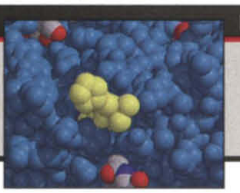
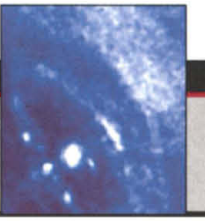


PAGE 1976
How acetaminophen works?



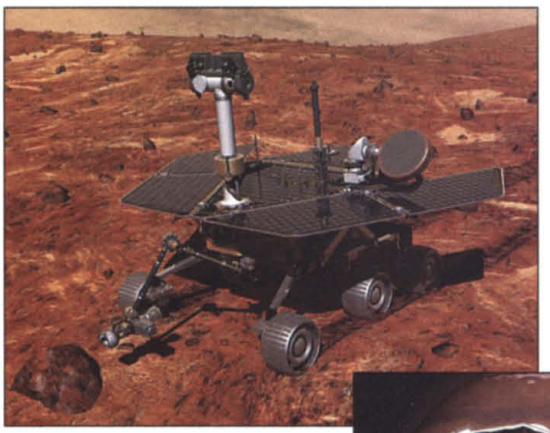
1979
Crab Nebula in action

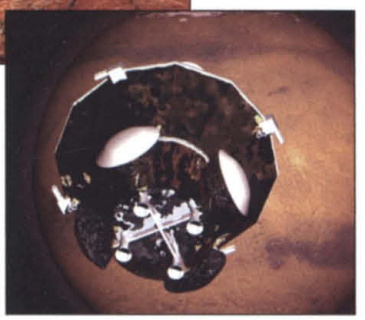
SOLAR SYSTEM EXPLORATION

France, Italy Threaten to Rain on Parade of Missions to Mars

PASADENA, CALIFORNIA—A carefully crafted international program to explore Mars is in danger of coming apart at the seams. Italy and France might soon scale back or cancel several collaborative projects with the United States, forcing a major revamping of Red Planet exploration in this decade and beyond. More immediately, design troubles on U.S. and European rover missions threaten to push back launches scheduled for next year.

The history of Mars missions is littered with technical failures, delays, and budget troubles, and many planetary scientists are taking the latest news in stride. But partial or full withdrawal of Italy and France would be a significant blow to an international effort to send increasingly sophisticated rovers and orbiters every 2 years to chip away at Mars's geological and atmospheric secrets. The missions are also meant to establish communications systems for more ambitious efforts, such as a sample return. But fiscal constraints, compounded by cost overruns, have led the French and Italian space agencies to reconsider their participation. "It is very, very serious," says Orlando Figueroa, NASA's Mars program director.





Red mess? A NASA rover (*above*) needs a better parachute by next year, and a 2007 French mission (*inset*) has financial problems.

The decade's lineup of missions is impressive. Next year NASA intends to launch two Mars rovers, and the European Space Agency (ESA) will launch an orbiter and a British-built lander; meanwhile, a Japanese spacecraft is expected to arrive in Mars orbit. In 2005, NASA plans to launch an orbiter with an important Italian instrument, followed in 2007 by a telecommunications spacecraft built with Italy. The same year, a group of countries led by France will launch a science orbiter and four small landers. A NASA-Italian science orbiter and a sophisticated NASA lander and rover are planned to follow in 2009, with a sample-return mission sometime in the next decade.

But Italy's space agency, ASI, might back out of its promise to provide NASA's 2005 spacecraft with a radar that would look for water in the top few hundred meters of the planet's crust. ASI president Sergio Vetrella warned NASA earlier this year that Italy might be forced to cancel the $20 million–plus instrument. "This is already practically under construction, only now we have to fight [as if this were] a new initiative," complains Giovanni Bignami, ASI's departing scientific director, whose resignation takes effect next month.

Locating the water on Mars is critical for NASA's long-term research program, says Jack Farmer, an astrobiologist at Arizona State University in Tempe. Figueroa says that it is too late to replace the radar instrument, but he's hopeful that ASI will make a firm commitment by the end of this month.

Italy also might decide not to join NASA in building the first martian telecommunications satellite for a 2007 launch and a synthetic aperture radar as part of a 2009 NASA-ASI science orbiter. Vetrella declined to comment, but Figueroa is preparing for the worst. He says NASA might combine the 2007 and 2009 orbiters into a single U.S. communications satellite.

French participation also might be on the ropes. France is leading a primarily European effort to send a science orbiter to Mars in 2007. It would conduct a test of orbital capture, setting the stage for a sample return with the United States, and would place four small craft on the surface to study the structure and composition of the planet's interior. The orbiter would include space for a NASA Scout mission, the details of which have yet to be determined.

But cost overruns recently prompted the French research minister to order a scaled-back version from CNES, the country's space agency. Options include postponing it by 2 years, reducing the capability of the orbiter, and scrapping the orbital-capture effort, according to Richard Bonneville of CNES. The landers remain the mission's highest priority.

U.S. officials and scientists are concerned, but they are playing down the impact on NASA's efforts—particularly its plans for a sample-return mission, which isn't likely until well into the next decade. "We're trying to structure the sample return so it doesn't necessarily require the French," says Farmer. The loss of the Scout opportunity would not hinder NASA's plans for another dedicated Scout mission, Figueroa adds.

Meanwhile, ESA is considering a more aggressive role in Mars exploration. Its current plans are to launch an orbiter dubbed Mars Express in 2003. A scientific advisory committee has recently sketched a set of follow-on missions, beginning with a rover called ExoMars in 2007 or 2009. It would be followed by a streamlined sample-return mission in 2011 and a more ambitious sample return in 2015.

Delegates from ESA member countries will vote on this plan next month; a funding decision will be made in late 2004. "We believe that if ESA takes a leadership role, other countries will come in," says Paul Clancy, who plans future programs at ESA's European Space Research and Technology Centre in Noordwijk, the Netherlands.

Whatever the fate of this initiative, scientists and engineers already have their hands full with near-term missions. Researchers from the University of Leicester and the Open University in the United Kingdom are currently racing to get their lander, called

CREDITS: (TOP TO BOTTOM) JPL/NASA; FINNISH METEOROLOGICAL INSTITUTE

Beagle 2, ready by the end of the year for integration into Mars Express. But tests of Beagle 2's balloons, which cushion its landing, did not go as expected, says Rudi Schmidt, ESA's Mars Express mission manager.

At the Jet Propulsion Laboratory (JPL) here, workers are attempting to solve a similar set of daunting technical problems involving the two rovers that are the centerpiece of the $800 million mission slated to be launched by NASA next summer. Recent tests on the airbag designed to cushion the fall proved successful, but the parachute to decelerate the speeding capsule has failed ground tests. Tests on three new parachute designs are slated for October. "If we don't have a parachute, we're not going to fly," says Chris Jones, JPL's planetary projects director.

Principal investigator Steven Squyres of Cornell University in Ithaca, New York, says he's philosophical about Mars exploration. He's confident that the NASA team will be able to solve the parachute problem and that the long-term issues will sort themselves out. Mars missions have "always been extremely difficult," he says. "But believe it or not, we have a more stable situation than anytime in the past 15 years." –ANDREW LAWLER

With reporting by Alexander Hellemans in Naples, Italy, Judy Redfearn in Bristol, U.K., and Daniel Clery in Cambridge, U.K.

CANCER IMMUNOTHERAPY

Select T Cells, Given Space, Shrink Tumors

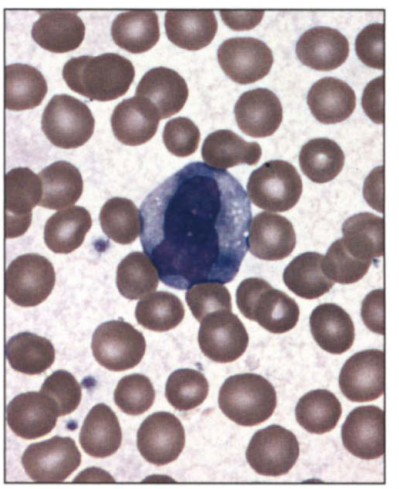
Tumors normally fend off any attacks by the immune system. But now scientists have found a way to give immune cells an edge, thereby shrinking tumors throughout the body, from the skin to the liver. The work, reported online by *Science* this week (www.sciencemag.org/cgi/content/abstract/1076514), breathes life into cancer immunotherapy, a field that has struggled to achieve success in humans.

For nearly 2 decades, immunologist Steven Rosenberg and his colleagues at the National Cancer Institute (NCI) in Bethesda, Maryland, have sought to fight tumors with T cells, the immune system's first line of defense. They have extracted cells from a patient's body, selected or modified them to improve their potency, and reinfused them. But the T cells often disappeared with little effect.

Rosenberg's new protocol, which incorporates a blast of chemotherapy and a more refined selection of immune cells than before, has had dramatically better results in a group of patients with metastatic melanoma. Although the therapy failed in some patients, in others it shriveled tumors. Of 13 volunteers, all of whom were expected to die within a few months, 10 remain alive 6 to 24 months after the first treatment.

"It's essentially what all of us have been striving for in immunotherapy," says James Mulé, an immunologist at the University of Michigan Medical School in Ann Arbor. Still, "it's really hard to predict how this will turn out" in the longer term and in larger groups of patients.

Unlike foreign intruders such as bacteria, tumor cells are the patient's own and hence are less viciously attacked by the immune system. However, the tumor surfaces of certain cancers have antigens, molecules that awaken the immune system and induce it to respond. Melanoma is one of these.



Top gun. A tumor-fighting T cell (center), surrounded by red blood cells, proved to be a vicious attacker of melanoma.

The researchers obtained tumor samples from each patient and searched for T cells that had infiltrated the tumors. Collecting as many as 50 T cell samples from a single tumor, they tested each against another tumor sample from the same patient. Rosenberg's team handpicked the two or three T cell samples that most effectively killed cancerous cells, and allowed the top T cells to multiply.

The NCI group decided that, to be effective, the selected T cells would have to make up the bulk of cells in each patient's immune system, at least temporarily, and persist long enough to act. The team administered chemotherapy to wipe out substantial numbers of existing immune cells and then reinfused the highly aggressive T cells.

Unlike many previous studies, this one not only relied on a type of T cell called a CD8 cell, which recognizes antigens and reacts, but also used CD4 cells. These "helper" T cells might have enabled the CD8 population to expand and retain its cancer-killing capacity.

In six patients, all tumors decreased in size by at least 50%: One 18-year-old remains disease-free 2 years after his treatment. The NCI group saw some tumor shrinkage in four others. Cells infused into two middle-aged men survived at unexpectedly high levels 4 months later; in one of the men, 97% of all immune cells were, for a brief time, the type infused. "[Rosenberg's] got numbers that nobody's seen before," says Bernard Fox, an immunologist at the Earle A. Chiles Research Institute in Portland, Oregon.

Still, although the treatment reached metastases buried in the lungs and liver, it didn't work well for everyone, and Rosenberg doesn't know why. "We have an enormous effort now trying to answer that question," he says. Another challenge is monitoring side effects: Four volunteers experienced a loss of skin pigmentation, and one suffered inflammation in the eye, signs that the therapy was attacking not only cancerous cells but normal pigment-producing cells as well. And it remains unclear whether one of the therapy's successes—enabling infused cells to persist—will have untoward effects.

Despite the hefty challenges that remain, Rosenberg and others hope this improved protocol can be adapted for other cancers and possibly even immune disorders such as AIDS. Offering infused T cells some elbowroom and handpicking only those most likely to succeed might improve the odds in battling once intractable diseases.

–JENNIFER COUZIN

CREDIT: S. ROSENBERG/NCI

BIOTERRORISM

NAS Censors Report on Agriculture Threats

When the U.S. Department of Agriculture (USDA) wanted to know if terrorists could disrupt the U.S. food supply, it turned to the National Academy of Sciences (NAS). This week, an academy panel made public its analysis—or at least most of it. Missing from the panel's report are eight hypothetical case studies that the academy excised because the material was