

a cell, the RNA translates itself into a large protein, which is then cleaved to produce a cluster of smaller ones. Those proteins attack critical cells such as neurons in the central nervous system.

The researchers—Jeronimo Cello, Aniko Paul, and Eckard Wimmer of the State University of New York, Stony Brook—built an almost perfect replica of the virus, reading the recipe available in a public database of the letters that make up the virus's chemical code. Because RNA is chemically unstable, the scientists converted the RNA sequence to DNA, replacing every uracil base with a thymine. Then they ordered short stretches of carefully arranged bases from one of the many companies that churns out such piece-meal DNA. Cello took about a year to layer these fragments together to form the first third of the virus. Once he established that these stretches stayed oriented correctly, he hired a DNA synthesis company to assemble the remaining portion, which it did in 2 months. To distinguish the synthetic virus from natural strains, the group inserted 19 markers, minor mutations that weren't expected to alter polio's behavior.

DNA in hand, the researchers immersed it in enzymes to convert it back to the RNA at polio's core. The artificial poliovirus acted much like its natural counterpart: It multiplied, and antibodies could block it from entering cells. Mice injected with the synthesized virus became paralyzed after about a week, as did animals infected with normal poliovirus. But the artificial version was less lethal: Between 1000 and 10,000 times more virus was needed to kill an animal. The team suspects that one or more of the 19 markers are hobbling the virus.

The research might throw a wrench into polio eradication plans. "It erodes the underpinning of the whole eradication concept," says Peter Jahrling, a smallpox researcher at the U.S. Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland. Last month the World Health Organization (WHO) announced that it had erased

the disease from the European continent, and, according to Bruce Aylward, WHO's coordinator of the Global Polio Eradication Initiative in Geneva, "the goal is to stop immunization" once the disease is fully eradicated. But given the possibility of recreating the virus, researchers who favor continued immunization, such as Donald A. Henderson, an adviser to the U.S. government on bioterrorism policies, hope that WHO will reconsider its stance.

Then there's the question of whether one could reconstruct other pathogens whose sequences are publicly available. Smallpox, among the most feared bioterror agents, is far more massive than polio at 185,000 bases and far more complex. LeDuc, for one, doesn't believe that rebuilding it is imminently doable. But given the new results, others aren't so sure. "In principle, yes, [it's] possible to synthesize smallpox," says Vadim Agol, a virologist at the Russian Academy of Medical Sciences in Moscow.

Despite such nightmarish scenarios, scientists have no plan to stop posting new genetic sequences online. Wimmer says that no concerns were raised to him about publishing the paper. As Cello says, "By releasing this you alert the authorities ... [about] what bioterrorists could do."

—JENNIFER COUZIN

EMBRYONIC STEM CELLS

Stem Cells Not So Stealthy After All

Human embryonic stem (ES) cells get no free pass from the immune system, contrary to some researchers' early hopes. As the cells differentiate, they express increasing levels of the telltale tags the body uses to distinguish between native and foreign cells. The findings, published online this week by the *Proceedings of the National Academy of Sciences*, confirm that a patient's immune system would be likely to reject transplanted tissues derived from ES cells. Scientists hoping to use the cells to treat Parkinson's disease, diabetes, and other maladies will therefore have to find ways to reconcile the body's defense system with the transplanted cells.

Earlier evidence from human embryos raised the slim but tantalizing possibility that ES cells might be "immune privileged," unrecognizable by the body's defenses against foreign cells. One study reported that the embryo cells that give rise to ES cells do not express the so-called MHC proteins that help the immune system identify an invader; another produced inconclusive results. That led some researchers to hope that transplanted tissue derived from ES cells might remain under the radar of the immune system.

Although the new results are not unexpected, they lay that hope to rest, says Hugh

Pasteur Loses A French civil court has found the Pasteur Institute in Paris to be responsible for a woman's death last year from Creutzfeldt-Jakob disease (CJD). Pascale Fachin contracted the brain-wasting disease in 1985 from contaminated human growth hormone (HGH) prepared by Pasteur scientists (*Science*, 31 May, p. 1587). The Montpellier court in southern France ordered Pasteur and the endocrinology group Association France-Hypophyse to pay nearly \$800,000 in damages to the family of the 30-year-old Fachin, half of it immediately.

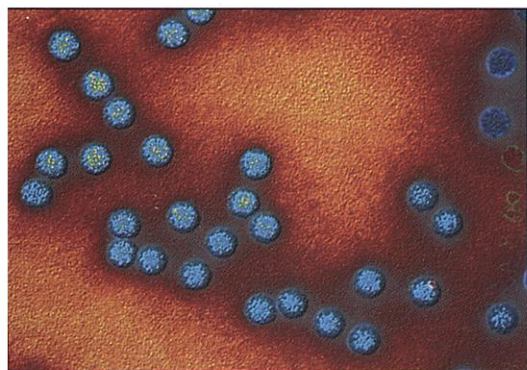
The institute plans to appeal, arguing that it could not be responsible for the contamination because it was "of a biological nature." The institute's insurance company has refused to cover the damages because it considers Pasteur to be the producer, not supplier, of HGH—a question the court ruling does not resolve. A defeat at the appellate level could unleash a flood of similar claims against the institute from other families of CJD victims.

Space Fantasy Russia's space industry has fallen on hard times since the breakup of the Soviet Union. And even its former competitors, the United States and Europe, are scrambling to pay for current projects such as the international space station. But last week, Russian officials made headlines around the world when they said that they have begun talks with European and U.S. space officials on a 2015 flight to Mars involving a six-person crew.

Nikolay Anfinov, R&D director of the Institute for Machine Building, and Vitaly Semenov, head of the Rosaviakosmos Keldysh Center, laid out a proposal for a 440-day flight—and a 2-month tour of the Red Planet—at a Moscow space conference. They estimated that the mission would cost a mere \$20 billion. If true, that would be a real bargain, as the U.S. Apollo project cost \$100 billion in deflated, 1960s dollars.

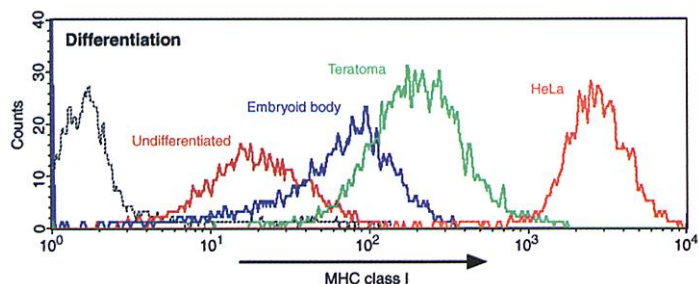
Not surprisingly, Western officials are skeptical. "NASA has received no plans or proposals," says one agency official, who adds that Russia has enough trouble meeting its obligations for the space station without bankrolling a trip to another planet.

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According to plan. Poliovirus reconstructed from its genetic sequence is indistinguishable from the original, shown here.

CREDITS: (TOP TO BOTTOM) GRC/NASA; GELDERBLON/VE OF SCIENCE/PHOTO RESEARCHERS INC.



Out of hiding. As they differentiate, human ES cells express increasing levels of immune system proteins.

Auchincloss, a transplant surgeon at Harvard Medical School in Boston, who notes that he has frequently heard scientists claim that MHC proteins aren't expressed in ES cells. "As simple as the data are here, it's something that we didn't know before," he says.

Graduate student Micha Drukker, cell biologist Nissim Benvenisty, and their colleagues at the Hebrew University of Jerusalem looked for MHC molecules in three human ES cell lines. Two were derived at the University of Wisconsin, Madison, and the third at Monash University in Melbourne, Australia. The team used a fluorescent-tagged antibody that attaches to MHC molecules and measured the amount of fluorescence that showed up in three stages of ES cell development: undifferentiated ES cells; so-called embryoid bodies that form as ES cells begin to differentiate; and teratomas, which are tumors formed by differentiated ES cells. As a control, they also tested a non-ES human cell line called HeLa.

The team found very low, but consistent, expression of MHC class I molecules on the undifferentiated ES cells. However, as the cells differentiated, they produced higher levels of the proteins. Although the levels are not as high as in the HeLa cells, they are high enough that they would probably trigger an immune reaction, says J. Andrew Bradley, a transplant surgeon at Cambridge University, U.K.

Even though ES cells aren't invisible to the immune system, scientists have several potential avenues around the problem of transplant rejection. They could genetically alter ES cells so that MHC proteins would not be expressed, build up a cell bank—similar to a blood bank—of cells with a range of MHC profiles, or use nuclear transfer techniques—better known as cloning—to create genetically matched ES cells for individual patients.

But each approach has its drawbacks. "It is hard to imagine an ES cell line bank that would have a match for all patients," Auchincloss says. Genetically altering ES cells to develop a "universal donor" cell that would not express MHC proteins is not only technically difficult but could leave the resulting tissue more susceptible to infections and

tumors—two things MHC molecules help the body fight against. And deriving genetically matched stem cell lines for individual patients using nuclear transfer techniques is not only controversial but would likely be too expensive for treating large numbers of patients, says Bradley.

The news is not all bad, Bradley notes. The relatively low levels of MHC expression might at least mean that tissues derived from ES cells would be less prone to rejection than today's whole-organ transplants.

—GRETCHEN VOGEL

SOLAR SYSTEM ORIGINS

Diamond Dust Dearth Raises Doubts

Most experts agree that the solar system's most ancient rocks from asteroids and comets should be sprinkled with microscopic diamond dust, a remnant of ancient stars. The less altered the rock since the gas and dust of the solar nebula came together, the more star dust should survive. But a group of researchers reported this week that at least some of the most primitive, unaltered rock in the solar system contains no diamond star dust at all. The finding raises questions about just how star stuff came to form the solar system. "It really was an unexpected result," says microscopist Lindsay Keller of NASA's Johnson Space Center in Houston, who was not in on the (non)discovery. "Why nanodiamonds are not there is uncertain."

During the past few decades, researchers

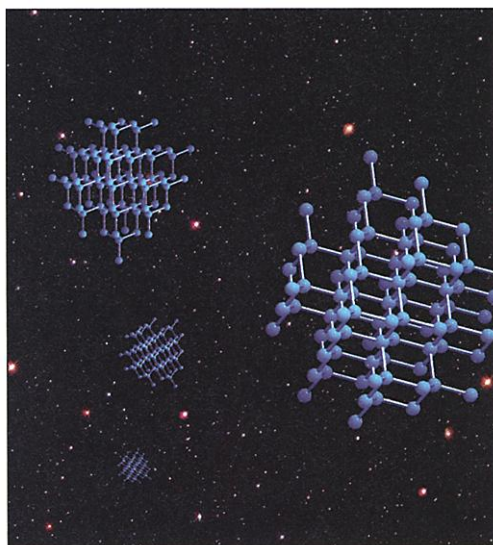
have found interstellar dust grains in some less altered meteorites by doing what one cosmochemist called "burning down the haystack to find the needle": dissolving a meteorite until only the hardy mineral bits condensed in the atmospheres of stars long ago—silicon carbide, graphite, and diamond—remain. The diamond flecks are so small (3 nanometers in diameter, on average) that a single grain might contain just a couple of thousand carbon atoms. Three years ago, microscopist Zurong Dai of Georgia Institute of Technology in Atlanta and his colleagues decided to extend the diamond hunt to microscopic interplanetary dust particles (IDPs) that flaked off asteroids and comets and now sift down through the stratosphere.

IDPs are too small for the "burn down the haystack" approach, so in an analytical tour de force Dai and his colleagues exposed the nanodiamonds by careful acid dissolution and identified them by measuring their distinctive atom-to-atom distance under high-resolution transmission electron microscopy. As they reported in this week's issue of *Nature*, they found plenty of nanodiamonds in two famous primitive meteorites—Murchison and Orgueil—as well as in two primitive micrometeorites retrieved from antarctic ice and four large, "cluster-type" IDPs from the stratosphere. But they found none in five smaller IDPs, although they were just as compositionally primitive as the cluster IDPs—and therefore also presumably came from the outer parts of the solar system, where stellar nanodiamonds are most likely to have survived. "We should have found nanodiamonds in every [sample] we looked at, but we didn't," says cosmochemist John Bradley of Lawrence Livermore National Laboratory in California, a co-author on the Dai paper. "That's puzzling."

The absence of nanodiamonds in half the IDPs examined has "no easy explanation," says Bradley. The simplest answer, the group writes, would be that most nanodiamonds were not formed around ancient stars at all but in the inner parts of the disk-shaped solar nebula as the solar system formed. That could leave detectable numbers of nanodiamonds in IDPs that formed closer in but not in more distant ones. The catch is that, if popular theories about chemical conditions in the early solar system are correct, diamonds shouldn't have been able to form there.

Alternatively, the asteroids or comets that produced the smaller IDPs might have been altered enough to have lost their nanodiamonds. If such bodies turn out not to be primitive, meteoriticists will lose one of their main sources of information about the formation of the solar system—a sacrifice they would hate to have to make.

—RICHARD A. KERR



Sky with diamonds. Rather than star dust, nanometer-sized diamonds may be a product of the newborn sun.