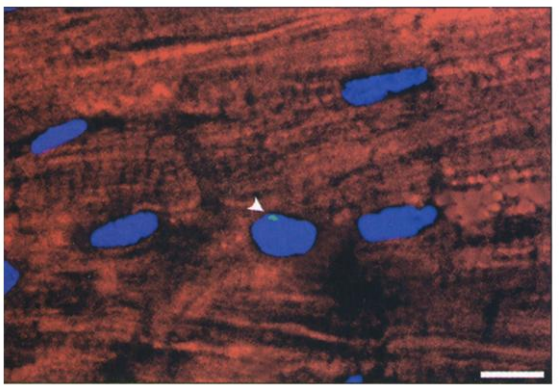
Cardiologist Philip Binkley of Ohio State University, Columbus, calls the study an "ingenious and novel demonstration that the heart can recruit new cells that may be a

benefit in remodeling the heart and possibly improving cardiac function." Several types of cells appeared to regenerate, including cardiac muscle, smooth muscle, and endothelium, Anversa says. Cells containing the Y chromosome appeared "perfectly indistinguishable" from neighboring cells that lacked a Y.

Suspecting that healing the heart might be a job for stem cells, Anversa's group then searched the heart tissue for three molecular markers characteristic of the versatile cells. They found cells bearing these markers both in transplanted and control hearts, suggesting that undamaged hearts harbor populations of such cells. The transplanted hearts contained even higher numbers of the cells, some of which came from the donor and others from the recipient, suggesting that the heart recruits stem cells from other parts of the body to aid in regeneration.

But it is unclear whether these are bona fide heart-specific stem cells and, if so, exactly how they promote regeneration of heart tissue. Nor do the researchers know where the cells originate or how they migrate. Before they can claim to have found stem cells, Anversa says, the team must isolate the cells and demonstrate in vitro that they are self-replicating and capable of differentiating into many types of tissue—work that is now under way.

Discovering how the heart might repair damaged tissue could have enormous, if distant, implications for treating heart disease. But as yet it's not even clear that the new cells help the transplanted organ, Binkley cautions. "Having recipient cells enter the [heart] could have certain detrimental effects," Binkley says, such as clogging up blood vessels. Only additional studies, he says, can determine if such cells are more balm than bane.



Help from afar? A cell containing a Y chromosome (arrow) has taken up residence in heart tissue from a female donor.

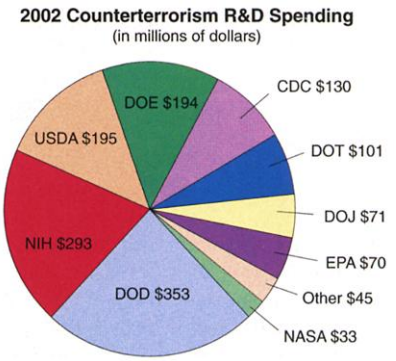
—CAROLINE SEYDEL

Caroline Seydel is a freelance science writer in Los Angeles.

U.S. BUDGET

Spending Triples on Terrorism R&D

NASA may be best known for sending a man to the moon. Now it wants to show that it's no slouch when it comes to fighting terrorists. The U.S. space agency is one of 11 federal agencies (see pie chart) to share in a record $1.5 billion that Congress has showered on terrorism-related R&D for 2002 in response to the 11 September and anthrax attacks. The money—nearly triple last year's spending—will be used for everything from new laboratories for studying potential bioweapons to developing hacker-proof computer systems.



Spreading the wealth. Eleven U.S. agencies will share a record $1.5 billion in terrorism-related research funds.

The money is a windfall for researchers, who earlier last year were fighting to overturn proposed cuts in many terrorism-related R&D budgets. Even after the attacks, the White House paid scant notice to research in its $40 billion emergency recovery package that was approved by Congress. But the Senate took up the cause with a vengeance, labeling as urgent more than $800 million in new terrorism-related R&D projects. "We heard from everyone—university scientists, industry, [federal] researchers—about things they could do to reduce the threat if only they had some money," says an aide to one Senate Democrat.

The final package, mostly inserted late last month into the 2002 appropriations for the Department of Defense, contains $711 million for R&D. That freshet of funds, when combined with spending approved earlier, will push 2002 spending on terrorism-related R&D up 157% over the $579 million spent in 2001, according to an analysis by the American Association for the Advancement of Science (publisher of *Science*).

Most of the new money will be used to expand existing programs aimed at preventing terrorist attacks. The military, for example, gets a 50% increase for its multifaceted terrorism research efforts, to $353 million. The Centers for Disease Control and Prevention, which has played a high-profile role in investigating the anthrax mail attacks, gets $1 billion overall for security-related expenses, including $130 million for studying anthrax and other potential bioweapons. That 256% increase "is hopefully just a down payment for research too long neglected," says one science society lobbyist.

The bioterrorism budget at the National Institutes of Health will soar by nearly 500%, to $289 million. The total includes $75 million for a new highly secure laboratory to work with dangerous pathogens. The Department of Agriculture is also slated to get new laboratories; of $113 million in new funds, $73 million is set aside for an animal biocontainment facility at the National Animal Disease Laboratory in Ames, Iowa, and improvements at the controversial Plum Island Animal Disease Center in New York (*Science*, 26 May 2000, p. 1320). The Department of Energy will devote $78 million of its $126 million in new funds to help prevent nuclear terrorism.

The country's space agency gets $33 million for work on two fronts: information systems that terrorists can't penetrate, and imaging systems and other technologies to better detect enemies. And the Environmental Protection Agency gets $70 million to, among other things, develop better methods to clean up after any bioweapons are unleashed.

—DAVID MALAKOFF

STEM CELL RESEARCH

Rat Brains Respond to Embryonic Stem Cells

In the heated ethical debates over embryonic stem (ES) cells, Parkinson's disease often figures large. Advocates for more research say ES cells offer the best hope for treating or even curing this devastating and deadly disease, which gradually robs patients of their ability to move. The advocates hope that scientists will someday be able to turn ES cells into dopamine-producing cells, replacing those that are lost in the disease. So far, however, evidence that ES cells can make this switch has been limited to experiments in lab culture, not animals.

Now, in a paper published online on 8 January by the *Proceedings of the National Academy of Sciences*, a team of neuroscientists reports that, indeed, mouse ES cells can become dopamine-producing neurons in the brains of rats. These experiments are the first to show that the specific type of neurons missing in Parkinson's disease can develop from an ES cell in an animal's brain and lead to partial recovery.

But the work does not mean doctors will soon be injecting human ES cells into Parkin-

CREDIT: (BOTTOM) F. QUAINI *ET AL.*, *N. ENGL. J. MED.* 349, 8 (2002)