State honors. Chinese President Jiang Zemin, center, awards top science prize to Wu Wenjun, left, and Yuan Longping.

annual prize. But the central government declined for the third straight year to pick a first-place winner in two other categories—natural sciences and technological innovation—because none of the nominees met the criteria for having achieved "at the world level."

Members of the selection committee said their decision reflects the fact that China's basic research enterprise still trails the rest of the world and that most projects lack the creative spark needed to achieve fundamental advances in science. Greater investment in large, cooperative basic research projects would help close the gap, says an official with the science and technology ministry.

The top prize for international collaboration went to U.S. physicist Wolfgang Panofsky, former director of the Stanford Linear Accelerator Center in California, and Indian plant geneticist Gurdev Khush of the International Rice Research Institute in the Philippines. Hundreds of Chinese scientists and technicians received awards in one of the five categories, which include scientific and technological advancement. **–DING YIMIN**

Ding Yimin writes for *China Features* in Beijing.

INDIA

Work Starts on First Science Satellite

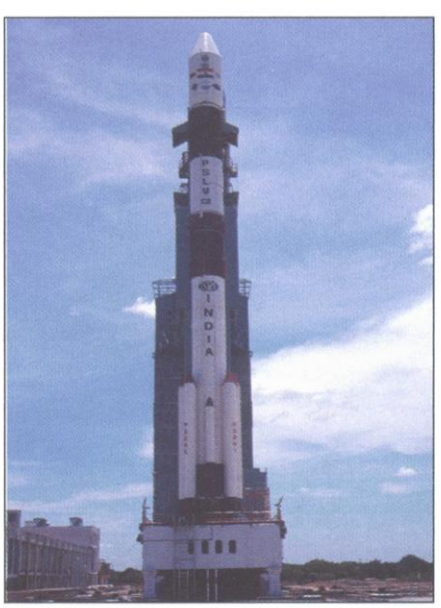
NEW DELHI—Indian astronomers have begun to design the country's first satellite dedicated to basic space science after receiving the green light last month from the Indian government. If successful, the payload will be launched in the second half of the decade on a domestically built rocket.

The project, dubbed Astrosat, aims to orbit four instruments to make broadband observations and surveys in the x-ray and ultraviolet (UV) regions of the spectrum. It would be funded by the Indian Space Research Organization, overseeing work by scientists at ISRO's satellite center, the Indian Institute of Astrophysics in Bangalore, and the Tata Institute of Fundamental Research (TIFR) in Mumbai. No price tag has been put on the mission. "We have to develop the prototype instruments in this period and show that we can indeed successfully make them in India," says Prahlad Chandra Agrawal, an astrophysicist at TIFR.

The instruments include soft x-ray and UV imaging telescopes as well as a large-area xenon-filled proportional counter and a cadmium-zinc-telluride array for long-duration studies over a broad range of spectral bands. The proposed payload is an order of magnitude more complex than one Agrawal's team built for an Indian satellite launched in 1996 to study x-ray sources within binary stars, and scientists say the large-field images should shed light on formation rates for low-redshifted stars. However, it falls well short of the high-resolution imaging and capabilities of the current generation of orbiting x-ray facilities, including NASA's Chandra X-ray Observatory and the European Space Agency's XMM-Newton.

"It's not something that we or the Japanese would be interested in doing at this point," says Peter Serlemitsos of NASA's Goddard Space Flight Center in Greenbelt, Maryland, which in the 1980s developed the foil mirror that the Indians hope to deploy on one of the x-ray instruments. "But if you're going to start a program, this isn't a bad way to do it. It should let them get their foot in the door."

Indian scientists are confident that they can make the mirrors and related optical devices. But they plan to seek outside help in developing other portions of the payload, in particular the photon-counting detector for the UV telescope. ISRO officials say that they hope to have designs completed in 18 months and to launch the satellite in "about 5 years" on ISRO's existing polar satellite



Looking up. India hopes to launch its first basic science satellite on this domestic rocket.

CREDITS: (TOP TO BOTTOM) JU PENG/XINHUA NEWS AGENCY; P. BAGLA

ScienceScope

Abbey Hits the Road One of NASA's top dogs has been sent to the doghouse. Space agency chief Dan Goldin last week removed George Abbey (below) as head of the Johnson Space Center in Houston, Texas, and transferred him to an undefined job at NASA headquarters in Washington, D.C.

Abbey played a key role in choosing Goldin for NASA's top job while he worked at the White House under former President George Bush in the early 1990s. He then served as Goldin's right-hand man in Washington before becoming space center commander in 1996.

The surprise fall from grace comes as NASA is struggling with major space station cost overruns—estimates run as high as $4 billion—which will likely force Goldin to make major cuts in other programs. Abbey and his center play a key role in station development. Goldin says only that it was time "for a change" and "reform." Rumors swirled this week over whether Abbey's removal was approved—or ordered—by the White House. Meanwhile, Goldin is still waiting to hear who his own successor will be.

Egalitarian Elitism The U.K.'s Royal Society is looking to inject more diversity into its hallowed rolls. Society president Sir Robert May this week prepared to announce a change in the nominating process that he hopes will net the elite group more researchers from less prestigious labs outside the biology and physics mainstream.

The society funds select researchers, advises the government, and has recently sought to raise its profile as a communicator in explaining how science shapes society. But May believes the nominating process—which leads to the election of 42 new fellows each year—has favored researchers working in traditional disciplines at science bastions such as Cambridge and Oxford universities. As a result, May notes, the process has missed such worthy candidates as computer scientist Tim Berners-Lee, inventor of the Web.

To "make it easier for us to pick up scientists in newly emerging disciplines," May says, he drafted a letter this week to U.K. university vice chancellors announcing that, from now on, nominees will need endorsements from just two current fellows, not six. This should help the society, May says, "not to overlook the Tim Berners-Lees of tomorrow."

Contributors: Vladimir Pokrovsky and Andrei Allakhverdov, David Malakoff, Andrew Lawler, Richard Stone

launch vehicle. The project has won the support of Indian Prime Minister Atal Behari Vajpayee, who in December touted his government's intention to build "a multiwavelength observatory to conduct front-ranking research in astronomy." –PALLAVA BAGLA

MICROBIOLOGY

Possible New Route to Polyketide Synthesis

For researchers prospecting for new drugs, one class of natural compounds—the polyketides—has long been the mother lode. These drugs, including such therapeutic mainstays as the antibiotic erythromycin, the immunosuppressive drug FK506, and the cholesterol-lowering drug lovastatin, have combined sales exceeding $10 billion per year. Now, researchers may have hit another rich vein: an improved method of synthesizing and engineering polyketides.

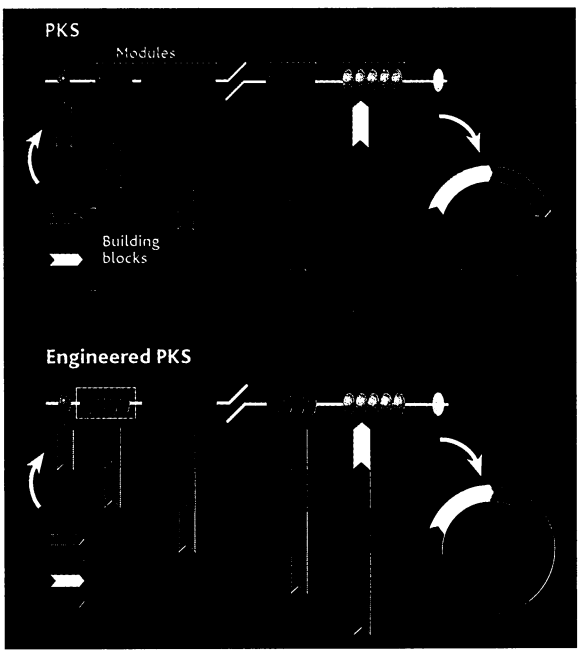
The compounds are difficult to synthesize, forcing drug companies to rely on production by their natural sources—unusual soil bacteria and fungi. Some of these microbes can be cultured readily, but many others are slow-growing and finicky, which makes them difficult to grow in the huge vats needed for industrial production. They're also tricky to alter genetically, hampering efforts to tweak the polyketide-synthesizing enzymes so that they make new variants. But on page 1790 of this issue, chemical engineer Chaitan Khosla of Stanford University and his colleagues report that they've engineered the common lab bacterium *Escherichia coli* to pump out a polyketide at rates potentially useful for industrial drug production.

Because *E. coli* is both easy to grow and highly amenable to genetic manipulation, the results offer a possible way of producing polyketides from exotic microbes in a much more tractable host. They also offer an opportunity to engineer new versions. "I think it's a real breakthrough," says bioorganic chemist Heinz Floss of the University of Washington, Seattle.

To pull it off, Khosla and his colleagues, Stanford graduate student Blaine Pfeifer, David Cane of Brown University in Providence, Rhode Island, and two others, had to overcome a series of formidable hurdles—adding the machinery for two new metabolic pathways and crippling another in *E. coli*.

The first problem was getting *E. coli* to make the enzyme that synthesizes the researcher's target polyketide, which forms the core of erythromycin. In nature, the bacteria that produce polyketides, in this case, a soil bacterium called *Saccharopolyspora erythraea*, rely on an unusual enzyme. This enzyme, polyketide synthase, sequentially joins a series of small building blocks to form the eventual product, which is a circular molecule. The enzyme itself consists of three very large proteins. As a result, the researchers had to introduce three *S. erythraea* genes into *E. coli* and fine-tune growth conditions just to make the enzyme.

The next challenge was getting the polyketide synthase to work in *E. coli*. These enzymes behave much like an assembly line, passing a growing polyketide chain from one active site to the next to add the next building block. The enzyme uses a cofactor compound called phosphopantetheine to carry out this transfer. But on its own, *E. coli* couldn't add the phosphopantetheine to polyketide synthase. To coax it to do so, the researchers added a gene from the soil bacterium *Bacillus subtilis* that produces another enzyme that attaches the cofactor.



Mix and match. By swapping or changing the modules that contain the active sites of polyketide synthases, researchers could engineer the enzymes to make novel polyketides in *E. coli*.

SOURCE: KOSAN BIOSCIENCES INC.

Finally, two modifications were needed to provide *E. coli* with the building blocks it needed to make the polyketide. To supply one, called propionyl coenzyme A (propionyl-CoA), the Stanford team knocked out key *E. coli* genes to cripple a metabolic pathway that breaks down that compound. To supply the other, called methylmalonyl-CoA, the Stanford team borrowed a gene from a third soil bacterium. If any one of their tricks had failed, the researchers would have had to start over. "We kept our fingers crossed to the very end," Khosla says.

Their efforts paid off, resulting in a bacterial strain that can pump out the polyketide at rates approaching those of industrial *S. erythraea* strains. In addition, by replacing one component of the *S. erythraea* polyketide synthase with a portion of an enzyme that makes a different type of drug, the Stanford team generated a hybrid enzyme that makes a polyketide unlike any found in nature. "They've demonstrated the feasibility of a directed approach" to making new polyketides, says microbiologist Joan Bennett of Tulane University in New Orleans, Louisiana, president-elect of the Society for Industrial Microbiology.

If *E. coli* can be used as a factory for making either natural or designer polyketides, the work could lead to a big payoff for Khosla and a company he co-founded, Kosan Biosciences of Hayward, California. Kosan owns the patent for the method and has the option of commercializing the discovery under a license agreement with Stanford. "We're going to ask now if we can use *E. coli* on a very large scale," says microbiologist Richard Hutchinson, Kosan's vice president of new technology.

Khosla and his colleagues still have a way to go to get industrial polyketide production by *E. coli*. They need to coax the microbe to add sugars to the polyketide to generate a complete erythromycin molecule. And if they accomplish that, Floss cautions, there's a chance that the antibiotic will kill the bacteria producing it. Khosla maintains that there are ways around those problems, such as having chemists add the sugars or stitching erythromycin-resistance genes into *E. coli*. "The important thing for people to realize is that it's not difficult anymore" for researchers to devise and produce new polyketides, Khosla says. If so, then the work may trigger another gold rush of polyketide prospectors.

–DAN FERBER

CELL BIOLOGY

Nobel Laureates Lobby for Stem Cells

Eighty Nobel Prize winners have signed a letter urging President Bush to allow government-funded researchers to work on human pluripotent stem cells. In a letter faxed to the White House on 22 February, they argue that the cells—which have the capacity to develop into any tissue type—could help treat a variety of diseases. The Bush Administration is under pressure from antiabortion groups to block federal funding for work on embryonic stem cells.

Scientific teams around the world are