

SPACE RESEARCH

Mir Gets New Lease on Its Scientific Life

After more than 7 months in mothballs, the Mir space station is once again open for business. A Netherlands-based company called Mir Corp. is helping to fix up the aging and trouble-plagued facility to make it ready for researchers—and eventually rich tourists. But it could be a short-lived venture: The Russian government, which owns the 14-year-old facility, has not decided how long to keep it in orbit, and U.S. space officials say privately they would love to see it shut down once and for all.

Mir Corp. has pledged to spend at least \$20 million on the venture. It is backed by several wealthy American investors, including Washington, D.C.-based telecommunications millionaire Walter Anderson, and the majority shareholder is the Russian space company Energia, which operates Mir for the Russian government. As a start, Mir and Energia bankrolled the launch on 4 April of a Soyuz spacecraft carrying two cosmonauts to Mir. They will check out life-support systems on Mir's collection of pressurized modules, fix a small leak, and conduct some 50 Russian science and technology experiments. Mir Corp. officials hope that a successful mission will help convince Western governments and companies to reactivate experiments they already have on board and attract new paying customers.

Jeffrey Manber, Mir Corp. president and a former Washington representative of Energia, argues that Mir offers opportunities "ranging from industrial production and scientific experimentation to space tourism and in-orbit advertising." With completion of the international space station expected to slip from its scheduled 2004 date, Manber says Mir can serve as a temporary substitute for companies and governments that have set aside money for experiments: "There is already equipment on Mir which can be used very cost effectively."

Manber admits that doing science aboard Mir won't be a big moneymaker, and the company ultimately hopes to lure wealthy and adventurous tourists to visit the station. That idea received an unexpected boost last week from U.S. Transportation Secretary

Rodney Slater, who applauded the company's efforts to create a space tourism business during a speech to aerospace industry officials in Colorado Springs, Colorado.

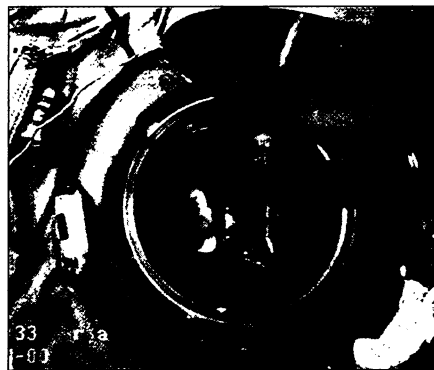
But many U.S. aerospace industry officials, NASA managers, and others familiar with Mir are skeptical about the company's prospects. Mir has suffered computer and power shutdowns, a fire, and a collision with a resupply vehicle that damaged one of its modules. And Russia's financial troubles

prevented significant upgrades during the 1990s. Moreover, the U.S. government in recent years has encouraged the Russians to deorbit Mir and concentrate the country's limited resources on building and launching its portion of the international station.

"There's a tough road ahead," says Manber, acknowledging the uncertain status of the facility. He is hopeful,

however, that the current mission will be followed this fall by a crew conducting experiments on behalf of Western scientists. But for now, Mir is proving that space stations can have many lives.

—ANDREW LAWLER



Back in business. Cosmonaut Alexander Kaleri waved as he entered Mir last week.

GENOME SEQUENCING

Claim and Counterclaim On the Human Genome

J. Craig Venter stole the show last week. The day before Venter appeared at a hearing of a House science subcommittee on 6 April to review research on the human genome, his company, Celera Genomics Corp. of Rockville, Maryland, issued a press release announcing that it had "completed the sequencing phase of one person's genome." The notice, which had a ring of finality about it, indicated that Celera's computers are poised to assemble the human data into a complete genome—a formidable task that Venter predicted at the hearing would take "3 to 6 weeks." Sometime later this year, he says, he will make the data available on Celera's Web site. Celera's stock, which had fallen abruptly in mid-March, soared.

It was an effective bit of propaganda: Celera released no new scientific data, but left the impression that it has bagged the human genome—just as it bagged the genome of the fruit fly in collaboration with the Berkeley *Drosophila* Genome Project earlier this year. But members of the nonprofit consortium that aims to complete

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to inactivate or "knock out" the *VR1* gene that they found that the resulting mice are impervious to capsaicin-induced pain.

For example, capsaicin injected into the hind paw of a normal mouse causes the animal to lick and shake the tender paw. However, the mutant mice barely reacted to the injection, and their paws did not swell or become inflamed as much as they do in normal mice. When researchers laced the drinking water of normal mice with capsaicin, the normal mice took one sip, rubbed their snouts, and stayed clear of the water bottle. The mutant mice, however, drank happily, says Caterina, who is now at Johns Hopkins University.

The mutant animals also tolerated high heat better, including having their tails immersed in a hot water bath and their paws put in contact with a hot plate. The animals did eventually react in both tests, showing that sensitivity was lessened, not eliminated, Caterina notes. This suggests that other heat-sensing channels play a role as well, he says.

Another type of test suggests that *VR1* plays a role in the extra sensitivity to heat usually displayed by inflamed tissues. Mustard oil painted onto the paws of normal mice causes them to become inflamed and very sensitive to heat—just as sunburned skin is seared by warm water or sunshine. But in the mice lacking *VR1*, the mustard-oil treatment did not enhance the response to heat, although the animals still displayed the hypersensitivity to touch that develops in inflamed tissues. Because touch-sensitive pain must be triggered by other neuronal responses, says Julius, the finding suggests that blocking *VR1* would not relieve a common, painful condition—extreme sensitivity to touch, such as that accompanying shingles.

The mouse work suggests, however, that such inhibitors may help combat another type of especially troubling pain, the chronic internal pain that can accompany tissue damage. Julius and his colleagues suspect that *VR1* receptors might contribute to such pain. They found, for example, that neurons carrying the receptors can be excited by the acidic environment produced by inflammation. But neurons from *VR1*-deficient mice bathed in an acidic solution did not react as vigorously as neurons from normal mice did. Thus, the researchers hope that blocking the *VR1* receptor might help relieve chronic internal pain.

The fact that the *VR1* knockout mice seem otherwise normal is encouraging for drug development, Campbell says. "It would appear that the [*VR1* receptor] molecules are specific to pain-sensing neurons," he says. That could lead to drugs with few side effects—perhaps only an inability to taste Tabasco sauce.

—GRETCHEN VOGEL

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'

ScienceScope

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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