The Lamb That Roared

A lamb cloned from a single cell of an adult sheep demonstrated the power of cloning technology, surprising both researchers and the public, and igniting a fierce debate about ethics

A year ago, few researchers would have guessed that science's most stunning achievement in 1997 would come from a barn. But in late February, a bleating, white-nosed lamb swept into the public eye: 7-month-old Dolly, the first animal cloned from an adult cell. She electrified both the research community and the general public, for although animals had been cloned before, creating a sheep from a single cell of a 6-year-old ewe was a stunning technological feat that many had thought impossible.

Cloning is of practical import, as it can be used to quickly create herds of identical animals that churn out medically useful proteins; the first such animals—a handful of transgenic sheep clones—are described on page 2130 of this issue. But the implications of cloning technology go much further, opening up new avenues of research in cancer, development, and even aging. Indeed, Dolly forces a reexamination of what it means to grow old, for although she is now 18 months old, her DNA, taken from the donor cell, may be almost 8 years old.

Next generation. These clones were derived from transgenic fetal cells and carry foreign genes.

According to conventional wisdom, adult cells cannot give rise to new, mature organisms. So after Dolly's debut, researchers scrambled to understand how she was created. Scientific societies convened their own impromptu meetings to discuss both the scientific and ethical implications of the work, and companies specializing in transgenic animals saw their stock value jump overnight.

But despite Dolly's soft brown eyes, some feared that she was a wolf in sheep's clothing, come to steal humankind's individuality and autonomy. She sparked calls for a ban on human cloning in the United States, Switzerland, China, and other nations, and to some, she raised the sci-fi specter of cookie-cutter clones grown for spare parts. But whether welcomed or feared, cloning in 1997 forced scientists and the public alike to rethink their basic ideas about life, and to confront the implications of our growing ability to manipulate life's blueprint.

As is true for many breakthroughs, cloning represents the convergence of advances in several disciplines over several decades. Painstaking progress in sheep reproductive biology, genetic manipulation, and cell culture all paved the way for Dolly. But the critical technique is nuclear transfer, in which the intact nucleus of one cell is absorbed into an egg whose own nucleus has been removed.

Researchers seeking to unlock the secrets of embryonic development had been working to perfect this technique for 40 years, starting with experiments in frogs in 1952. They transferred the nuclei of embryonic or tadpole cells into frog eggs and succeeded in raising cloned tadpoles and even adult frogs. But the older the frog cell donating the DNA, the less likely was the resulting clone to develop normally. When donor cells from an adult were used, no frog clone ever developed beyond the tadpole stage. And in mice, the typical mammalian model organism, results were even more discouraging. At the time, researchers couldn't get viable young from anything but nuclei taken from very early embryos—the two- to four-cell stage. So most biologists came to accept that mature cells could not give rise to entire organisms, especially in mice. Only an egg cell possessed that mysterious power, called totipotency.

But those working with cows and sheep were not quite persuaded. A team of researchers at the Roslin Institute outside Edinburgh, Scotland, for example, suspected that previous failures were caused by donor DNA that was in a different stage of the cell cycle than the recipient egg cell. They used nuclear transfer to clone sheep from embryonic cells, and in 1996 announced the birth of two cloned lambs. Next, they cloned sheep from fetal fibroblast cells. And in partnership with a local biotechnology company, they attempted what everyone had said was impossible: to clone a sheep from adult cells.

To do this, the team used cultured udder cells, taken from a 6-year-old ewe, and then starved them, forcing most of their genes to enter an inactive phase that the researchers hoped would match the cell-cycle stage of the recipient eggs. Once the udder-cell nuclei were transferred into the eggs, still-unknown factors coaxed that "inactivated" 6-year-old DNA to go back in time, so to speak, and apparently become totipotent once more, directing the eggs to develop into lambs. Out of 277 such eggs, only one produced a healthy living animal: Dolly.

To a startled public, Dolly made the horrors of science fiction clones seem all too possible. If she could be cloned from an udder cell, people wondered, then why not a dictator from his nose, as was attempted in the movie *Sleeper*, or a spare self as a reservoir of replacement body parts? Such things are safely in the realm of fiction, of course, but many people, scientists included, became concerned that cloning people would dehumanize our species and spoke out against it.

Yet upon reflection it's clear that just as identical twins grow up to be individuals, clones would never be truly identical. Even Dolly is not an exact replica of the ewe used to clone her, because she did not develop in that ewe's uterus nor receive its genes in the cellular organelles called mitochondria.

For now, Dolly stands alone. No one, not even the Roslin team, has made a second animal from an adult cell. Of course, most biomedical researchers work with mice—and mouse nuclear transfer results are still dismal. So attention is focused on the handful of labs worldwide working on cloning in livestock. Most are starting with fetal cells, whose DNA can more easily be made totipotent. So far, several firms say they too have cloned either sheep or cows from fetal cells, and one group has cloned monkeys from embryonic cells.

Nuclear transfer experiments are under way in other species too, ranging from zebrafish to rabbits. Among basic researchers, the Scottish group's success has inspired new experiments looking at how DNA changes as a cell matures. Clarifying the nature of totipotency may spark insight into what makes cells and organisms age, and how cell growth can go awry, as in cancer. Researchers are watching Dolly closely, for although so far she seems the 18-month-old she's supposed to be, her DNA may make her age prematurely.

Cloning experts point out that the true identity of Dolly's progenitor cell is not known for sure—it's possible that it was a stem cell, known to be able to develop into several

ILLUSTRATION: TERRY E. SMITH

kinds of tissues. Even if that's true, the ability to restore totipotency to easily harvested adult cells would offer a potentially simple method to replace lost or damaged cells.

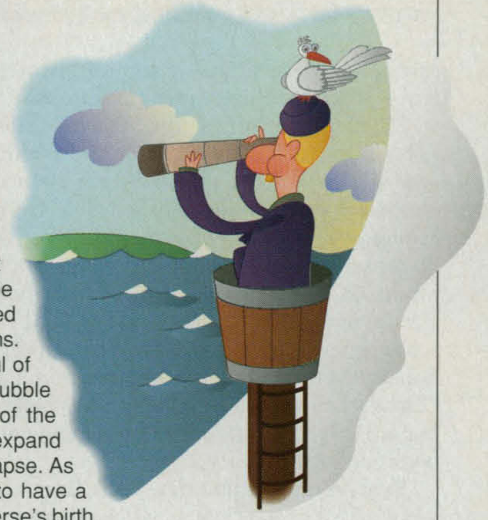
Meanwhile, the Roslin team has taken the next step toward making cloning economically useful by cloning sheep carrying foreign genes. Three sheep carry a marker gene, and two have both the marker gene and the gene for the human factor IX protein, which some hemophiliacs take to aid blood clotting. These sheep were cloned from transgenic fetal fibroblast cells, not adult cells, so they are most remarkable not as clones, but because they developed successfully despite having undergone genetic manipulation.

On the drawing board are flocks of sheep that make factor IX and other useful proteins in their milk. Other scientists are developing nuclear transfer techniques to create other types of genetically tailored livestock, opening the door to better animal models of genetic diseases, animals as organ donors, and possibly leaner, faster growing livestock.

Indeed, as with all breakthroughs, it's not possible yet to foretell exactly where cloning will lead. Although initial reactions were universally against all human cloning, there have been whispers that such cloning may one day have a place in giving infertile couples genetic offspring. Whatever direction the research takes, however, the public is likely to demand a say in how cloning is applied. Biologists, ethicists, and others will be wrestling with the implications of this birth in a barn for years to come.

–Elizabeth Pennisi

New Research Horizons



What fields will rise to prominence in 1998? *Science* surveyed the research world and found six likely prospects.

Forecasting future shocks. Climate researchers made a sharp call on 1997's massive El Niño, but the burgeoning field of long-range climate prediction has its reputation on the line once more: New predictions for this winter have been posted, from warmth in Minnesota to drought in southern Africa. Such seasonal forecasts pale before the new frontier of decadal predictions, based on understanding the slow mood swings of the oceans.

The expanding universe. Views of a handful of distant stellar explosions, taken this year by the Hubble Space Telescope, suggest that the ballooning of the universe has slowed so little over time that it may expand forever, rather than going to blazes in a final collapse. As more observations come in, expect these data to have a chilling effect on mainstream theories of the universe's birth.

Personalized prescriptions. The surge of interest in genotyping technologies—and in the firms developing them—is reviving pharmacogenetics, a decades-old vision of tailoring drugs to a patient's genetic makeup. Thanks to DNA chips and arrays, rapid DNA analyses may soon be able to reveal genetic variations affecting drug metabolism and side effects. These technologies are already changing how clinical trials are conducted and may eventually revolutionize how medications are prescribed.

Ribosomal inspection. At long last, researchers are beginning to get a detailed look at the inner machinery of the ribosome, the cell's protein factory. Advances in the techniques of structural biology are revealing the intricate dynamics of this large complex of RNA and proteins. Higher resolution images of the ribosome are likely to yield the exact nature of some of the many steps involved in protein production.

Diversity debate. Experiments with artificial ecosystems have bolstered the traditional view that biodiversity improves ecosystem functions. But recent work on natural ecosystems suggests that biodiversity may not be crucial to such functions as how nutrients cycle, while research in microbial communities suggests that high biodiversity makes ecosystems more predictable. As humans continue to wipe out species, expect more research on the science of why biodiversity matters.

Designer crops. The United States leads in transgenic crops, but Europe is fast catching up, with more than 100 trials—ranging from maize to strawberries—approved in Britain. A few transgenic crops have earned European Union approval and will soon be on the market. But will reluctant European consumers bite? Expect a battle for acceptance, as lobbyists press for new labeling rules.

THE RUNNERS-UP

We honor nine surprising discoveries that both change ideas about the natural world and offer great potential benefits to society.

First Runner-Up: Pathfinder's Triumphal Mars Landing

When it comes to Mars exploration, getting there has always been half the battle. From the start of the space age to the beginning of 1997, 19 missions set out—and more than half failed. No mission had touched down on martian soil since 1976. So on the 4th of July this year, when the Mars Pathfinder lander sent back images of the first robot to roam the surface of another planet, jubilation was the order of the day. But Pathfinder was more than just a stunning technological achievement: It returned a bounty of scientific information from an intriguing part of the Red Planet and did so on the cheap. As the first of NASA's "faster, cheaper, better" Discovery missions, Pathfinder broke through a history of martian jinxes and high costs. The landing captivated audiences worldwide and vindicated NASA's gamble on a new, smaller scale approach to solar system exploration.

Pathfinder's technological victory was all the more impressive given its Rube Goldberg approach to landing on Mars. Previous landers have relied on an expensive rocket to first get into orbit around their targets, but Pathfinder blazed straight into the martian atmosphere behind a simple heat shield, popped open a parachute while still at supersonic speeds, and then began searching for the surface using onboard radar. At literally the last second, the craft fired its three small retrorockets and cut the parachute loose from the lander. Encased in airbags, the lander plummeted the last 30 meters in a free fall, finally bouncing to a stop—right side up.

When the rover started returning data, color images of the martian landscape—released in real time on CNN and in almost real time on the World Wide Web—entranced the public. To geologists, the images also revealed traces of the great flood that a billion years earlier had sculpted a distant hill, stacked nearby boulders, and left meter-scale ripples in the ground. Compositional measurements made by Sojourner on rocks such as Barnacle Bill and Yogi revealed that they contain a surprising amount of silica, suggesting that geological forces had reprocessed the rocks sometime in martian history. And Sojourner's discovery of rounded pebbles that may have been water-worn in flowing streams added evidence that Mars's

NASA

The big picture. Pathfinder scanned Mars from horizon to horizon.

surface was warmer and wetter in its earliest days—when life might have gotten a start.

Mission engineers at the Jet Propulsion Laboratory in Pasadena, California, managed all this with less than $270 million and within a 3-year development schedule. Such economy runs counter to the old bigger-is-better culture of spacecraft design, which produced, for example, the $3.3 billion Cassini mission to Saturn. And Pathfinder's achievements are the first in what NASA hopes will be a series of blockbusters from the Discovery program. Next up, on 5 January, Lunar Prospector lifts off for its mapping orbit around the moon.

Synchrotrons shine new light. Beams of x-rays and ultraviolet light have long been used to reveal the atomic structure of materials. But by all accounts 1997 was a banner year for a new generation of stadium-sized machines known as synchrotrons, which produce the brightest beams yet and can illuminate the structural secrets of matter—both living and inert—down to individual atoms. This year saw the commissioning of SPRing-8, the world's most powerful synchrotron, in Nishi-Harima, Japan, and marked the first full year of operation of the second most powerful machine, the Advanced Photon Source in Argonne, Illinois. And synchrotrons around the globe yielded some striking breakthroughs in the structure of materials.


ARGONNE NATIONAL LABORATORY

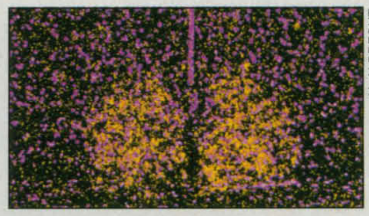
Shining light. Bright beams at the Advanced Photon Source reveal the structure of matter.

Among the highlights: An international team used the European Synchrotron Radiation Facility (ESRF) in Grenoble, France, to produce an atomic-scale map of the nucleosome core particle, thus gaining new insights into how this DNA-protein complex manages to coil meters of DNA inside each cell. A Swiss and French team used the ESRF beam to solve the structure of bacteriorhodopsin, a membrane protein whose small crystals had defeated previous attempts to determine its structure. And a group at Oxford University solved the largest x-ray crystal structure to date, that of the bluetongue virus, made up of more than 1000 separate proteins.

Despite such smashing results, budget woes threaten a new ultraviolet synchrotron, the Advanced Light Source, in the United States. But worldwide, synchrotrons show no signs of slowing—another 26 are in the works.

Keeping time. As the days ticked by in 1997, those studying organisms' internal clocks marked time with periodic bursts of discovery. Researchers isolated several new genes that help keep daily rhythms, including the first two mammalian clock genes. And one fruit fly clock gene was found to be active throughout the fly, suggesting that many cells, not just those of the brain, can keep time.

Before this year, only three clock genes had been identified, two in the fruit fly (*per* and *tim*) and one in bread mold, called *frequency* (*frq*); these genes code for proteins whose concentrations rise and fall on a cycle


U. ALBRECHT

Clocking in. Active mammalian clock gene (yellow) lights up a mouse brain at 11 a.m.

Bumper Crop for Pop Science

Most scientists think the general public pays scant attention to research, but in 1997 several science stories became hits in popular culture, as the mass media—particularly television and the Internet—discovered that the process of discovery itself can be a rich source of entertainment as well as information.

Space science was perhaps the most popular story, as a string of marvels, mishaps, and milestones drew eyes upward in numbers probably not matched since the days of the Apollo moon project. In March and April, there was Hale-Bopp—for once, a comet whose brightness exceeded its ballyhoo. The comet turned even urbanites into backyard astronomers, and nearly doubled previous records for visibility and endurance. Lasting even longer, however, were the travails of Russia's dilapidated Mir space station. This space-based soap opera repeatedly stopped the hearts of Mir watchers, as a rotating cast of astronauts battled fires, computer breakdowns, and other calamities.

Then on the 4th of July, the Mars Pathfinder lander bounced down on the Red Planet, announced on CNN with much fanfare and 24-hour live coverage from NASA's mission control room. Pathfinder's intrepid Sojourner rover wasn't equipped to search for signs of life, but Sojourner and its lively band of handlers at mission control charmed TV and World Wide Web audiences anyway. The "hits" pummeling Pathfinder Web sites peaked at millions per hour, with the grand total now nearing 1 billion. As with many hit TV shows, there was a toy tie-in: Mattel's Hot Wheels version of the rover went flying, not crawling, off store shelves.

Space exploration may have mimicked high-adventure science fiction, but reproductive biologists' exploits in a petri dish in Scotland evoked, for many, the genre's cautionary side. Dolly—the ewe cloned from an adult mammary-gland cell—sparked hasty calls from politicians for a moratorium on human cloning, forced ordinary citizens to reconsider the meaning of individuality, and became a staple of late-night TV comedians. Like headless tadpoles in Britain, genetically engineered soybeans in Germany, and the new film *Alien Resurrection*, the cloning story tapped public fears of genetic technologies. Scientists may wish that ordinary citizens knew more about science than they do—but they can hardly deny the strength of its grip on the public imagination.

ILLUSTRATIONS: TERRY E. SMITH

Scorecard '96

Last year, *Science*'s editors gazed into the future to predict the hot fields of the next 12 months. Here's how our favorites fared this year, showing whether our crystal ball was cloudy or clear.

The cure for cancer. Promising new results boosted bold new therapies, such as blocking the growth of blood vessels that feed tumors, or designing a virus to kill cancer cells. But clinical trials are proceeding slowly, and it may be years before such tactics pan out.

Advanced Photon Source. Several beamlines saw first light this year, while other groups used this x-ray synchrotron to probe everything from protein structure to the behavior of catalysts in water (see second runner-up, p. 2040).

Computer security. Although worried Web users kept a wary eye on information security, there were no major new breaches of the encryption codes used to safeguard business data.

Synthetic carbohydrates. New clinical trials were launched to see if these sugar-based molecules may work as a cancer vaccine, coaxing the immune system into attacking the natural carbos that decorate tumor cells.

Quantum error correction. New schemes for correcting errors in unimaginably fast quantum computers leaped forward, as theorists moved beyond correcting mistakes in memory to protecting logic operations. And the first experimental realizations of quantum error correction are in the publication pipeline.

Supersymmetric particles. A fire at CERN slowed the search for the elusive signs of supersymmetry. Optimists still see hints of the particles in the modest amount of data gathered and predict that their signatures will turn up next year at CERN.

set to 24 hours by sunlight. Then, last May, researchers reported two new genes in bread mold, *white collar-1* and *-2*, which turn on the transcription of *frq*, thus participating in a feedback mechanism that keeps the clock ticking. Later that month, another team isolated the first timekeeping gene from a mammal—a mouse gene called *Clock*—which also appears to regulate circadian rhythms.

In September, two teams independently discovered a gene that resembles *per* in mice and humans. Having similar genes in such divergent species as humans and flies implies that the genes that make up the clock's gears and springs may have been conserved since the earliest days of biological time. Finally, in the closing days of 1997, researchers found that *per* is active not only in the brains of flies, but in many other tissues as well, suggesting that many independent clocks are ticking away in the body—and that the brain is only one of many timekeepers.

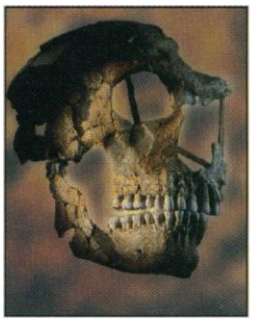
Violence at a distance. They are the most violent events in the universe, and for 30 years they ranked high on the cosmic mystery top 10. Gamma ray bursts, sudden explosions of high-energy radiation occurring almost daily at random positions in the sky, were first detected in the early 1960s. But gamma ray detectors couldn't accurately determine their location or distance from Earth. Some astronomers thought the bursts were far-off events, others that they occur in our own galaxy.

Then on 28 February, the Italian-Dutch satellite BeppoSAX simultaneously detected a burst in both gamma ray and x-ray wavelengths, using two separate detectors. An x-ray telescope aboard the satellite was also able to catch the afterglow of the burst and pinpoint its position. Alerted via the Internet, Dutch astronomers at an observatory in the Canary Islands found a dimming optical light source at the burst position, coinciding with what appeared to be a distant galaxy.

Ten weeks later, on 8 May 1997, it happened again—a second BeppoSAX detection was linked with an optical source. This time, American astronomers using a Hawaii-based telescope were able to study the light of the burst in great detail and to peg its distance at several billion light-years. It seems that gamma ray bursts occur in the far reaches of the universe, making them by far the most energetic events in the cosmos, exceeded only by the big bang itself. But what distant cataclysms cause these bursts? They might be the collision of two dense neutron stars, but their true nature remains a mystery to be solved another year.

A glimpse of Neandertal DNA. Ever since the first skeleton of a Neandertal was discovered in Germany's Neander Valley in 1856, anthropologists have wondered whether this burly human was ancestral to living humans or an evolutionary dead end. Many more Neandertals have turned up since, but the bones alone haven't settled the mystery.

Then in July a team in Munich announced that it had recovered and analyzed a snippet of DNA from the arm bone of that original Neandertal. The researchers had pieced together a 379–base pair sequence from the mitochondrial DNA (mtDNA) in the cell's energy-producing organelles. This Neandertal mtDNA spelled out a sequence very different from that in living humans, supporting the view that Neandertals were not our ancestors, but a separate species that went extinct.

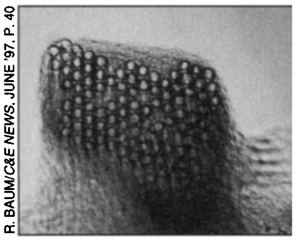


K. GARRETT/NAT'L GEOGRAPHIC SOCIETY

Distant relation. mtDNA suggested that Neandertals are not our ancestors.

Only one small part of the genome was reconstructed, but at 30,000 to 100,000 years old this is the oldest DNA extracted from a human. And it is a triumph for the besieged field of ancient DNA. Earlier, spectacular claims of analyzing DNA from insects in amber have not been replicated, and many had almost given up on the idea of extracting useful DNA from ancient fossils. But this work was replicated in a U.S. lab, convincing even skeptics that it is the real thing.

Nanotubes on a roll. Since their discovery in 1991, nanometer-sized tubes of carbon have been seen as the right stuff for everything from future electronic devices to ultrastrong materials. In 1996, researchers developed a laser-based method to produce high yields of single-walled nanotubes (SWNTs), and in 1997 they brought the tubes closer to their potential by testing, tweaking, and filling them.



R. BAUM/C&E NEWS, JUNE '97, P. 40

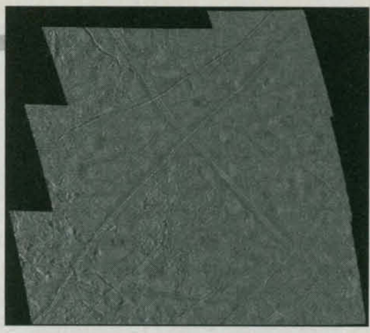
Tubing it. Nanotubes are in demand.

Cousins of the spherical buckminsterfullerene (C_{60}, Molecule of the Year in 1991), nanotubes are sheets of graphite—carbon atoms arrayed in adjoining hexagons—that are rolled up and capped at the ends. Those made of only a single wall of carbon are prized for their regular structures and predictable behavior. For example, theorists predicted early on that depending on their architecture, SWNTs should be semiconductors or metals, key building blocks for electronic devices. Scientists confirmed both predictions in 1997. Individual nanotubes were found to be excellent conductors, a property that could be enhanced by doping their outer surfaces. And a slightly different bonding arrangement between a single pair of polygons was shown to turn a nanotube into a simple semiconducting electronic device. Other researchers demonstrated their ability to manipulate the tubes by stuffing them with gas or with gallium nitride rods.

Also this year, a French and U.S. team came up with a cheaper way to produce SWNTs using a simple electric arc discharge, a feat that's likely to make these cylinders easier to come by and therefore study. But no known method can produce the tons of SWNTs needed for a commodity material, so the push to make larger batches of tiny tubes will continue.

The other ocean. This year planetary scientists gathered solid evidence that our ocean is not alone. The Galileo spacecraft orbiting Jupiter returned images of the surface of the jovian moon Europa, revealing what looks like an icy crust floating on a watery ocean.

Absolute proof of a deep sea might be beyond Galileo's abilities, but the newly credible case for liquid water—the crucial ingredient for life—raises the prospect of alien stirrings beneath Europa's icy surface.


JPL

Deep water. Europa's jumbled, icy surface hints at an ocean below.

The signs of a europan ocean were varied. Faults, rifts, and jumbled crustal blocks suggest that the surface layer of ice was thin when last disturbed; in one spot, iceberglike blocks seem to have floated in a now-frozen sea. And some large impact craters appear to have punched through thin ice, leaving flat blemishes rather than rimmed craters.

These and other clues suggest that when the europan surface was last disrupted, the ice was only 10 to 20 kilometers thick, leaving 100 kilometers or more below for liquid water. And large areas nearly unblemished by the drizzle of small impactors suggest that all this disruption was recent or even ongoing. An intensive campaign by Galileo during the next 14 months may turn up more evidence, but look for proposals to send a spacecraft to orbit this moon to probe for the final answer.

Genomes galore. The growing tower of microbial genetic data was buttressed by two more cornerstones this year, and geneticists also pushed closer to what once seemed a pie-in-the-sky goal—analyzing whole genomes.

Researchers sequenced the entire genetic codes of two well-studied microbes, the common gut microbe *Escherichia coli* and the soil bacterium *Bacillus subtilis*. These bacteria—each with a genome more than 4 million bases long—have been laboratory workhorses for generations of biologists. Now, scientists can link decades of physiological and biochemical work to the genes involved.

Politicians Sweat Over Global Warming

Scientific uncertainty is nothing new to policy-makers. But this year it occupied center stage as the global warming issue, long smoldering on the scientific sidelines, spread to the political arena. Earlier this month, politicians, scientists, and lobbyists gathered in Kyoto, Japan, to face up to a burning question: If human emissions of carbon dioxide and other greenhouse gases will warm the world, what should be done about it? While the answer depends in part on science, 10 days of arduous debate at Kyoto—as delegates hammered out a historic accord—made it plain that the science is only the start.

Well before Kyoto, scientists had already aired their views in a report by the Intergovernmental Panel on Climate Change (IPCC)—the most comprehensive international assessment ever on an environmental question. But while the effort was impressive, it was hardly conclusive. The report said warming due to a doubling of greenhouse gases, expected sometime late in the next century, could range from 1.5 to 4.5 degrees Celsius—from moderate to outright catastrophic. And scientists still can't be sure just what the effects of climate change will be on various regions of the world.

Given that uncertainty, most policy-makers agreed that emissions need to be restricted—but how much, and who will bear the cost? Kyoto provided a few answers, including emission reductions ranging from 6% to 8% below 1990 levels by Japan, the United States, and Europe, as well as the inclusion of all six major greenhouse gases in the tally. Of special interest to scientists, a clean development fund would channel new energy-saving technologies to developing countries. Such a fund—intended as the first step toward participation by poorer nations—may thrust science back into the center of the debate. But it won't provide any quick fixes for negotiators when they reconvene in November 1998 in Buenos Aires to tackle several unresolved issues, including whether and how developing nations will participate in the treaty.

ILLUSTRATION: TERRY E. SMITH

This was also the year when whole-genome sequencing took off. Once a maverick approach, this shotgun method has become commonplace in organisms with fewer than 2 million bases. This year, it yielded genomes of three archaea (primitive microbes often adapted to extreme environments) and several pathogens, such as *Helicobacter pylori*, infamous as the cause of ulcers, and *Borrelia burgdorferi*, the spirochete behind Lyme disease. More than 40 other microbial genome efforts are under way.


D. M. PHILLIPS/VISUALS UNLIMITED

In the bank. *Escherichia coli* has been sequenced.

This output has been both empowering and humbling. With whole genomes to compare, researchers can classify genes into functional or ancestral families. From these studies, biochemists are tracking down new proteins in key metabolic pathways, providing insight into such questions as how pathogens gain access to their hosts. Yet even in familiar *E. coli*, about a third of the putative new genes are of unknown function, which stakes out a new challenge for the years ahead.

Neurons in the news. In 1997, researchers homed in on clues to the workings of the central nervous system, clues that may one day lead to new treatments for ailments ranging from Parkinson's disease to spinal cord injuries.

This year, scientists fingered the first genetic cause of Parkinson's, tying a mutation in a gene called α-synuclein to a heritable form of the disease in a large Italian family. The work not only put to rest a long-standing debate over whether genes play a role in Parkinson's, but also pointed to a possible mechanism for the disease, involving abnormal processing of the protein.

Other research shed light on the biology of the dopamine-producing brain cells that die in Parkinson's. Work from a Swedish lab using mice showed that a receptor protein called Nurr1 is needed for both proper development of dopamine-producing cells and the synthesis of a healthy amount of dopamine.

There were advances in Alzheimer's disease too: Researchers identified a potential new player, novel brain lesions called "AMY plaques," that may contribute to the disease. And this year also raised hopes that injured spinal cords may one day be rewired. Groups from London and San Diego linked the sprouting of nerve fibers in the severed cords of adult rats with some return of function—a feat long thought impossible.

–The News and Editorial Staffs

For an expanded version with references and links, see Science Online *at* www.sciencemag.org/content/vol278/issue5346/#special