The renewed attention to financial conflicts has already had an impact. Last week Harvard Medical School, which was considering a proposal to relax its strict limits on faculty members' involvement in outside commercial ventures, decided to table the proposal. In a 25 May memo to faculty explaining this decision, medical school dean Joseph Martin wrote, "I believe that the most important role academic medicine can have in clinical research today is to try to bolster the public's faith in the veracity and ethical underpinnings of this noble endeavor."

Frist was not impressed with HHS's efforts, however. He took the government officials to task for not moving more rapidly to increase surveillance and enforcement of clinical research rules. "I am very disappointed" with HHS's progress to date, Frist said, adding that "your response absolutely must be more comprehensive."

Even so, one intrepid witness—Savio Woo, president of the American Society of Human Gene Therapy in Milwaukee—offered a contrary view. He suggested that it would be unwise to rush forward with some new regulations and warned that doing so could have damaging consequences. By requiring even small clinical trials to be managed by someone other than the principal investigator, Woo said, the government could impose "excessive costs that will stifle academic clinical research." Innovative studies of rare diseases would be hit hardest, he added.

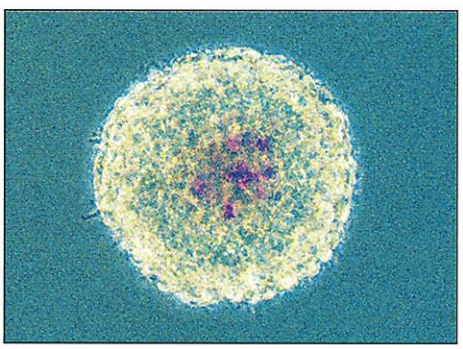
–ELIOT MARSHALL

DEVELOPMENT

Brain Cells Reveal Surprising Versatility

When a team of scientists reported last year that stem cells from the brains of adult mice could become functional blood cells, many scientists were intrigued, if a bit skeptical. Now, these versatile cells have shown even more surprising abilities: When injected into embryos, it seems, they can develop into nearly every type of tissue in the body. The work, described on page 1660, leaves a number of questions open. Even so, the cells' apparent flexibility is "amazing; it's really quite spectacular," says developmental biologist Janet Rossant of Mount Sinai Hospital in Toronto.

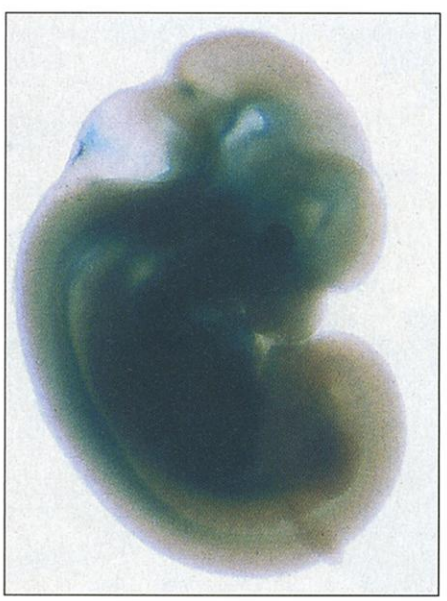
Scientists are amazed because decades of study had suggested that as development proceeds, cells become more and more specialized, and more restricted, in what they can do. According to widely accepted dogma, only embryonic stem (ES) cells, which are isolated before key differentiation steps occur, can become any tissue in the body. The latest results are another blow to that idea, showing that cells from adult animals are "able to revert into essentially ES cells" when they receive certain signals from the environment, says developmental neuroscientist Derek Van Der Kooy at the University of Toronto.



The findings may also have political implications. Because of the broad developmental potential of ES cells, researchers want to explore whether they can be used to provide replacement tissues for treating conditions such as spinal cord injuries, Parkinson's disease, and diabetes. But because human ES cells have to be taken from embryos, the U.S. Congress currently prohibits using federal funds to produce them. If certain molecular signals can indeed induce adult stem cells to develop into many different kinds of tissue, the work may fuel the arguments of the opponents of ES cell research who have testified that federal funding of human ES cell research is unnecessary, because cells from adults are equally promising. However, most scientists caution that the research on both adult and embryonic stem cells is too premature to compare the potential of the two.

Clues that adult stem cells might have wider abilities than expected began to accumulate last year, as researchers reported that mouse brain cells could become blood and cells taken from bone marrow could become muscle (*Science*, 25 February, p. 1418). Scientists have had trouble replicating some of these findings, and developmental neuroscientist Jonas Frisén and his colleagues at the Karolinska Institute in Stockholm decided to put adult stem cells to an even more rigorous test: to see if they could duplicate the characteristic feat of mouse ES cells, which can incorporate into another embryo and contribute to all the tissues of the resulting chimeric mouse.

Postdoctoral researcher Diana Clarke began by removing cells from the brains of adult mice and culturing them for about a week, to separate stem cells from fully differentiated cells, which die in culture. She and her colleagues then injected early mouse embryos either with neurospheres, aggregates of neural stem cells that form in culture from single cells, or with a group of dissociated cells, and allowed the embryos to develop until embryonic day 11. Because the researchers had derived the stem cells from mice that express a bacterial enzyme called β-galactosidase, they were able to follow their fates by applying a sugar derivative that releases a blue dye when cut by the enzyme. The team found blue-stained descendents of the stem cells in various organs—including the heart, liver, intestine, and nervous system—in six of the 600 embryos injected with dissociated cells, and 11 of the 94 embryos injected with neurospheres.



Multitalented. When scientists inject stem cells *(left)* from the brains of adult mice into an early mouse embryo, their progeny (stained blue) contribute to nearly every tissue in the body.

They had even better success with a different model. Mouse ES cells can incorporate themselves into developing chicks, and when Clarke injected neurospheres into the

CREDITS: (TOP TO BOTTOM) CLAS JOHANSSON/KAROLINSKA INSTITUTE; DIANA CLARKE/KAROLINSKA INSTITUTE

amniotic cavity of early chick embryos, she and her colleagues found progeny of the mouse cells in the liver, spinal cord, stomach, and kidneys of about one-quarter of the surviving embryos.

Both sets of experiments produced a puzzling result, however: Neural-derived cells did not appear in the blood systems of either the mouse or chick embryos. In light of last year's results, that is a "glaring, interesting conundrum," says neuroscientist Fred Gage of the Salk Institute for Biological Studies in La Jolla, California. The cells' absence in the bloodstream "doesn't mean they can't" become blood, he says, "but it leaves open the possibility that they don't."

Even more important, several researchers say, is the question of exactly what type of cell formed the various other tissues. Frisén and his team cannot tell whether the cells that contributed to the various embryonic tissues are some sort of rare, undifferentiated cell or whether something in the embryonic environment actually reprograms a cell that had already begun to differentiate. Scientists would dearly love to know the answer to that question, as it would help them understand what molecular factors allow stem cells to change their fates.

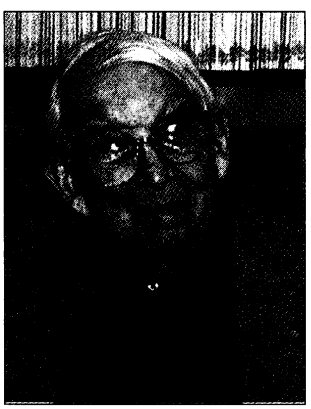
Rossant notes that it would also be nice to know whether the neural-cell chimeras would continue to develop into normal adults as ES-cell chimeras can, and especially whether the neural cells could become mature sperm and eggs. Nevertheless, she says, the work "is another demonstration that adult stem cells have more potential than we thought. Now we have to figure out how to harness that potential."

–GRETCHEN VOGEL

MATHEMATICS

Statistical Physicists Phase Out a Dream

For decades, the Holy Grail of statistical mechanics has been a mathematical problem known as the Ising model. Introduced in the 1920s by German physicist Ernst Ising, the Ising model is a powerful tool for studying phase transitions: the abrupt changes of state that occur, for instance, when ice melts or cooling iron becomes magnetic. Although they've learned much from approximate solutions and computer simulations, physicists have long sought an exact mathematical solution to the Ising model, which would provide much more information about such still-mysterious transitions.



Ernst Ising. His phase-change model is doomed to be inexact.

CREDITS (LEFT TO RIGHT): S. KOBE; C. THOMAS/NASA

Unfortunately, it looks as if that's not in the cards. Sorin Istrail, a theoretical computer scientist at Celera Genomics in Rockville, Maryland, has proved that the Ising model —at least in its most general, three-dimensional (3D) form—belongs to a class of problems that theorists believe will remain unsolved forever. "People have always thought the 3D solution was just around the corner," says Alan Ferrenberg, a computational physicist at the University of Georgia, Athens. "It really means now that numerical analysis is the only way we've got to approach [the Ising model]."

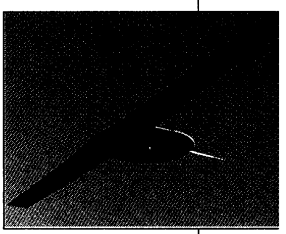
The Ising model deals with objects—say, atoms—laid out in a regular array, such as a rectangular grid or a honeycomb arrangement. The array can be 1D (think of beads on a string), a 2D grid, or a 3D lattice. What makes the model so useful is that it helps physicists understand how a large system of objects, each interacting only with its nearest neighbors, can combine to create a large-scale order. In a ferromagnet, for example, each atom has a magnetic moment that points either up or down. Pairs of neighbors with opposing moments raise the total energy of the system, while those with parallel moments lower it.

Solving the model means counting the number of arrangements that add up to each given energy level. Some versions of the Ising model can be solved exactly. Ising himself solved the 1D ferromagnetic model—and found it had no phase transition. In 1944, the Norwegian chemist Lars Onsager discovered an exact formula for the 2D model, which does possess a phase transition. But scientists have never been able to extend Ising's and Onsager's solutions to the physically realistic realm of three dimensions. "We now know why," says Istrail. "What these brilliant mathematicians and physicists failed to do, indeed cannot be done."

While working at Sandia National Laboratories, Istrail proved that computing the energy states for the general 3D Ising model is what computer scientists call an NP-complete problem—one of a class of recalcitrant calculations that theorists believe can be solved only by arduous brute-force computations. In effect, an exact solution to the Ising model would provide the key to efficient algorithms for solving thousands of other computational problems, ranging from factoring large numbers to the notorious traveling salesman problem, in which the salesman must find the most efficient route through a given number of cities. Al-

ScienceScope

Defenses Raised In February, President Clinton alarmed academic researchers in math, engineering, and computing—fields that get major military funding—by proposing to slash the Department of Defense's (DOD's) applied research spending by 8%, while boosting basic funding by 4% (*Science*, 11 February, p. 952). But leaders of the House and Senate panels that oversee DOD's budget promised to do more to keep innovative ideas flowing (such as drone aircraft, right)—and last week they followed through.



On 25 May, the House Appropriations Committee approved a bill providing $3.4 billion to applied studies, about 2% below this year's level, while giving basic research a 12% increase to $1.3 billion. Earlier, a Senate panel approved even rosier numbers, giving applied and basic science increases of 5% and 10%, respectively.

"We are pleased that Congress has recognized the importance of basic research, but we will continue to push for overall increases," says Caroline Trupp Gil of the American Chemical Society and the Coalition for National Security Research, a lobbying alliance. Computer researchers, for instance, will be pushing to raise some program budgets to requested levels when the full House and Senate vote on the bills later this month.

Hair of the Bear DNA samples taken from grizzly bear hair may help resolve a bitter dispute over the size of the bear population in and around Wyoming's Yellowstone National Park. Last month, federal scientists released a preliminary count of bears in Yellowstone's Lake area based on hairs found on barbed wire fur catchers. The figure—84 individuals, compared to 44 estimated in the 1980s from bear tracks—benefits from "a much more sophisticated technology" for tracking bear numbers, says Chuck Schwartz, head of the Interagency Grizzly Bear Study Team.

Schwartz now wants to do a Yellowstone-wide hair study to help pin down grizzly population trends—information that could prove pivotal in the debate over whether the animals should be removed from the U.S. endangered species list (*Science*, 23 April 1999, p. 568). A similar new study in Montana's Glacier National Park proved useful, but it's "not an inexpensive proposition," Schwartz says. A baseline bear count could cost $1 million, with more surveys needed to establish trends.