

NEUROSCIENCE

Hot Pepper Receptor Could Help Manage Pain

Bite into a hot pepper, and the pain that engulfs your tongue and palate really does feel like a burn. Several years ago, scientists uncovered the apparent reason: a cell-surface protein that in cultured cells responds both to heat and to capsaicin, the active ingredient in chili peppers. But cultured cells don't experience pain, and researchers weren't sure of the molecule's importance in animals. Now, genetically altered mice that possess an amazing tolerance for hot sauce



Hot stuff. Mice lacking the VR1 receptor are impervious to the burn of hot peppers and are less sensitive to high temperatures.

have demonstrated that the protein plays a key role in several kinds of pain. The finding may eventually aid in the development of new pain-killing drugs.

In work described on page 306, neuroscientists Michael Caterina, David Julius, and Allan Basbaum of the University of California, San Francisco, Martin Koltzenburg of the University of Würzburg, Germany, and their colleagues genetically altered mice to remove the receptor that responds to heat as well as to capsaicin and other so-called vanilloid compounds. The mice behaved normally in most respects, but showed less sensitivity to high temperatures and drank capsaicin-laced water freely. Their neurons also failed to respond to normally noxious stimuli.

Those traits, Julius says, show that the receptor is not only "an essential part of vanilloid sensitivity" but also plays an important role in several other kinds of pain. Indeed, neurosurgeon James Campbell of The Johns Hopkins University School of Medicine in Baltimore says that the receptor is a promising drug target. "If we go after these receptors, we may be able to control [certain kinds of] pain," he says.

Researchers knew that neurons containing the capsaicin receptor, dubbed VR1 (for vanilloid receptor 1), respond to capsaicin and other painful stimuli in culture. But it was only after Julius and Caterina decided

ScienceScope

Looking East Germany's Max Planck Society, which recently completed an expansion into the former East Germany, is now stretching even farther eastward. Society officials announced last week that they will set up a joint "junior research group" with Poland's Academy of Sciences.

The collaboration between Germany's premier basic-research organization and Warsaw's year-old International Institute of Molecular and Cell Biology is seen as a possible model for joint efforts in other fields and with other central European countries. The new research group will be led by a scientist under age 35—chosen after a global search—and will include several Polish postdocs and young researchers. Max Planck, which will pay for salaries and equipment costs, has set up similar groups in France, Israel, and China.

"We want to show that outstanding biology can be done in Poland," says Polish biochemist Maciej J. Nalecz, the director of the Polish academy's Institute of Experimental Biology. "We also want to keep outstanding biologists in Poland." In a reciprocal move, Poland hopes to set up its own satellite research group at the Max Planck Institute of Molecular Cell Biology and Genetics in nearby Dresden.

Vaccine Trial Convinced that vaccines caused his grandson's autism, Representative Dan Burton (R-IN, below) said last week he will ask the National Institutes of Health and other health agencies to investigate his theory.

Burton, who chairs the House Committee on Government Reform, held a 7-hour hearing on autism and vaccines on 6 April. It included testimony from parents, a touter of vitamin cures, and a practitioner who said that stretching the heads of autistic children relieves symptoms. Also on hand was Andrew Wakefield of the Royal Free and University College Medical School in London. In 1998, Wakefield and colleagues published a paper—since refuted by larger studies—that linked one kind of autism to measles, mumps, and rubella vaccination. But when an infectious disease specialist testified that the link was highly unlikely, Burton accused him of conflict of interest because his research was funded by a vaccine maker.

Such badgering drew attention. "I'm troubled by this hearing," said Henry Waxman (CA), the committee's ranking Democrat. "This was structured to satisfy the chair's point of view."



ficient" way to determine which BACs to sequence, and in what order.

The result, announced in simultaneous press briefings last week in Beijing and Tokyo, is a map that covers some 80% of the rice genome at least four times over—a good enough draft to enable gene prediction programs to find many of the estimated 30,000 genes, Mahairas says. Neither the UW team nor Monsanto would reveal how long the project took or how much it cost. Mahairas would only say that "the whole approach worked very, very rapidly."

Sasaki, who has seen the data, says the quality of the sequence varies from BAC to BAC, but "it's still very valuable." Rod Wing, a molecular biologist at Clemson University in South Carolina who has been scrambling to determine the optimal set of rice BACs for the sequencing consortium, is more circumspect: "We're going to have to look at the data very closely" to determine how best to use both the public and Monsanto sets. Some partners may take up where Mahairas left off, using the Monsanto BACs directly in their sequencing efforts; Wing, on the other hand, is considering using the company's data to make the sequencing of his own BACs more efficient.

Although some researchers wonder whether Monsanto will be as forthcoming with the data as promised, Hood insists it will. He describes the project as a "win-win situation": Monsanto gets a jump start on finding the genes with commercial value, and the consortium saves several years and perhaps as much as \$100 million.

Rockefeller's Toennissen holds out Monsanto's data-release policy as a model for other public-private collaborations. Some details are unclear, but as early as next month, the consortium will have access to much of Monsanto's data. Once a piece of Monsanto sequence goes into the consortium's public database, anyone—even competitors—can use it, no strings attached, says Sasaki. Until then, however, other academic researchers who want to use Monsanto's sequence must agree to give the company an option to negotiate nonexclusive rights to license any patents derived from its use. "It would be nice if other companies followed suit and made their fundamental genomics information available under similar circumstances," says Toennissen.

DuPont, for example, has a private rice database, as does Novartis. Neither has released these data, but Novartis did help to launch the public rice effort by supporting Wing's research. Says Michael Bevan, a plant molecular geneticist at the John Innes Centre in Norwich, U.K., Monsanto's actions "certainly put other companies on the spot."

—ELIZABETH PENNISI

With reporting by Dennis Normile in Tokyo, Pallava Bagla in India, and Li Hui in China.

a "draft" version of the human genome this year quickly tried to pour cold water on Celera's boast.

Eric Lander, for example, director of one of the largest of the publicly funded sequencing centers, based at the Massachusetts Institute of Technology, advised reporters that a lot of work remains to be done. He was quoted in *The Boston Globe* as saying that Celera had only produced "a small fraction of the data required"—less, in fact, "than has been produced by the international public sequencing consortium."

A week earlier, the public consortium had indulged in some propaganda of its own. The National Human Genome Research Institute (NHGRI) announced that the nonprofit labs had sequenced the 2-billionth base pair of human DNA. As the genome is about 3 billion base pairs long, NHGRI director Francis Collins interpreted this to mean that the job was two-thirds done. Although the milestone is impressive, researchers say, it does not give an accurate reading of how near to completion the project is.

Indeed, Venter went out of his way in testimony last week to downplay the consortium's achievements. "Mr. Chairman," Venter said, "I find myself in the peculiar position of warning you that in the race to complete a draft human sequence, the publicly funded Human Genome Project may be at a stage where quality and scientific standards are sacrificed for credit. ... Analysis of the public data in GenBank reveals that it is an unordered collection of over 500,000 fragments of average size 8000 base pairs. This means that the publicly funded program is nowhere close to being 'done.'" Venter suggested that Congress urge the consortium's researchers to "keep their standards at the highest levels ... and not rush to publish preliminary data for the sake of claiming priority."

Asked if there is any chance that the competing genome teams might still come together to finish this project, Venter said last week: "I keep trying to come to the dance, but the others are still taking lessons." This prompted a member of the public consortium to respond: "We all want to go to the dance, but we can't agree on the music." Given the harsh criticisms flying back and forth, collaboration seems unlikely.

In fact, the competition could be moving to a new arena: Celera announced last week that it is immediately directing its army of 300 sequencing machines to analyze the genome of the mouse—which is widely seen as being critical for understanding the human genome. The public consortium began a mouse sequencing project late last year. Celera expects to finish its work on the

mouse long before the public consortium, which is aiming to be done by 2005. But the consortium's mouse genome will be completed to fine detail and, unlike Celera's, it will be released on public Web sites.

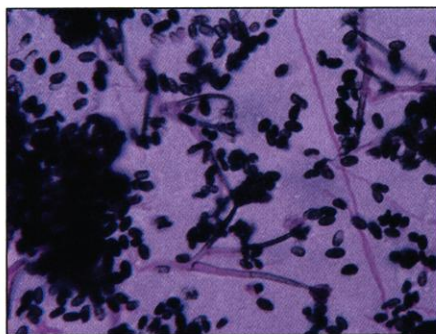
—ELIOT MARSHALL

PUBLIC HEALTH

A Mold's Toxic Legacy Revisited

In 1995, the Centers for Disease Control and Prevention (CDC) in Atlanta set off a cascade of alarms when an agency task force linked certain toxin-producing molds to a cluster of cases of sometimes fatal lung bleeding, or pulmonary hemorrhage, in infants. But last month, the CDC published the findings of two expert panels that identified what they called "serious shortcomings" in the initial investigation and concluded that "a possible association between acute pulmonary hemorrhage ... and [mold] exposure ... was not proven."

The reexamination is already stirring debate. Investigators involved in the original



Culprit? Uncertainty remains about whether toxic molds, like *S. chartarum*, trigger pulmonary hemorrhage in infants.

study are preparing a rebuttal of the CDC report to be posted on the Internet (gcr.meds.cwru.edu/stachy). And resolving the issue is important, because sick infants may be just the tip of the iceberg of much broader public health problems. Toxic molds, which cause allergies and asthma attacks in sensitive individuals, have also been linked to the elusive sick building syndrome, which, in turn, has led to lawsuits and efforts to clean up mold-contaminated buildings—both costing millions of dollars.

Dorr Dearborn, a pediatric pulmonologist at the Rainbow Babies' and Children's Hospital in Cleveland, triggered the original investigation in November 1994 when he alerted the CDC to a cluster of eight babies the hospital had treated for a normally rare bleeding of the lungs. The CDC immediately sent in a task force to look for possible causes. The team focused on the infants'

Hit or Missile? A few well-designed balloons could burst the Pentagon's planned nuclear missile defense, according to a report issued this week by the nonprofit Union of Concerned Scientists. The controversial \$7 billion system would send anti-missile missiles (right) crashing into enemy warheads sailing through space (*Science*, 16 April 1999, p. 416). But an 11-member panel led by Andrew Sessler, a physicist at Lawrence Berkeley National Laboratory and former head of the American Physical Society, says adversaries could bewilder the interceptors by making modest changes to warheads.



A shroud filled with chilly liquid nitrogen, for instance, could make a warhead virtually invisible to the interceptors' heat-seeking infrared eyes, the panel predicted. Similarly, hiding a warhead inside one of a flotilla of radar-reflecting balloons would bamboozle the system. In two tests against simpler targets, the panel noted that interceptors have scored just one hit.

Pentagon planners say they will "study" the report. But shield skeptic Representative Thomas Allen (D-ME) says it demonstrates that the expensive defense "will be obsolete by the time it is deployed." The next missile test is slated for June, and the Clinton Administration could decide by October to deploy the system's first phase, which could be in place by 2005.

Policing Science Indian scientists have drafted first-ever codes of conduct for researchers and scientific institutions. The 15-point scientists' code, drafted this week by 450 researchers at a National Symposium on Ethics in the Administration of Science in Hyderabad, says researchers shouldn't "cook" results, pad their publications list, or "yield to political or social pressures." And the 16-point institutional code calls for protecting whistleblowers by creating systems that "institutionalize dissent." Conferees also recommended that the government establish an independent Office of Research Integrity to investigate misconduct.

The next step is to present the recommendations to India's Department of Science and Technology, says Pushp Bhargava, president of the Society for Scientific Values, which sponsored the conference. He and other researchers hope the agency will eventually formulate an official "Charter for Scientists."

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