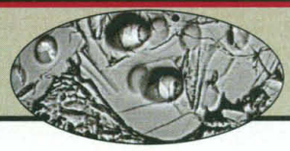
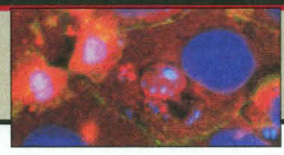
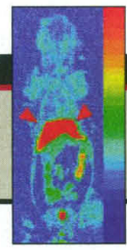






mune response.

Most gene therapists at the meeting agreed that Gelsinger's reaction was unusual. For example, Robert Warren, a clinician at the University of California, San Francisco, said that he had not seen serious toxicity—except in one patient who lost blood pressure—in the more than 40 cancer patients he has treated with adenovirus vector. Ron Crystal of Cornell University's New York Hospital said that he had administered similar vectors 140 times and seen a serious immune reaction only in one cystic fibrosis patient in 1993.

One researcher publicly challenged the notion that Gelsinger's reaction was unusual. Art Beaudet, chair of molecular and human genetics at Baylor College of Medicine in Houston and a member of RAC's special working group, said: "You don't need to evoke anything weird" in this case. Because adenovirus is known to trigger an immune response and because the Penn team kept raising the dose, Beaudet suggested, a sharp immune reaction might not be so strange. Thomas Caskey, a research executive at Merck & Co. of Whitehouse Station, New Jersey, also told *Science* that he thought the Penn trial had been "pushing the edge of the envelope." Beaudet and Caskey are both testing a new, "gutless" adenovirus vector stripped of all native genes, which they say has eliminated most toxic immune responses in animals. It hasn't been used in clinical trials, however.

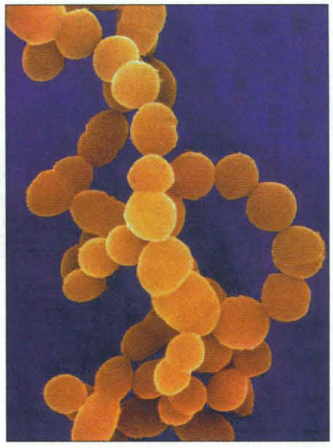
Members of the RAC and the special working group praised the investigators for sharing data and ended the session with mild proposals. Summing up, Verma urged clinicians to adopt a common index for dosing patients and a standard measure of virus particle concentration. These are "obvious" ideas, he said. Others suggested that RAC assemble a database on vectors and their effects; that clinicians screen patients more carefully; and that researchers collect better data on the fate of vectors in the body.

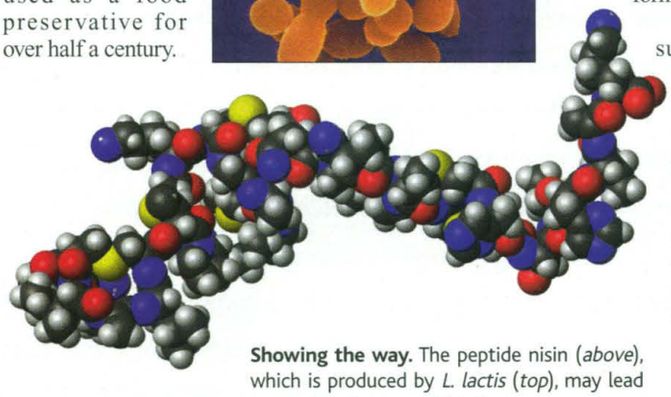
Gelsinger's death "did some damage to gene therapy, and it did some damage to clinical research," a key federal official said when the public meeting was over. The Food and Drug Administration has already announced that it found "deviations" from the protocol in Penn's conduct of the trial, including a decision to treat Gelsinger even though he had an ammonia level before the trial that was 30% to 60% higher than the agreed limit. The FDA is expected to issue a report and possibly a reprimand soon. The RAC and another NIH advisory group are thinking about how to improve the monitoring of gene therapy and will send recommendations to the NIH director for action early next year. **–ELIOT MARSHALL**

MICROBIOLOGY

Promising Antibiotic Candidate Identified

The ever-increasing resistance of pathogenic microbes to antibiotics has raised the specter of a "postantibiotic era" in which doctors are powerless to treat many bacterial infections. Even vancomycin, a longtime antibiotic of last resort, appears to be losing its punch. Now researchers have come up with a possible replacement—one that they say could lead to a whole new generation of antibiotics. It's not a brand-new invention, however. In fact, it has been used as a food preservative for over half a century.





Showing the way. The peptide nisin (*above*), which is produced by *L. lactis* (*top*), may lead researchers to new antibiotics.

The compound, nisin, is a peptide—a small proteinlike molecule—produced by *Lactococcus lactis*, a bacterium that can turn milk sour, to kill its competitors. Microbiologists have known for decades that nisin is an effective killer, but they never knew exactly how it worked. On page 2361, a Dutch-German team provides an answer. They show that the peptide latches onto a molecule on many bacterial cell membranes known as Lipid II—the same target used by vancomycin. The result suggests that nisin, or derivatives of it, could one day replace vancomycin as a broad-range antibiotic. And because nobody has ever found a bug that is resistant to nisin, the researchers hope that nisin and related compounds might trump the problem of bacterial resistance. "This looks like a very significant contribution," says biochemist Norman Hansen of the University of Maryland, College Park.

Nisin is only one of many antimicrobial peptides that have recently caught researchers' interest; others have been isolated from frog skin, insects, and plants, for instance. Most kill bacteria by sticking to and punching a hole in their fatty cell membranes. Some studies suggested that nisin might work the same way. But whereas large quantities of the other peptides are needed to do the job, limiting their usefulness, nisin always stood out because it is effective at concentrations up to 1000 times lower, making it a popular preservative for dairy and many other products. "There has always been this question about why nisin is different," says Tomas Ganz, who studies antimicrobial peptides at the University of California, Los Angeles.

Other work had suggested that might be because nisin has a different mode of action: Like vancomycin, it might bind to Lipid II, which is a precursor of the bacterial cell wall, a tough protective layer that lies outside the membrane. The binding would rob bacteria of their ability to build cell walls, eventually killing them.

The new study, from biochemists Eefjan Breukink and Ben de Kruijff of Utrecht University in the Netherlands, together with colleagues at three other institutions, indicates that both explanations are in fact partially correct. For example, the researchers found that nisin resembles magainin, a peptide antibiotic derived from frogs, in that it kills *Micrococcus flavus* bacteria within a few minutes by forming pores in the cell membrane. But they also found that van-

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comycin interferes with nisin's ability to make these holes, presumably because it competes with the peptide in binding to Lipid II. Conversely, when the researchers fused the bacterial membranes to artificial membranes loaded with extra Lipid II, nisin's pore-forming power was bolstered.

Apparently, says Breukink, Lipid II is a special key that nisin uses to punch its deadly holes—a key that other antimicrobial peptides lack. He does not yet know exactly how Lipid II helps nisin form pores. But he is sure that the peptide attaches to a different part of the lipid than vancomycin does, which may explain why bacteria have become resistant to vancomycin but not to nisin.

Now that researchers know that Lipid II is such an Achilles' heel for bacteria, they can try to devise a whole range of compounds that exploit it. The low doses needed would reduce the risk of side effects, Ganz says, and could help make the drugs economically feasible. And by tinkering a little with the nisin gene, researchers could easily produce many slightly different derivatives, for instance if resistance arises. "This holds the promise of giving access to huge numbers of antibiotics through relatively simple means," says Hansen.

But many hurdles will have to be overcome. For one, nisin can only kill *Streptococcus*, *Staphylococcus*, and other so-called gram-positive bacteria. Another problem is that peptides have a short lifetime in the body and a higher risk of triggering allergic reactions than conventional antibiotics have. Still, the new study may help motivate the pharmaceutical industry to overcome such obstacles, says Hansen: "They just have never recognized the potential of these antimicrobial peptides." **–MARTIN ENSERINK**

SPACE

Europe Lofts X-ray Observatory

To the relief and delight of engineers and x-ray astronomers, Europe's new space workhorse, the Ariane 5 launcher, deposited a $640 million x-ray observatory into orbit on 10 December. If all goes well, the European Space Agency's X-ray Multi-Mirror Mission (XMM) will capture images of very distant sources of fluctuating x-rays, such as those produced by black holes or supernova explosions.

Onlookers at the Kourou, French Guiana, spaceport had their hearts in their throats as the Ariane 5 rocket lifted off. They remembered the fireworks caused by the first Ariane 5, which exploded in June 1996 while carrying a squadron of four space probes. The launch proceeded smoothly, however, and XMM was gradually brought into its final, elongated, 48-hour orbit that will keep it largely out of Earth's radiation belts, reports Giovanni Bignami, science director of the Italian Space Agency, who witnessed the launch. "The solar panels have also opened with no problem," he says.

The 10-meter-long spacecraft carries a set of three x-ray telescopes that together contain 58 mirrors with a total surface area of 120 square meters. These mirrors focus the x-rays onto charge-coupled device (CCD) cameras that capture images of the observed objects and also measure the wavelength of the x-rays. Two telescopes are also connected to diffraction gratings that spread out the x-rays according to wavelength so that researchers can study

Heart of gold. An engineer puts together XMM's many-mirrored scope.

x-ray spectra with a much higher precision than that from the CCDs. XMM's scopes have lower resolution than those of Chandra, the x-ray observatory launched by NASA in July, but they excel at sensitivity —they are 5 to 15 times more sensitive depending on the wavelength and can pick up fainter or more fleeting signals. Bignami, who was the principal investigator for the prime focus CCD cameras until 1998, expects that because of its elongated orbit and better shielding procedures, the CCDs will not suffer the same radiation damage that has slightly impaired some of Chandra's detectors. The CCDs can be closed off with an aluminum shield whenever XMM enters the radiation belts near Earth or during a solar flare.

Like Chandra and Astro-E—a Japanese observatory that will be launched to look at shorter wavelength x-rays in January (*Science*, 30 July, p. 652)—XMM will focus its attention on x-ray producers such as hot gases, supernova remnants, jets of material squirting out of exploding stars, and massive black holes at the centers of galaxies. Astronomers are anxiously anticipating XMM x-ray data from enigmatic black holes. Because their x-ray outputs can fluctuate rapidly, XMM's sensitivity will be an advantage

CREDITS: (LEFT TO RIGHT) ESA; COBE/NASA/ESA

ScienceScope

Cell Division The American Society for Cell Biology (ASCB)—a small but aggressive group whose members include such scientific leaders as molecular biologists Harold Varmus and Bruce Alberts—has decided to strike out on its own. The ASCB board voted last week to split from the 67,000-member umbrella group known as the Federation of American Societies for Experimental Biology (FASEB) in 2001.

The 9000-member ASCB can use its "limited resources more effectively" if staffers don't have to spend time coordinating with FASEB's policy review process, says ASCB president Randy Shekman. The society will continue to work with FASEB, he notes, but will focus on its own key interests. For example, FASEB took no position this year on federal funding of human stem cell research, while ASCB lobbied intensively in favor of government backing for the controversial studies. FASEB issued no comment on the ASCB's departure.

Tanning Salon Warning: Building the space station could be hazardous to your health. That's the message from a National Research Council panel, which last week urged NASA to find a way to warn spacewalking construction crews of impending solar storms (right). Flares and coronal mass ejections from the sun can unleash massive streams of charged particles, which could pack enough energy to harm astronauts working outside the relative protection of the space shuttle or station modules. The risk of injury is rising, as the sun will reach the peak of activity in its 11-year cycle in 2001.

Researchers, however, do not yet have a good grasp on predicting solar storms. So the panel, chaired by Boston University physicist George Siscoe, urged NASA and other agencies to use satellites, such as the existing Solar and Heliospheric Observatory (SOHO) and spacecraft slated to begin monitoring the sun next year, to anchor an early warning system that would tell astronauts when to stay indoors. NASA solar research chief George Withbroe, who requested the report, says he is confident the new space-based sentinels—which will provide more detailed data than SOHO alone—will soon give Earth-bound researchers a better grip on predicting solar events.