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BIOMEDICINE

NIH Sets Rules for Funding Embryonic Stem Cell Research

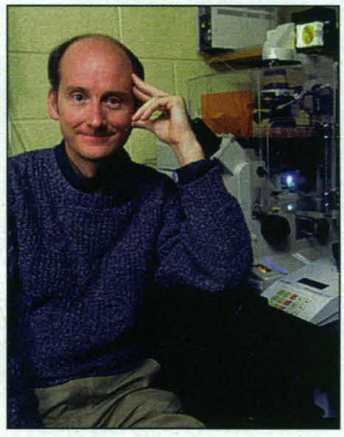
The National Institutes of Health (NIH) moved closer to funding work using embryonic and fetal stem cells last week, issuing proposed guidelines* that would allow publicly funded scientists to use these controversial materials. The carefully worded plan would rely on private labs to produce cell lines from embryos. But it would allow grantees to use the cells as long as they were derived according to strict requirements. The new rules are slightly more permissive for fetal stem cells, allowing publicly funded scientists both to derive and use them.

Despite NIH's cautious approach, the guidelines are already under attack: Anti-abortion activists have said they will try to get Congress to intervene next year and block support for all embryonic stem cell research. And even if that move fails, it could still be months before stem cell lines that meet NIH's requirements are available for widespread use.

Many scientists believe that embryonic stem cells, which can become almost any cell in the body, hold great promise for basic research in developmental biology as well as for treating a range of diseases. But the cells have been controversial because researchers derive them from early embryos or fetal tissue. Federal law allows NIH to fund some research on fetal tissue but prohibits work that might harm a human embryo. In January, NIH's parent agency, the Department of Health and Human Services, ruled that the law did not forbid research on stem cell lines, because they cannot develop into a person once they are removed from the embryo (*Science*, 22 January, p. 465).

In accord with that ruling, NIH published guidelines in the *Federal Register* on 2 December that spell out detailed criteria for other fetal tissue research. To monitor the field, the guidelines also would establish a Human Pluripotent Stem Cell Review Group, which would evaluate any newly derived cell lines to ensure they are in compliance with NIH rules. The guidelines are "a very thoughtful and very thorough response" to the political situation, says stem cell researcher Roger Pedersen of the University of California, San Francisco. And although he objects to a few of the requirements as unduly specific, "overall, it's a positive thing," he says.

cell lines would have to meet before NIH-funded researchers could use them. For example, embryonic cell lines could come only from frozen "excess" embryos created during fertility treatments at private clinics; embryo donors would have to sign strictly worded consent forms; and the process of obtaining embryos for research would have to be separate from clinical procedures. Slightly different terms apply to fetal tissue: Federally funded scientists would be free to derive and work on such cell lines as long as they followed ethical standards similar to those already in place



On standby. Wisconsin's Thomson is ready to share embryonic stem cells when NIH gives the green light.

NIH GUIDELINES FOR RESEARCH ON EMBRYONIC STEM CELLS

Deriving new cell lines from embryos	Prohibited
Research on privately derived cell lines from embryos	Allowed
Deriving new cell lines from fetal tissue	Allowed
Research on cell lines from fetal tissue	Allowed
Research that would use stem cells to create a human embryo	Prohibited
Combining human stem cells with animal embryos	Prohibited
Use of stem cells for reproductive cloning	Prohibited
Research on stem cells derived from embryos created for research purposes	Prohibited

But that specificity means existing cell lines probably won't meet NIH requirements. Indeed, the two scientists who derived cell lines described in papers last November (*Science*, 6 November 1998, p. 1014) agree that the consent process they used differed slightly from the NIH requirements and would be unlikely to pass muster. John Gearhart of The Johns Hopkins University School of Medicine, who derived his cell line from fetal germ cells, notes that his team's consent form does not include the required statement that the cells could be used "for many years." The review panel might not accept the document as equivalent. The new guidelines also require that all identifiers associated with the embryos be removed before the cell lines are derived. Although the donors at Hopkins were anonymous, Gearhart says, he retained certain identifiers because the Food and Drug Administration would require information on the source if the cells were ever used to treat patients.

James Thomson of the University of Wisconsin, Madison, who derived his cell lines from embryos, agrees that he "would probably have to derive new lines" to meet the guidelines, and he told *Science* that he intends to do so. But that would delay research. Thomson estimates it would take 6 months to derive, test, and grow enough cells to distribute to outside researchers.

Both Thomson and Gearhart were funded in part by Geron Corp. of Menlo Park, California, but the University of Wisconsin's Wisconsin Alumni Research Foundation (WARF) owns the patent on Thomson's work and is "completely free to distribute cells to academic researchers," Thomson says—"and we plan to do so." Geron holds an exclusive license for certain potentially profitable uses of the cells, says Carl Gulbrandsen, patents and licensing director for WARF, but the university retains the right to distribute the cells for research.

CREDIT: JEFF MILLER/UW-MADISON NEWS & PUBLIC AFFAIRS

* www.nih.gov/news/stemcell/draftguidelines.htm

The university is setting up an independent, not-for-profit institute to handle requests. Gearhart has said he will decide whether to distribute his cells to other researchers once final guidelines are in place.

The NIH's proposal could still run into trouble in Congress, however. Many observers expected the controversy to explode this fall. Representative Jay Dickey (R–AK) had proposed to amend NIH's appropriation bill specifically to bar work on embryo-derived cells. At the same time, a Senate advocate of stem cell research, Arlen Specter (R–PA), had proposed language that would be more permissive than NIH, permitting researchers to derive cell lines from human embryos as well as use them. Congressional leaders prevailed on both legislators to withdraw their proposals, however, and the appropriations bill signed into law last week is silent on the issue. As part of the compromise, Senate Majority Leader Trent Lott (R–MS) has promised a debate on Specter's bill in February. Both sides are gearing up.

In the meantime, NIH is accepting public comment on the draft guidelines through the end of January. Once the final version is in place, NIH will begin accepting proposals for work on both embryonic and fetal stem cells, says Lana Skirboll, the NIH's associate director for science policy. Barring congressional intervention, she predicts the first grants could be funded as soon as next spring.

–GRETCHEN VOGEL

PLANETARY SCIENCE

Yet Another Loss to The Martian Gremlin

Failure at Mars is becoming drearily familiar: Since 1960, the United States, the Soviet Union, and Russia have launched 29 missions toward Mars, only eight of which could be called real successes. The dogged Russians and Soviets are zero for 16, engendering talk of a martian gremlin that lies in wait for unsuspecting spacecraft. Until this year, however, the Americans seemed to have dodged the gremlin, with an impressive eight successes out of 11 attempts. But in September confusion over English and metric units doomed Mars Climate Orbiter. And over the past weekend the Mars Polar Lander (MPL) went missing, giving the United States just two successes in the last five tries.

While scientists mourned the loss of a chance to study martian water ice up close, mission planners at NASA and the Jet Propulsion Laboratory (JPL) in Pasadena, California, were at least as discouraged by the prospect that they may never know what sealed MPL's fate. In the wake of the loss, they offered two scenarios. MPL could have reached the surface intact but landed on a slope so steep that it tipped over. Or, just after it broke off radio communication with Earth, as intended, 12 minutes before its planned landing, it could have suffered some onboard problem—perhaps due to some undiscovered flaw in current designs that might turn upcoming Mars missions into gremlin bait as well.

CREDIT: NASA/JPL/CALTECH

Lost duo. Why Mars Polar Lander became the year's second martian casualty, after Mars Climate Orbiter *(top)*, may never be known.

A complex sequence of mechanical operations was scheduled after the communications break. Outside Mars's atmosphere, MPL should have separated from a structure that had supported it during the cruise to Mars. It should have made a fiery entry behind its heat shield, deployed its parachute, jettisoned the heat shield, radar-locked onto the surface, and separated from the parachute. Then, using rockets to decelerate, it should have made a gentle touchdown on the surface.

With no word from the lander, engineers don't know how any of that went. MPL had no way of communicating during its entry, descent, and landing, unlike its predecessor Mars Pathfinder, which landed successfully in 1997. Pathfinder's mission, notes project scientist Matthew Golombek of JPL, was to test a new airbag-cushioned landing method, so mission engineers documented spacecraft performance to the very end. In the case of MPL, spacecraft designers economized by leaving out the somewhat complex and expensive equipment needed for continuous communications. After all, two Viking spacecraft had successfully made rocket-braked landings on Mars in 1976, using much older technology.

Even if MPL did make it down, other hazards awaited it. Like all other landings on Mars, it would have touched down on little-known terrain. According to Richard Zurek, MPL project scientist at JPL, images of the landing zone made by the orbiting Mars Global Surveyor showed a relatively smooth surface. But because a picture element in most of those images encompasses 4 meters, plenty of lethal hazards—car-sized potholes or meter-high ledges, for example—could be hiding in the apparently innocuous terrain. "We can't capture [lander-scale hazards] with the images we have," says Zurek. "That's a risk you take when you go to Mars. We're going to places on Mars we haven't been before. You can't guarantee success."

–RICHARD A. KERR

TISSUE ENGINEERING

Growing Human Corneas in the Lab

If the eyes are the windows to the soul, the cornea is the windowpane, a tough but transparent layer of tissue that lets light through but protects the interior of the eye from the elements. But although a smudged window is easy to clean, a cornea clouded by injury or disease can impair vision and lead to blindness. Surgeons can often replace damaged corneas with healthy ones from organ donors. But the supply barely meets the demand, and few corneas remain for researchers, who need them to study corneal wound healing and eye diseases. That leaves none for toxicity testing of drugs and household products. As a result, manufacturers often test them on animals, usually rabbits. Now, researchers have taken a big step toward alleviating the cornea shortage.

On page 2169, cell biologist May Griffith of the University of Ottawa Eye Institute, Mitchell Watsky of the University of