

The Runners-Up >>

2 REPROGRAMMING CELLS. The riddle of Dolly the Sheep has puzzled biologists for more than a decade: What is it about the oocyte that rejuvenates the nucleus of a differentiated cell, prompting the genome to return to the embryonic state and form a new individual? This year, scientists came closer to solving that riddle. In a series of papers, researchers showed that by adding just a handful of genes to skin cells, they could reprogram those cells to look and act like embryonic stem (ES) cells. ES cells are famous for their potential to become any kind of cell in the body. But because researchers derive them from early embryos, they are also infamous for the political and ethical debates that they have sparked.

The new work is both a scientific and a political breakthrough, shedding light on the molecular basis of reprogramming and, perhaps, promising a way out of the political storm that has surrounded the stem cell field.

The work grows out of a breakthrough a decade ago. In 1997, Dolly, the first mammal cloned from an adult cell, demonstrated that unknown factors in the oocyte can turn back the developmental clock in a differentiated cell, allowing the genome to go back to its embryonic state.

Various experiments have shown how readily this talent is evoked. A few years ago, researchers discovered that fusing ES cells with differentiated cells could also reprogram the nucleus, producing ES-like cells but with twice the normal number of chromosomes.

Recently, they also showed that a fertilized mouse egg, or zygote, with its nucleus removed could also reprogram a somatic cell.

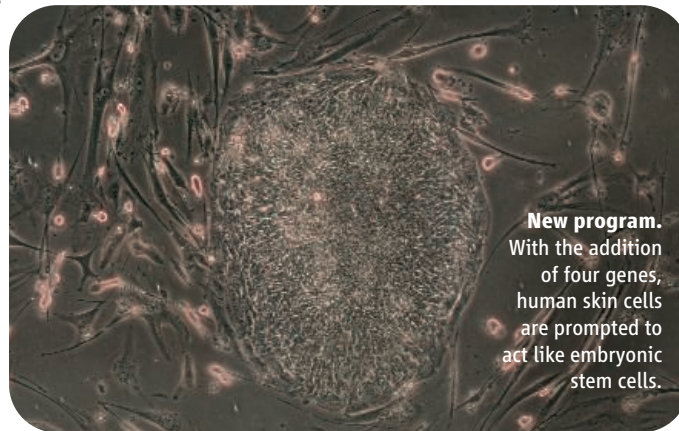
Meanwhile, the identity of the reprogramming factors continued to puzzle and tantalize biologists. In 2006, Japanese researchers announced that they were close to at least part of the answer. By adding just four genes to mouse tail cells, they produced what they call induced pluripotent stem (iPS) cells: cells that looked and acted like ES cells.

This year, in two announcements that electrified the stem cell field, scientists closed the deal. In a series of papers in June, the same Japanese group, along with two American groups, showed that the iPS cells made from mouse skin could, like ES cells, contribute to chimeric embryos and produce all the body's cells, including eggs and sperm. The

work convinced most observers that iPS cells were indeed equivalent to ES cells, at least in mice.

Then in November came a triumph no one had expected this soon: Not one, but two teams repeated the feat in human cells. The Japanese team showed that their mouse recipe could work in human cells, and an American team found that a slightly different recipe would do the job as well.

The advance seems set to transform both the science and the politics of stem cell research. Scientists say the work demonstrates that the riddle of Dolly may be simpler than they had dared to hope: Just four genes can make all the difference. Now they can get down to the business of understanding how to guide the development of these high-potential cells in the laboratory. In December, scientists reported that



HOW'D WE DO?
Rating the predictions we made last year in "Areas to Watch"

World-weary? Hardly. Four spacecraft returned torrents of data from around the solar system. The Venus Express orbiter probed the vicious atmosphere of Earth's near-twin. On its way to Pluto, New Horizons snapped pictures of Jupiter. The Mars Reconnaissance Orbiter revealed unforeseen hazards for future landers. And Europe's Earth-orbiting COROT discovered its first planet orbiting another star, showing that COROT can detect exoplanets as small as Earth.

Skulls and bones. In 2007, paleoanthropologists unveiled the long-awaited postcranial bones of a 1.7-million-year-old *Homo erectus* from Dmanisi, Georgia, bits of a putative gorilla ancestor, and new early *Homo* specimens from Africa. But the world still waits for publication of the skeleton of the enigmatic *Ardipithecus ramidus*, a 4.4-million-year-old Ethiopian hominid that may shed light on the murky roots of the human family tree.

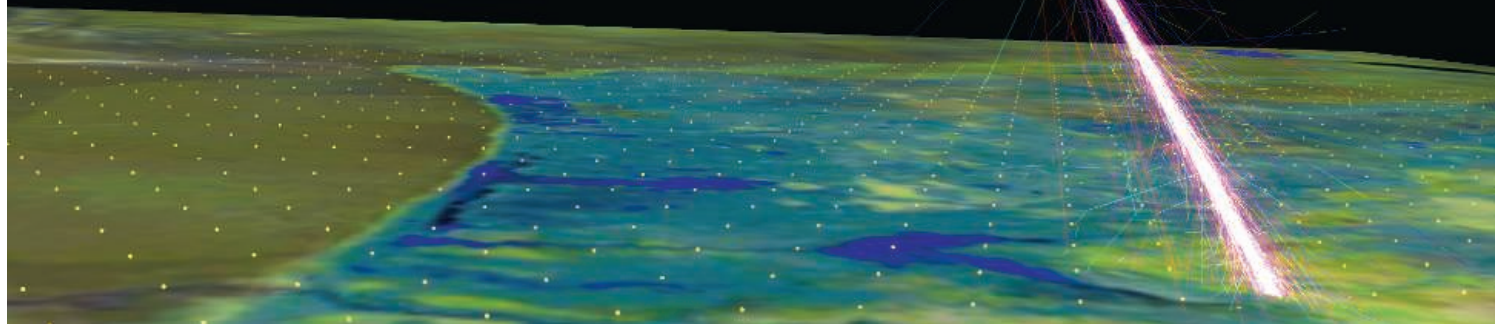
Loads of new primate genes. The published genome sequence of the rhesus macaque did help clarify genetic changes that led to humans, but the analyses of the genomes of the gorilla, orangutan, marmoset, gibbon, galago, tree shrew, and mouse lemur have yet to appear. Eventually, though, these sequence maps will bring a host of evolutionary insights.

A climate of change? High-profile reports, an agenda-setting meeting in Bali, Indonesia, and a

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Debris trail. High-energy cosmic rays streaking into Earth's atmosphere shed clues to their source.



CREDIT: M. SUBBARAO, D. SURENDRAN, AND R. LANDSBERG/KICP/ADLER PLANETARIUM AND ASTRONOMY MUSEUM/UNIVERSITY OF CHICAGO

they had already used mouse iPS cells to successfully treat a mouse model of sickle cell anemia. The next big challenge will be finding a way to reprogram human cells without using possible cancer-causing viruses to insert the genes.

Politicians and ethicists on both sides of the debate about embryo research are jubilant. Supporters hope the new technique will enable them to conduct research without political restrictions, and opponents hope it will eventually render embryo research unnecessary. Indeed, several scientists said the new work prompted them to abandon their plans for further research on human cloning.

Officials at the National Institutes of Health said there was no reason work with iPS cells would not be eligible for federal funding, enabling scientists in the United States to sidestep restrictions imposed by the Bush Administration. And President George W. Bush himself greeted the announcement by saying that he welcomed the scientific solution to the ethical problem.

But it's much too early to predict an end to the political controversies about stem cell research. Some researchers say they still need to be able to do research cloning to find out just what proteins the egg uses for its reprogramming magic. And now that science has come a step closer to the long-term goal of stem cell therapy, mouse models won't be adequate for animal studies. Rather, researchers will need to test cell transplantation approaches with primates, a move that will inevitably stir up resistance from animal-rights activists.



Nobel Peace Prize placed global climate squarely in the public eye, but policy-makers in the United

States, China, and India haven't passed mandatory limits on greenhouse gas emissions that scientists say are needed. (See "Global Warming, Hotter Than Ever," p. 1846.)

Whole-genome association studies.

In work that made up part of this year's Breakthrough of the Year (see p. 1842), more than a dozen large-scale comparative studies of human DNA showed the technique's enormous promise for

tracking down genes linked to disease.



Light crystals.

Physicists hope to explore high-temperature superconductivity and other bizarre properties of solids by emulating them in optical lattices, artificial "crystals" based on corrugated patterns of laser light.

The year's hundreds of papers on optical lattices did not include a superconductor stand-in, but a grand entrance can't be far off.



3 TRACING COSMIC BULLETS. What's smaller than an atom but crashes into Earth with as much energy as a golf ball hitting a fairway? Since the 1960s, that riddle has tantalized physicists studying the highest energy cosmic rays, particles from space that strike the atmosphere with energies 100 million times higher than particle accelerators have reached. This year, the Pierre Auger Observatory in Argentina supplied key clues to determine where in space the interlopers come from.

Many physicists had assumed the extremely rare rays were protons from distant galaxies. That notion took a hit in the 1990s, when researchers with the Akeno Giant Air Shower Array (AGASA) near Tokyo reported 11 rays with energies above 100 exa-electron volts (EeV)—about 10 times more than expected. The abundance was tantalizing. On their long trips, protons ought to interact with radiation lingering from the big bang in a way that saps their energy and leaves few with more than 60 EeV. So the excess suggested that the rays might be born in our galactic neighborhood, perhaps in the decays of super-massive particles forged in the big bang. But researchers with the Hi-Res detector in Dugway, Utah, saw only two 100-EeV rays, about as many as expected from far-off sources.

The Auger team set out to beat AGASA and Hi-Res at their own games. When a cosmic ray strikes the atmosphere, it sets off an avalanche of particles. AGASA used 111 detectors spread over 100 square kilometers to sample the particles and infer the ray's energy and direction; Auger comprises nearly 1500 detectors spread over 3000 square kilometers. The avalanche also causes the air to fluoresce. Hi-Res used two batteries of telescopes to see the light; Auger boasts four. In July, the Auger team reported its first big result: no excess of rays above 60 EeV.

Auger still sees a couple of dozen rays above that level, however. Last month, the team reported that they seem to emanate from active galactic nuclei (AGNs): enormous black holes in the middles of some galaxies. The AGNs lie within 250 million light-years of Earth, close enough that cosmic radiation would not have drained the particles' energy en route. Auger researchers haven't yet proved that AGNs are the sources of the rays, and no one knows how an AGN might accelerate a proton to such stupendous energies.

Expect the controversy to continue. Hi-Res researchers say that they see no correlation with AGNs. With Japanese colleagues, they are completing the 740-square-kilometer Telescope Array in Millard County, Utah, which has 512 detectors and three telescope batteries. But with a much bigger array, the Auger team will surely be first to test its own claims.