during the menstrual cycle.

Still, researchers have a great deal of work to do to find out what all the genes identified by the Kinzler-Vogelstein team do in normal angiogenesis, and whether any will be suitable targets for drug therapy. But the Hopkins workers are likely to have lots of help. "This paper will no doubt set off a flurry of work by other investigators," predicts Folkman. **–JEAN MARX**

MARINE CONSERVATION

Virginia Gets Crabby About Harvest Limits

Virginia is at odds with other Atlantic coastal states over a plan to protect horseshoe crabs. Virginia officials have refused to accept a quota on their harvest, arguing that it's not based on good science. Now, the Department of Commerce has scheduled a moratorium, to go into effect next month, that is aimed at preserving what many believe is a dwindling population.

The horseshoe crab is not really a crab at all, but a distant relative of spiders. Birdwatchers prize horseshoe crabs because their eggs provide nourishment for hungry migratory birds. Medical companies use crab blood to test injectable drugs for contamination. And the fishing industry uses crabs as bait for conch and eel. As demand from the growing conch fisheries has increased, crab harvest has skyrocketed, growing from 500 tons in 1990 to 3000 tons in 1997.

Ebb and flow. States disagree over how to protect horseshoe crabs.

The Audubon Society and other conservation groups fear that this demand may account for what appeared to be a sharp decline in horseshoe crab populations, originally noticed by volunteers in 1992. In response, Delaware and New Jersey officials in 1997 instituted stringent restrictions on their harvest. When fishers began landing their crabs in Maryland to avoid the restrictions, that state imposed its own 75% cut. That shifted the trade to Virginia, which now accounts for about a quarter of the harvest. In 1998, Maryland, Delaware, and New Jersey decided a coastwide management plan was needed, so they asked the Atlantic States Marine Fisheries Commission (ASMFC) to design one.

The scientists charged with the task soon realized that there was a lack of good data on horseshoe crab populations, says Jim Berkson, a fisheries scientist at Virginia Polytechnic Institute and State University in Blacksburg who participated in the stock assessment committee. But they were alarmed by the still-increasing harvest, fearing long-lasting effects on a species that takes 9 to 11 years to reach sexual maturity.

In February, ASMFC voted for a 25% reduction of the average harvest levels from 1995 through 1997. This was a compromise between the 50% cut desired by Maryland and other states and the status quo sought by Virginia. Virginia officials objected to what they said amounted to a 75% cut in what the state's conch industry needed. They argued that state laws require them to base their decisions on good science—which, they said, was absent here. State officials also argued that the problem needed to be quantified before a quota was established.

That position didn't pass muster with the commission, which saw it as a delaying tactic. In May, it found Virginia "out of compliance" and asked the Department of Commerce to shut down Virginia fisheries for not adhering to the commission's quota. "The bottom line is that decisions are made with whatever information is available," says Dieter Busch, director of ASMFC's Interstate Fisheries Management Program. Virginia's Marine Resources Commission has since reduced the legal harvest in half, to 355,000 crabs. But that still isn't good enough for federal officials. Last week the Department of Commerce proposed a moratorium for September, the start of the fall harvest.

Virginia hopes to convince the Atlantic commission at a meeting next week to ease its quota, and the fishing industry is watching closely. "We're hopeful," says Rick Robins, who runs Chesapeake Bay Packing in Newport News, Virginia, the largest exporter of conch. "But we're prepared to seek an injunction," he says, if the commission stands firm.

–ERIK STOKSTAD

AGRICULTURE

Variety Spices Up Chinese Rice Yields

The results of Chinese field trials reinforce the accepted scientific wisdom that planting different varieties of a crop in the same field holds down the spread of certain diseases and improves yields. And this time researchers seem to have convinced farmers, too.

Zhu Youyong, a plant pathologist at the Phytopathology Laboratory of Yunnan Province at Yunnan Agricultural University in Kunming, China, and colleagues report in the 17 August issue of *Nature* on a 2-year experiment that involved mixing two varieties of rice in the same field. Their work, involving thousands of local rice farmers, found an 18% rise in overall productivity, including greater profits for a premium-priced variety that is particularly susceptible to rice blast from a fungus.

Mixing it up. Monocultural plantings of rice, common in Yunnan Province and elsewhere, are more vulnerable to disease.

Most Yunnan farmers plant one variety of hybrid rice, with a few devoting some land to a more glutinous rice used for desserts and other regional specialties. Following Zhu's suggestion, however, farmers planted a single row of glutinous rice in the middle of a group of either four or six rows of hybrid rice. The experiment started on 812 hectares in 1998 and expanded to 3342 hectares in 1999. Monoculture control plots were grown at 15 small sites throughout the region.

The results show the power of variety. Researchers calculated that it would take an average of 1.18 hectares of monoculture cropland to produce the same amounts of hybrid and glutinous rice produced in 1 hectare of mixed crops. The most striking change was for individual glutinous plants grown in a mixed environment: They yielded up to 89% more rice than their monocultural cousins. What's more, because the glutinous rice fetches a premium price, the value per hectare of the mixed fields was 14% greater than the hybrid monoculture plots and 40% greater than the glutinous monoculture plots. In both years, blast destroyed about 20% of the glutinous rice grain in the monoculture plots but only 1% in the mixed plots. Blast damage in the hybrid rice, although much lower in general, also dropped, with a grain loss of only 1% in the mixed plots versus 2.3% in monoculture plots. The damage from blast was so reduced in the mixed plots that farmers stopped their periodic fungicide spraying. "The farmers are very happy," says Zhu.

Christopher Mundt, a plant pathologist at Oregon State University in Corvallis and a co-author of the paper, explains that different types of rice blast attack different varieties of rice. In a monoculture field of rice,

CREDITS: (LEFT TO RIGHT) R. PRICE/CORBIS; J. SOHM/CORBIS

he says, the blast can spread "like a fire through a field of dry grass." The fungus has a harder time finding a compatible host in a mixed environment.

Martin Wolfe, a plant pathologist and research director of the Elm Farm Research Center, an organic farming research center in Hamstead Marshall, Newbury, U.K., supports the approach but notes that the mixture must be tailored to local growing conditions. "This is a useful tool," says Wolfe, who has written a commentary in the same issue. "But you can't just rush in and plant together anything you like."

The message from Zhu's study appears to be spreading through Yunnan Province, where this year 40,000 hectares were planted in the mixed pattern, he says. The payoff, he adds, is easy to measure for farmers: "more rice and more money." –DENNIS NORMILE

MICROBIOLOGY

A Weak Link in TB Bacterium Is Found

Easily the most successful human pathogen in the world, the bacterium that causes tuberculosis infects one-third of the world's population. Often acting in deadly combination with AIDS, TB kills 2 million to 3 million people per year, more than any other infectious disease. The secret of the pathogen's success is that it can linger undetected in the lungs for decades, hiding from the macrophages that aim to chew it up and spit it out. Now a team of researchers has uncovered a vulnerability in this resilient bug that suggests new ways to starve it out of its bolt-hole.

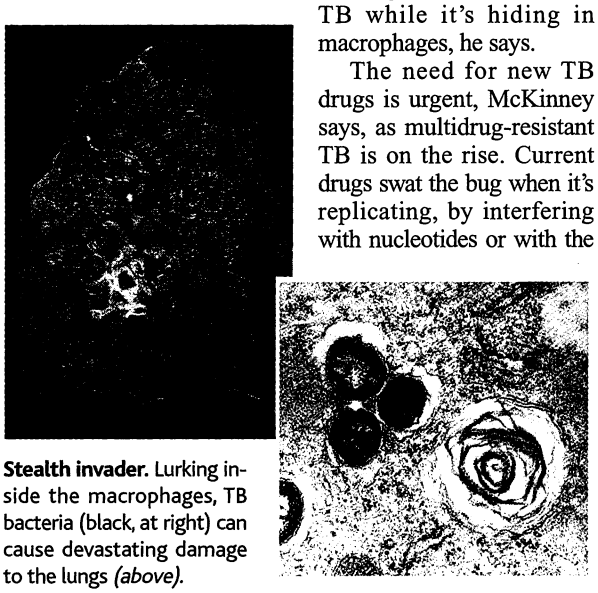
When *Mycobacterium tuberculosis* infects a person for the first time, it proliferates for a few weeks until the immune system marshals its defenses. The two then reach a stalemate, says John McKinney of The Rockefeller University in New York City, part of a four-institution team reporting its findings in the 17 August issue of *Nature*. This persistent state—the pathogen population doesn't increase, but the immune system can't get rid of the bacteria already ensconced—can last a lifetime, with the person suffering no obvious ill effects. But in 10% of those infected, TB will erupt into full-blown disease in response to various stresses or if the immune system is compromised.

During its latent days inside macrophages, the bacterium is stuck with a restricted diet: It eats carbon from lipids via a pathway called the glyoxylate shunt present in bacteria and plants. The TB bacterium also builds amino acids via the oft-memorized Krebs cycle, explains McKinney, but "we went after the glyoxylate shunt because it's the only [pathway the bacteria use for metabolism] not found in humans." Working with William Jacobs Jr. at the Albert Einstein College of Medicine in the Bronx, he created a knockout *M. tuberculosis* that lacks an enzyme called isocitrate lyase (ICL) that is critical for this pathway. Study collaborator David Russell of Cornell University in Ithaca, New York, discovered that ICL levels are elevated in *M. tuberculosis* when it's in its latent phase. Normal TB bacteria burrow into macrophages in mice and make themselves at home indefinitely, but McKinney's altered bacteria that can't produce ICL were wiped out by the animals' immune system.

"One of the things we don't understand is how *M. tuberculosis* can sit around in tissue for years or decades," says Jo Colston, an expert on microbial pathogenesis at the National Institute for Medical Research in London who was not involved in the study. "Obviously, if you can hit a protein that enables [the bacterium] to survive, that represents a potential therapy target."

McKinney and colleagues are searching for such compounds. In a second publication in the August issue of *Nature Structural Biology*, they describe the protein structure of ICL. They also identify two compounds that smother the active end of ICL and shut down the enzyme, thus preventing it from playing its part in the glyoxylate shunt. X-ray crystallographer James Sacchettini of Texas A&M University in College Station, a collaborator on both publications, says his group, working with research sponsor Glaxo Wellcome in the United Kingdom, will screen hundreds of thousands of additional compounds. Those that stymie ICL have potential to serve as drugs that can starve TB while it's hiding in macrophages, he says.

The need for new TB drugs is urgent, McKinney says, as multidrug-resistant TB is on the rise. Current drugs swat the bug when it's replicating, by interfering with nucleotides or with the



Stealth invader. Lurking inside the macrophages, TB bacteria (black, at right) can cause devastating damage to the lungs *(above)*.

CREDITS: (LEFT TO RIGHT) IMAGE FROM WEBPATH, COURTESY OF EDWARD C. KLATT; DAVID G. RUSSELL/CORNELL UNIVERSITY

ScienceScope

Defining Distress Plans by the U.S. government to change the way researchers characterize pain and distress in lab animals is drawing reaction from biomedical and animal-rights groups. In July, the U.S. Department of Agriculture (USDA) asked for comments on the new guidelines, which are supposed to help researchers spot and lessen discomfort in lab animals. Among other things, the plan defines "distress" as stress that has "negative effects on [an animal's] well being."

Last week, the Federation of American Societies for Experimental Biology (FASEB) said it would prefer a different definition, adopted by the National Research Council in 1992. It describes stress as "an aversive state in which an animal ... shows maladaptive behaviors." FASEB also wants practical rules that rely on the "professional judgement" of researchers and veterinarians.

The Humane Society of the United States and other groups, however, want USDA to adopt a Canadian-style scheme that ranks pain and distress into several categories, based on common lab procedures. "We need a scale with very clear-cut markers," says John McArdle, director of the Alternatives Research & Development Foundation of Eden Prairie, Minnesota. Other ideas may still surface, as USDA will receive comments until at least 8 September.

Orange Alliance At the urging of Senator Tom Daschle (D–SD), the National Institute of Environmental Health Sciences (NIEHS) is trying to team up with Vietnamese scientists to conduct studies of the health and environmental effects of dioxin. The chemical, implicated as a cause of cancer and other disorders, was present in the defoliant Agent Orange, which U.S. forces sprayed widely during the Vietnam war. Today, some Vietnamese carry tissue concentrations of dioxin that are up to 20 times higher than those found in people living in the United States.

This week, NIEHS gathered a group of epidemiologists and toxicologists in Monterey, California, to discuss research strategy and the resources needed to perform epidemiological studies in Vietnam. Later this year, NIEHS scientists plan to meet with their Vietnamese counterparts, with joint studies set to begin in 2002. "That is, assuming the Vietnamese are interested," says NIEHS's Chris Portier.

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