2000 was a banner year for scientists deciphering the "book of life"; this year saw the completion of the genome sequences of complex organisms ranging from the fruit fly to the human

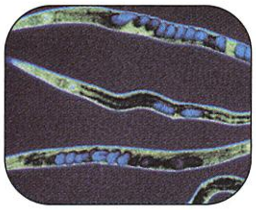
Genomics Comes of Age

Genomes carry the torch of life from one generation to the next for every organism on Earth. Each genome—physically just molecules of DNA—is a script written in a four-letter alphabet. Not too long ago, determining the precise sequence of those letters was such a slow, tedious process that only the most dedicated geneticist would attempt to read any one "paragraph"—a single gene. But today, genome sequencing is a billion-dollar, worldwide enterprise. Terabytes of sequence data generated through a melding of biology, chemistry, physics, mathematics, computer science, and engineering are changing the way biologists work and think. *Science* marks the production of this torrent of genome data as the Breakthrough of 2000; it might well be the breakthrough of the decade, perhaps even the century, for all its potential to alter our view of the world we live in.

The pace has been frantic. A year ago researchers had completely read the genome of only one multicellular organism, a worm called *Caenorhabditis elegans*. Now sequences exist for the fruit fly, the human, and plant geneticists' beloved benchmark weed, *Arabidopsis thaliana*. And drafts of the genomes of the mouse, rat, zebrafish, and two species of pufferfish are not far behind. Researchers have also been churning through the genomes of simpler organisms: Some five dozen microbial genomes are now on file, including those of the villains that cause cholera and meningitis. Most of these data are accessible to scientists free of charge, catalyzing a vast exploration for new discoveries.

As a result, genomics—the study of genome data—is now in hyperdrive. By comparing mouse to human, worm to fly, or even mouse to mouse, a new breed of computer-savvy biologists is hacking through the thickets of DNA code, discovering not just genes but also other important bits of genetic material, and even evolutionary secrets. We are learning, for example, that we have a lot more in common with Earth's other biota than we thought. Far from being a culmination, these genome libraries will break open decades of new laboratory investigations. And rather than investigate single genes, many 21st-century researchers will tackle whole families of genes and whole pathways of interacting proteins. Indeed, researchers are already studying how patterns of gene expression differ from one tissue to another and under different conditions.

This is a long way from the start of the 20th century, when geneticists were just rediscovering the seminal work of Gregor Mendel, a monk whose experiments with pea plants led to the first insights about heredity. It took until the 1950s for researchers to unmask DNA as the bearer of the genetic code. During the next 2 decades, biochemists developed the cloning and sequencing tools needed to fish out genes. By 1990, an insatiable hunger to know all the genes encoded in the DNA of humans prompted the establishment of the international Human Genome Project. It was biology's first foray into big science, and by almost any measure, it has been a great success. The genome achievements this past year epitomize this century-long and decade-long quest.

Genome count. The genomes of (*top to bottom*) a mustard-like weed, a nematode, a fruit fly, and humans are out, with more to follow.

Most remarkably, sequencing output has skyrocketed: In May 1999, the public archives contained about 700 million bases of the human genome; by May this year, the figure was more than 3 billion and just 3 months later, more than 4 billion. This is partly thanks to an increase in government, corporate, and foundation support. But new technology in the form of better automated sequencers, as well as intense competition between public and private sequencing efforts, also drove this acceleration.

Sequencing is also faster because gene wranglers have shifted their focus from turning out finished genomes, in which all the bases are in the right order, to generating draft sequence, with bases and even whole sections of DNA still missing or in the wrong place. So whereas human chromosomes 22 (finished late last year) and 21 (completed in May), as well as the *Arabidopsis* genome (published last week), have all undergone time-consuming "finishing" in which the pieces are put in the right order and discrepancies are resolved, most of the rest of the human genome data that are freely available to the public exist as draft sequence and are only now being cleaned up.

One of the first tests of the value of less-than-completely-finished sequences came in March, when academic experts and Celera Genomics of Rockville, Maryland, teamed up to publish the genome of *Drosophila melano-gaster*, a fruit fly long studied by geneticists. Even with some 1200 gaps where bases were missing altogether, the sequence yielded many new insights about how genomes work.

The *Drosophila* project also demonstrated the potential of whole-genome shotgun sequencing for large genomes. In this approach, the entire genome is chopped up into millions of overlapping pieces, which are sequenced and reassembled all at once. Shotgunning had worked for sequencing microbial genomes—smaller than 10 million bases—but until *Drosophila*, most sequencers had tackled larger genomes piece by piece, dividing each piece into small chunks for sequencing and assembly. The completion of the *Drosophila* genome convinced most that some combination of a whole-genome shotgun and the piece-by-piece approach might be the most efficient way to decipher big genomes.

The *Drosophila* project was hailed as a model of public-private collaboration. It stands in sharp contrast to the acrimony between Celera and the publicly funded international Human Genome Project over the sequencing of the human genome. That rivalry reached an all-time low in early spring, with

CREDITS: (TOP TO BOTTOM) JOSHUA MYLNE; JAMES KING-HOLMES/SPL/PHOTO RESEARCHERS; K. B. SANDVED/VISUALS UNLIMITED; SPIKE/PHOTODISC barbs flying in the press. But by June, relations had improved enough that the two groups jointly celebrated the near completion of a rough draft at the White House. Although the two groups are not working together per se, they have agreed to publish their work to date on the human genome sequence simultaneously, most likely in early 2001. Meanwhile, the Human Genome Project has released its sequence data free of charge through a publicly accessible database and is moving ahead with finishing the draft. It should have that job done by the end of 2003, if not sooner. Until its paper is published, Celera is making its human data available only to academic and commercial subscribers.

Already, researchers are using the new technology to study many genes or proteins at once. Dotting thousands of bits of genetic material on gene chips for studying the simultaneous expression of thousands of genes has resulted in new insights into the heterogeneity of cancer, the causes of aging, and the complexity of the immune system. And databases of genetic markers called single-nucleotide polymorphisms, or SNPs, which differ from one person to the next, should prove useful in tracking down disease genes and assessing an individual's susceptibility to certain diseases.

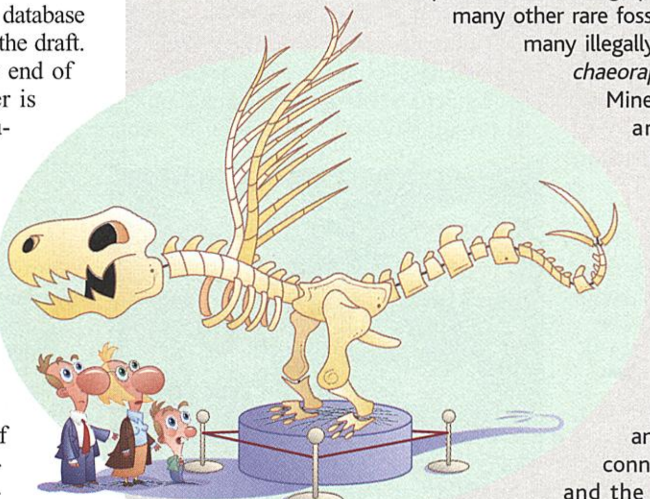
Yet, it's not the genes but the proteins they code for that actually do all the work. A host of promising procedures has cranked up the study of these workhorses, including microarrays made with protein spots instead of DNA spots. In 2000, during their search for new protein-protein interactions, researchers parlayed information about 27 nematode proteins with known roles so as to glean the functions of 100 others that had been complete mysteries. These efforts bespeak the coming era of proteomics, the identification and characterization of each protein and its structure, and of every protein-protein interaction.

This explosion of genetic knowledge comes with some heavy ethical and social baggage: It is not clear how society will deal with the growing potential to manipulate genomes, and many governments are grappling with how to protect individual rights once the technology exists for reading each person's genome. But the allure of this knowledge has made the quest irresistible. The world eagerly awaits the published draft of the human genome, with its genes outlined and its character explained. And almost as eagerly, the gene searchers are chasing down the genomes of many other organisms, a quest that will tell us more about our own genome as well as about our place in the grand library of life. —ELIZABETH PENNISI

Disappearing Discovery of the Year: *Archaeoraptor*

Hailed as "a true missing link" between birds and dinosaurs when it debuted in *National Geographic* in November 1999, *Archaeoraptor* soared off in a burst of media fame. But early this year the flying dinosaur fell to Earth in a jumble of parts from two distinct fossils—a primitive bird and a dinosaur. "It hurt us tremendously," says Jim Kirkland of the Utah Geological Survey, who worries that the public will think all feathered dinos are fake.

The 125-million-year-old fossil comes from Liaoning Province in China, a location that has produced stunning specimens of feathered dinosaurs and many other rare fossils (*Science*, 13 March 1998, p. 1626), many illegally smuggled out. In February 1999, *Archaeoraptor* surfaced at the Tucson Gem and Mineral Show, where Stephen Czerkas, an artist and amateur paleontologist, bought it for $80,000 from a dealer.



Czerkas wanted his friend Philip Currie, a paleontologist at the Royal Tyrrell Museum in Canada, to co-author a scientific paper on his find. Currie agreed—on the condition that the fossil be returned to China—and mentioned the specimen to *National Geographic*. But when Currie finally examined it, he realized he couldn't see a connection between the dinosaurian tail and the body. They still believed the parts came from the same animal.

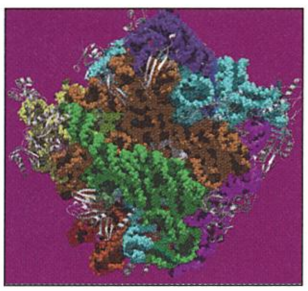
None of these problems sank in at *National Geographic*, which was preparing a feature story. When *Nature* and *Science* both turned down the scientific paper, *National Geographic* found itself in the awkward position of publishing the description of—and naming—the fossil; that's supposed to happen in a scientific journal, not in a mainstream magazine, and it annoyed paleontologists. "We were locked into a publication schedule at that point," says Barbara Moffet of the National Geographic Society's public affairs office. "The time ran out."

Archaeoraptor's demise came in December, when Xu Xing of the Institute of Vertebrate Paleontology and Paleoanthropology in Beijing notified *National Geographic* of a counterslab containing *Archaeoraptor*'s dinosaurian tail. It was attached not to a bird, but to a type of dinosaur called a dromaeosaur. In April, a panel of scientists convened by *National Geographic* examined that slab and concluded that *Archaeoraptor* was indeed a composite.

THE RUNNERS-UP

Science recognizes nine other major discoveries on scales ranging from the cosmic to the quantum.

First runner-up: Ribosome revelations. Researchers this year got their closest look yet at one of the cell's most important players, the protein factory called the ribosome. Each cell must precisely fit together two protein-RNA subunits so that the resulting macromolecule—the ribosome—can produce protein. Biologists have been eagerly awaiting a close-up of this complex for clues about how it makes protein with such stunning accuracy. Over the last 12 months, several groups have sharpened our blurry view, presenting structures in atomic detail. The new views show how the smaller subunit moves relative to the larger one to make possible the continued addition of amino acids to a nascent protein.



Ribosome up close. RNA does the work in the large subunit of the cell's protein factory.

The new close-up of the large subunit's structure revealed which piece is actually the cell's protein chemist. RNA itself acts as an enzyme, catalyzing the formation of the peptide bond that links one amino acid building block to the next amino acid down the line. This realization of RNA's active role helped bolster the theory that RNA

CREDITS: (TOP TO BOTTOM) ILLUSTRATION: TERRY SMITH; P. NISSEN *ET AL.*

molecules were among life's first, with proteins coming along later.

Other results this year drove home the antiquity of the ribosome. A study of all the ribosomal proteins in chloroplasts—the photosynthesis complexes in plants—found 25 with counterparts in bacteria and only four unique to plants, suggesting that the ribosome originated before plants and animals went their separate ways.

In addition, protein-RNA particles called snoRNAs have turned up in microbes called archaea. SnoRNAs typically hang out in a cellular compartment called the nucleolus, but archaea lack nucleoli, suggesting that snoRNAs predate nucleoli and were part of early life as well.

Finally, the cell apparently has several failsafe mechanisms when protein production goes off the rails. Investigations involving liver cells whose ribosomes had a defect showed that these cells grow in size but fail to replicate; thus they don't pass this defect on to progeny. Other studies demonstrated that another type of RNA, called tmRNA, can short-circuit aberrant protein synthesis and tag the incomplete product for immediate destruction.

Fossil find. Anthropologists have long agreed that the first humans—that is, members of the genus *Homo*—arose in Africa. Yet just when these early humans began to migrate out of Africa and inhabit other continents has been a matter of fierce debate.

In May, a team of Georgian and German prehistorians reported the first undisputed proof that humans indeed left Africa at least 1.7 million years ago. The spectacular find of two well-preserved skulls at Dmanisi, 85 kilometers south of the Georgian capital Tbilisi, united the anthropological community in a rare consensus about its great importance.

Don't look back. Fossils of early migrants.

Two lines of evidence convinced researchers that the team had clinched the case for the earliest human migrant. First, the skulls were found in sediments dated to 1.77 million years ago, supported by argon-argon dating of a 1.85-million-year-old volcanic layer just below. Second, the skulls closely resembled those of an early human species—called *Homo ergaster* by some scientists and early *Homo erectus* by others—known to have lived in Africa between 1.9 million and 1.4 million years ago.

The Dmanisi find, researchers say, demonstrates that *Homo ergaster* was on the move shortly after this new species arose in Africa and that some of our earliest ancestors were already restless wanderers.

One word—organics. Earlier this month, the chemistry Nobel Prize was presented for the discovery in the 1970s that plastics can be made electrically conductive. That discovery led to the finding that plastics could act like semiconductors—the workhorse materials of the information revolution—and it sparked research efforts to make

Peering Into 2001

Science's editors gazed into their crystal ball to predict six research areas to watch in the coming year.

Infectious diseases. Research into the planet's major scourges is moving out of the backwaters and onto the world stage. In 2000, the White House, the European Union, and the G-8 all announced multimillion-dollar initiatives to battle TB, malaria, and HIV, while the Bill & Melinda Gates Foundation chipped in, too. New drugs and vaccines will take years to develop, but expect a flurry of papers to pave the way.

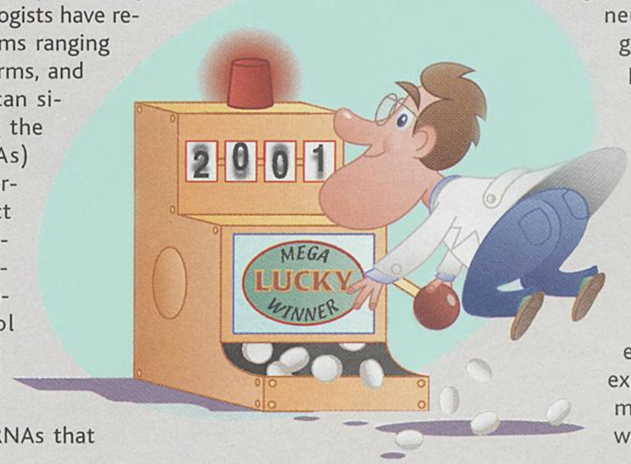
New views of the ocean. New satellites launched in the past 3 years to keep watch on the oceans should yield big dividends in 2001. Instruments such as SeaWiFS, which detects ocean chlorophyll, and Terra, NASA's giant new Earth-observing satellite, are mapping ocean temperatures, circulation, and photosynthesis by tiny ocean plants. This data gusher should yield insights into short-term climate changes such as El Niño, as well as the first global picture of seasonal ocean productivity.

RNA surveillance. Biologists have recently found that organisms ranging from molds to plants, worms, and perhaps even mammals can silence genes by degrading the messenger RNAs (mRNAs) they make. This "RNA interference" may help protect cells against invading viruses and some genetic damage. Scientists are also unraveling quality-control mechanisms such as "nonsense-mediated decay," by which cells remove error-containing mRNAs that produce defective proteins. In 2001, look for more progress toward understanding these fundamental cellular defense strategies.

Follow the money. Politicians everywhere are talking up research. Both U.S. presidential candidates raised hopes this fall, as did their Canadian counterparts, that science will be awash in new money in 2001. Likewise in the United Kingdom, although the largesse may favor the well endowed, while French bioscientists are basking in the best budget in a decade. Japan is poised to maintain a fast pace despite a prolonged economic slump, and China is rewarding its scientific stars and luring back those currently overseas. Germany and Italy anticipate more modest growth rates. Less encouraging is Russia, where efforts to shore up its crumbling scientific elite have so far fallen short.

Quark soup. Physicists at Brookhaven National Lab in Upton, New York, will be replicating a little piece of the universe as it was at the tender age of 10 microseconds. When gold atoms in the Relativistic Heavy Ion Collider (RHIC) smash together, the nuclei will reheat into a primordial plasma of free quarks and gluons, particles normally locked up in protons and neutrons. This new state of matter has been glimpsed at CERN, the European particle physics lab, but this year RHIC researchers will start painting a complete portrait.

On one hand or the other. Scientists trying to decipher how a cell tells its left from its right—or top from bottom—are likely to find some answers in the coming year. Cell biologists are working with flies, nematodes, and yeast to learn how proteins or RNA are directed to one side of a cell but not the other. And watch for the results from several teams attempting to replicate surprising experiments reported in 1999 that suggested mammalian embryos determine right from left with a system of swirling cilia.



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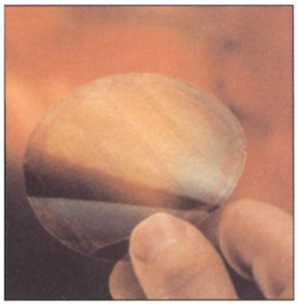


Powerful plastics. Novel organic materials make better chips and new lasers.

everything from lasers to computer circuits out of plastic and other organic molecules. This year, these efforts surged ahead on several fronts, raising hopes for applications such as wall-sized electronic displays and electronic price tags.

In the latest volley in the field of plastic electronics, researchers created a complex array of 864 organic transistors and other computer chip components on cheap and flexible plastic. As the complexity of circuit design increases, researchers are looking at plastic circuits for a host of applications.

Researchers also struck pay dirt in the field of organic lasers. Typically, new materials are made into lasers by "pumping" them with another powerful laser. But for real-world applications, organic lasers need to be powered by electrons, not photons. To work, such devices must inject large amounts of electrical current into a core material that then converts electrical energy to light. To get that current, one research team wedged an organic light emitter called tetracene between a pair of transistors. When switched on, those transistors injected enough current to coax the tetracene to lase.

New cells for old. Scientists performed some amazing tricks this year with stem cells and cloning, further undermining the old idea that a cell's developmental path is irreversible. In one surprising result, researchers showed that brain cells from adult mice can, when injected into early mouse embryos, become cells in the heart, stomach, liver, and other organs of a developing fetus. Other scientists found that cells from adult human bone marrow had become liver cells in patients who received transplants. In mice, transplanted bone marrow cells can travel to the brain and become neuronlike cells. If these multitalented cells can be tamed, researchers might be able to repair tissues damaged in spinal cord injuries, heart disease, and other maladies.

In other manipulations of cell fate, researchers managed to clone pigs from porcine skin cells—a step toward creating transgenic pigs for possible use as organ donors. Another team produced a fetal gaur, an endangered animal from India and southeast Asia, by injecting the nucleus of a gaur cell into the egg of a domestic cow and implanting the embryo in a cow's uterus.

Porcine progress. These piglets were cloned from an adult skin cell.

Worries that cloned animals might have cells with shorter-than-normal lifespans were assuaged when at least three groups showed that the carbon copies have telomeres that are as long as, or longer than, those of their noncloned counterparts. Telomeres are the DNA at the ends of chromosomes that become shorter with each cell division and help determine the lifetime of a cell and its descendants.

Water, water, everywhere. The solar system looked wetter and wetter this year as planetary scientists nailed down the existence of an ocean on Jupiter's satellite Europa and ferreted out signs of water shaping Mars from its earliest days until, quite possibly, the present. And where there's water, there's talk, at least, of alien life.

The long-proposed Europan ocean began to look very real after the Galileo spacecraft sped past the ice-covered moon early this year. Galileo picked up a weak magnetic field

Scorecard '99

Each year we predict six fields that will make headlines in the coming year. But forecasting is no exact science; here we rate whether our crystal ball was cloudy or clear.

Alzheimer's update. Last year's prediction of an "acid test" for β amyloid–containing plaques as the cause of Alzheimer's was premature. Inhibitors of the enzymes that make β amyloid are still in preclinical trials. Two other treatments—an antibiotic and a "vaccine" that dissolves the plaques—are beginning human trials. Still, it may be years before we know whether antiplaque therapies can help Alzheimer's patients.

X-ray specs. First, the good news: 2000 was a banner year for x-ray astronomy. X-ray satellites Chandra and XMM-Newton, both launched in 1999, have been unveiling black holes, supernovae, gamma ray bursts, and stellar dynamics. The bad news: In February, the launch of a third x-ray satellite, ASTRO-E, failed, leaving a huge blind spot in astronomers' x-ray vision.

Epigenetics. Even though only small steps were made in the study of how DNA is packaged and genes are expressed, 2000 still ranks as a banner year. Not just cancer researchers, but more plant scientists and evolutionary biologists now appreciate the role that chemical modifications of DNA may play in disease and in the survival of organisms. Next year, expect more insights into how RNA modulates gene expression and perhaps some therapeutic molecules.

Healing ecosystems. Two ambitious projects made mixed progress. Congress approved the first installment of a $7.8 billion plan to restore natural water flows in the Everglades, while an expert panel began to examine this scientifically controversial plan. In the Pacific Northwest, researchers dueled over whether removing dams or taking other measures such as reducing harvest is the best hope for Columbia River salmon. A Clinton Administration decision on if and when to breach dams was expected by year's end.

Nanocomputers. Researchers continued to improve their molecule-based electronic devices over the last year. Some promising new single devices made from carbon nanotubes and unusual molecules made their appearance, building on advances made in 1999. And new architectures and computing schemes continue to get attention. But having the individual gadgets does not make a computer—the challenge remains to wire them up into working circuits.

Polio persists. Much of western Asia, including all of China, was declared polio free on 29 October. However, the disease still stalked thousands of children in West and Central Africa and South Asia. And controversy persists over the oral polio vaccine, which is cheap and easy to administer but causes recipients to shed infectious virus particles and contaminate water supplies—a probable cause of a recent outbreak in the Caribbean, the first cases in the Western Hemisphere since 1991 (*Science*, 8 December, p. 1867).

CREDITS: (TOP TO BOTTOM) PHILIPS RESEARCH; ILLUSTRATIONS (GLOBES): TERRY SMITH; GLENN/BLACKSBURG, VA

Mars dribbles. Signs of water erosion boosted thoughts of life.

near Europa whose orientation depended on the changing orientation of Jupiter's much stronger field. Europa watchers could imagine only one material—salty ocean water—that could produce such a varying field.

Researchers continued to debate whether a past ocean washed over Mars, but excitement grew with reports of how water seems to have meandered along or beneath the planet's surface for eons. Striking images from the orbiting Mars Global Surveyor revealed springlike seeps that dribbled down crater walls within the past million years or so and are possibly still flowing. Apparently, water in some form—ice, brine, or a methane–water ice combination—still resides just below the surface. Other images from Surveyor and analyses of martian meteorites suggest that geologically recent volcanic activity has mobilized such subsurface water in the past few hundred million years. And earlier this month, Surveyor team members reported signs in the latest images that large areas of the martian equatorial region seem to have been covered by standing water about 4 billion years ago, implying a warmer and wetter climate back then.

Cosmic BOOMERANG. As 1999 drew to a close, cosmologists were almost shivering with anticipation. A preliminary map of the sky from a balloon-borne telescope named BOOMERANG had served up tantalizing evidence that we live in a flat universe that will expand forever instead of falling back on itself eons from now. By the end of 2000, a thorough analysis, which was soon strikingly confirmed by a second independent balloon experiment called MAXIMA, removed almost all doubt that the universe is flat, even as it called into question some fundamental assumptions about the state of the early universe.

According to the inflationary theory of cosmology, just after the big bang the newborn universe suddenly expanded like a balloon filled by a fire hose. For one test of the theory, astronomers look to the oldest light in the universe, the cosmic microwave background (CMB) radiation. When the universe first formed, a dense cage of matter trapped all radiation. Only after 300,000 years did the density of matter fall far enough to set the light free. That first light, the CMB, still retains the ripples of the earliest expansion. In a flat universe, most of these ripples in the CMB would appear almost exactly 1 angular degree across. That is precisely what both BOOMERANG and MAXIMA saw.

A surprise lurked in the data, however. The two balloon flights found additional

Inflationary science. Balloon-borne satellites take the cosmic temperature.

CMB fluctuations at a half-degree, but they found fewer of the smaller ripples than theorists had predicted. The shortfall implies that the simplest theory of the early universe cannot be correct. Either the estimates of the balance of normal matter and invisible "dark matter" are slightly wrong, or theorists must alter the properties of the engine driving inflation.

Good reception. Nuclear receptors—a large family of transcription factors that turn genes on and off upon binding specific ligands such as hormones—are implicated in cardiovascular disease, diabetes, and cancer. This year brought new insights into their involvement in the metabolism of cholesterol and fatty acids. Scientists identified new target genes and potential drugs that could block or enhance the receptors' signaling, perhaps leading to effective treatments for seemingly intractable diseases.

A few of these receptors also play key roles in the vexing problem of drug-drug interactions. In January, several papers reported that St. John's wort, the popular herb taken

Meltdown of the Year: The Wen Ho Lee Case

Was Wen Ho Lee the cagey superspy who shipped U.S. nuclear secrets to China? Or was he the innocent victim of racial profiling by overzealous spy hunters? Either way, Lee will be long remembered for triggering a political chain reaction with far-reaching consequences. And although the government's espionage case against Lee eventually imploded, it revealed flaws in everything from the Department of Energy's (DOE's) security practices to the media's reporting of the story.

Until *The New York Times* fingered him in a March 1999 story as the prime suspect in an espionage investigation at the Los Alamos National Laboratory, the Taiwan-born Lee had been a bit player in nuclear weapons science. But in 1996, Lee came under suspicion after U.S. officials learned that China had gotten hold of designs for the W-88, a powerful miniature warhead. Then, in December 1999, after investigators discovered that Lee had downloaded thousands of megabytes of information, he was arrested and charged with 59 counts of mishandling classified information (but not with espionage).

Over the next 278 days—which Lee spent shackled in solitary confinement—the feds' case gradually dissolved. An FBI agent recanted key testimony, then prosecutors refused to unveil secrets that they claimed were central to their case. In September, after Lee pled guilty to a single charge, the trial judge lambasted government officials, saying the case—and Lee's treatment—"embarrassed our entire nation."

Villain or victim? Espionage allegations against Lee rattled U.S. weapons labs.

The shock waves are still rippling through DOE's major science facilities. Congress has imposed widespread polygraph testing for weapons scientists and restrictions on foreign visitors to the labs. Lawmakers also dismantled DOE's nuclear weapons bureaucracy and welded together a new National Nuclear Security Administration. The changes have improved security, DOE officials say. But the controversy has also endangered science at the labs, by hampering international cooperation and recruitment of new staff.

Shock waves hit elsewhere too. In an unprecedented editors' note, *The New York Times* asserted that it was "proud" of its reporting on the Lee case, but that an internal review had "found some things we wish we had done differently." And Lee's ordeal has left many other Asian-American scientists feeling uneasy, wondering if their heritage alone makes them vulnerable to suspicion.

CREDITS: (TOP TO BOTTOM) MALIN SPACE SCIENCE SYSTEMS/JPL/NASA; NASA/NSBF; AFP/CORBIS for mild depression, interferes with the effectiveness of other drugs, including the antiretrovirals used to treat HIV infections and the immunosuppressive drugs vital to transplant recipients. A few months later a team in North Carolina reported that the herb exerts its effect through the so-called steroid and xenobiotic receptor (SXR). SXR responds to certain drugs, hormones, and other chemicals—including St. John's wort—by kicking production of the liver's detoxification enzymes into high gear, causing the body to break down and excrete other drugs. In work that demonstrated the central role of SXR, scientists in California created transgenic mice in which the mouse receptor PXR was replaced with the human SXR. The "humanized" mice reacted strongly to compounds that trigger reactions in humans but were impervious to compounds that normally ring alarm bells in mice—a potentially valuable tool for testing the safety of new drugs.

Powerful trigger. St. John's wort (*Hypericum perforatum*).

Biomedical Ethics on the Front Burner

It was a hot year for debates over research ethics. Controversy erupted in late 1999 after the death of 18-year-old Jesse Gelsinger in a gene-therapy clinical trial. The heat intensified as one review after another probed this experiment at the University of Pennsylvania (Penn). Federal investigators claimed that researchers had not followed established safety protocols. The university admitted "errors," instituted a new system for monitoring clinical trials in May, and awarded a significant financial settlement to the Gelsinger family in November (*Science*, 2 June, p. 1558, and 10 November, p. 1065).

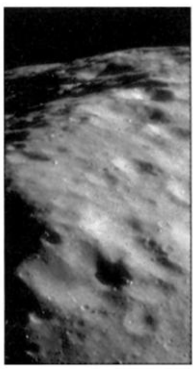
Because Penn and one of its clinicians had a financial stake in a gene-therapy company, questions about potential conflicts of interest arose at once. Two societies—the American Society of Gene Therapy and the American Society of Human Genetics—have explicitly asked members to avoid holding equity in companies that sponsor clinical trials they oversee. Now the Association of American Universities and the Association of American Medical Colleges are rethinking conflict-of-interest guidelines.

While deans focused on management issues, others took a look at international ethical standards, sparked by a long-running debate over the use of placebos in AIDS-prevention trials in the developing world. The U.S. National Bioethics Advisory Commission argued that it is acceptable to use placebos in some circumstances, provided that researchers arrange to share a successful treatment after the trial (*Science*, 6 October, p. 28). But an international ethics body meeting in Edinburgh, U.K., came to a different conclusion. In a revised Declaration of Helsinki, the World Medical Association said that placebos should be used only when there is no other therapy available for comparison (*Science*, 20 October, p. 418). If adopted, the Helsinki revision would dramatically change drug testing around the world.

The U.S. government, meanwhile, established an Office for Human Research Protections within the Department of Health and Human Services. Its new chief, Greg Koski, who trained as an anesthesiologist at the Massachusetts General Hospital in Boston, said in his first major speech last summer that industry-academia ties have "gotten entirely out of hand" and will require more careful scrutiny (*Science*, 25 August, p. 1266).

So NEAR ... After circling the 34-kilometer asteroid Eros for less than half a year, the NEAR Shoemaker spacecraft revealed the rock's deepest secret: Under a mask of rouge hides a heart containing some of the most primitive matter in the solar system. The discovery solves the decades-old mystery of what kind of asteroid can supply the most common meteorites falling to Earth.

Astronomers have long been frustrated in their search for the source of so-called ordinary chondrite meteorites, bits of the unaltered building blocks of the solar system. Their best telescopic gauge of asteroid composition—color at visible and infrared wavelengths—revealed little connection between ordinary chondrites and the most common type of asteroid, the S-type. Some researchers argued that exposure to the rigors of outer space had reddened the surfaces of ordinary chondrite asteroids so they resemble the mix of rock and metal that the reddish S-types seemed to be. NEAR Shoemaker ended the debate by directly measuring elemental composition from x-rays emitted by surface material. The composition of Eros does indeed match that of ordinary chondrites, it turns out, not the metal-rich compositions of more evolved rocks. Apparently, weathering under the blast of the solar wind reddened Eros to hide its true, primordial nature from astronomers.



Close-up. Eros revealed its true primitive nature.

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Quantum curiosities. Textbook wisdom once held that quantum mechanics ruled the small world, classical mechanics the large. Yet experiments reported this past year are overturning long-held dogmas about the quantum world and are helping physicists understand exactly what gives quantum-mechanical objects their bizarre properties.

The laws of quantum mechanics seem to defy everyday logic. For instance, the property called superposition allows a quantum object to assume seemingly contradictory properties at the same time, like Schrödinger's famous half-alive, half-dead cat. However, cats are big classical things, whereas quantum objects are small. Or are they?

In March, physicists announced that they had induced an electric current to flow around a superconducting loop of wire clockwise and counterclockwise at the same time. Although far from cat-sized, these current loops were a few micrometers across, much bigger than the atom-sized objects that physicists associate with quantum behavior and the largest objects ever seen to display superposition.

Dead or alive? Big things can exhibit quantum weirdness.

A new puzzle arose this year in the field of quantum computing, in which scientists use quantum mechanics to do the seemingly impossible. Until early this year, scientists were convinced that the power of quantum computers rests on a quantum property called entanglement, in which the fates of two quantum objects are linked. But in January, one scientist showed that you could still get quantum-computer power without using entanglement, leaving researchers scratching their heads.

–THE NEWS AND EDITORIAL STAFFS

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