EMBO reports

analysis

Research on human embryonic stem cells

NIH issues new guidelines a week after British recommendations

'Legal sophistry.' That is what Senator Sam Brownback (Republican, KS) calls the newly issued US guidelines governing taxpayer-funded research with human embryonic stem cells. To tell the truth, Senator Brownback has a point. The guidelines, issued on August 23, specify that researchers with grants from the National Institutes of Health may work only with cells from surplus frozen embryos that would otherwise have been discarded by fertility clinics (http://www.nih.gov/news/stemcell/stemcellguidelines.htm). Furthermore, the researchers may not extract the cells themselves, but must obtain them from privately funded middlemen who collect the embryos and distribute the cells. The announcement came only a week after the British government released a scientific report recommending stem cell research and said it would ask parliament for approval this fall.

The NIH guidelines attempt to reconcile two irreconcilable views

The NIH guidelines attempt the impossible: to reconcile two irreconcilable views, those of a significant minority of Americans who believe that human life begins at conception and those of the majority, who think otherwise. Thus, the rules are not notably rational. But for the lawyers and ethicists who danced endless hours on the head of a pin to devise them, rationality was not a priority. In the end, they settled for attempting to reassure those who oppose the research that at least their taxes will not be spent—directly—on creating human embryos for the purpose of destroying them.

Whether this contemporary exercise in medieval scholasticism will comfort ordinary citizens is unknown. Not unexpectedly, it did not work with the organized opposition. Every right-to-life advocate—from the National Right to Life Committee to the Pope—roundly denounced the new guidelines. One harsh critic compared NIH's decision to allow using surplus embryos to the Nazis justifying experiments with inmates of concentration camps on the grounds that they would be dead soon anyway.

Researchers and patient advocates, however, are jubilant at the prospect that publicly funded human embryonic stem cell research can finally go on after Congress in 1996 prohibited the NIH from funding research in which a human embryo is destroyed. NIH grantees have some catching up to do; a few private companies, notably Geron Corporation in Menlo Park, CA, have been working with embryonic cells for two years. John Gearhart of Johns Hopkins University, who was the first to isolate stem cells from human foetuses in 1998, declared, 'this is terrific. This is what I believe makes our country top of the heap in terms of scientific research.' Said President Bill Clinton, 'I think we cannot walk away from the potential to save lives and improve lives, to help people literally get up and walk, to do all kinds of things we could never have imagined, as long as we meet rigorous, ethical standards.'

After the first isolation of stem cells from human embryos, *Science* magazine in 1999 declared this discovery the 'Breakthrough of the Year.' Embryonic stem cells have been touted as a cure for just about everything that ails us. The possibilities range from spinal cord injury to diabetes to wound healing, and especially the ills of an ageing population: Alzheimer's, Parkinson's, heart disease, strokes, osteoporosis and, perhaps, even senescence itself. Even those who have no moral objection to research with embryos, are worried that applications like forestalling ageing could represent the start of the slippery slope towards turning human embryos into a commodity.

'Indeed, biotech companies can make more money by offering to use them for the burgeoning market of "enhancement" medicine', argued Lori B. Andrews, director of the Institute for Science, Law and Technology at the Chicago-Kent College of Law and expert on the legal and ethical issues posed by artificial reproduction. She points out that Geron is touting the artificial skin it is developing as a treatment not just for burn victims but also for people with sun damage and other age-related conditions.

The scientific report approved by the British government would open the door to cloning human embryos for purposes of disease therapy

The final guidelines are only slightly different from the draft proposed in December last year. NIH reports that it received >50 000 comments on that draft. According to an analysis by the American Society for Cell Biology (http://www.faseb.org/ascb/newsroom/SCGuidelineover.html), many of the comments were simple expressions of opposition to human embryo research in any form, rather than critiques. The new draft tries to address many of the critics' points without abandoning the medically and financially promising field of stem cell research. 'I think the attempt to find a compromise is reasonable. Restricting procurement to unwanted embryos makes sense, since it shows respect for the creation of embryos but does not treat them as persons with the same rights as children and adults', said Arthur Caplan, Director of

the Center for Bioethics at the University of Pennsylvania.

But how long that restriction can last is uncertain. Eventually researchers will want to create embryos from their patients' tissue, because cells transplanted from these embryos will not risk rejection by the patients' immune system. The scientific report approved by the British government already goes in this direction. It not only would allow extraction of stem cells from embryos but also opens the door to cloning human embryos via nuclear transfer—but for purposes of disease therapy only, rather than for reproduction.

Calls for the creation of human embryos to use in research would certainly raise hackles, even among those who are well-disposed to using surplus embryos. In addition, the opponents now have an increasingly powerful argument against it: a recent string of successes with stem cells taken from adults. Stem cell transplants from mouse pancreas, for example, have reportedly reversed diabetes in mice. Bone marrow transplants have mitigated the condition of people suffering from lupus and may lead to therapies for other immune system diseases. In fact, although there was some excitement about stem cell research in US financial markets after the guidelines were announced, most of it focused on companies planning to work with adult cells.

Opponents have a powerful argument against embryonic stem cells: successes with stem cells taken from adults

Whether US taxpayers will bestow stem cell research money on anybody, however, probably depends entirely on the results of the upcoming national elections. The guidelines govern current policy, but they can be overturned in a trice by congressional action or a presidential executive order. Congress is polarized on the issue, and so are the presidential candidates. Republican George W. Bush has declared himself opposed to federal funding for stem cell research that involves destroying a living human embryo. Democrat Al Gore, the sitting vice president, supports stem cell research, and so does the party's official platform. The present Republican-led Congress is following a firm policy of doing as little as possible between now and Election Day, although it will probably try to interfere with funding if the House remains under Republican control. But since all 435 members of the House of Representatives are up for re-election, and so is one-third of the Senate, majority sentiment might well be completely different after the election in November.

NIH recognizes these political realities. The agency's timetable for handing out grants for research on human embryonic stem cells is nothing if not deliberate. Potential stem cell grantees must run two gauntlets before their proposals even make it into the agency's usual pipeline for consideration. First, they will be vetted by the Human Pluripotent Stem Cell Review Group, a special NIH committee of scientists and ethicists that will make sure the research design observes the guidelines. A second committee of scientists will subsequently take a look at protocols and judge scientific merit. Only after passing muster with both committees will a proposal be considered for funding.

One NIH official has said that work might be funded as soon as early next year, but it seems far more likely that successful proposals will not get money until the next fiscal year, at the end of 2001. As further evidence that NIH is keeping its usual prudent eye on the results of the November 7 election, it has set the grant proposal deadline for November 15, and scheduled the first meeting of the Pluripotent Group for December.

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Toxins for terrorists

Do scientists act illegally when sending out potentially dangerous material?

In 1999, Tommy Nilsson, Rainer Pepperkok and Brian Storrie published results about protein export in cells they obtained by using shiga toxin. One month later, Nilsson (a group leader at the European Molecular Biology Laboratory in Heidelberg, Germany) received a request for the plasmids that his laboratory used to produce non-toxic fragments of the toxin. As a scientist, Nilsson shares his published knowledge and material with every colleague who asks for it. But one aspect of the request for the toxin constructs made him hesitate. The letter came from North Korea. After considering the request and discussing the matter with other colleagues, Nilsson decided not to send these plasmids to a country labelled as a 'rogue' state. 'You have to think about what consequences might arise from this,' he explained, 'because the material might fall into the hands of people working on biological weapons.' Indeed, he did not make his decision easily. 'I felt pretty bad about not sending it,' he said, 'because you are obliged to send out material after you have published it—that's the norm. And you must pay particular attention to requests from third world countries where any material, be it an antibody or a plasmid, may be of great help.'

Nilsson made his decision because he was uncertain about legal aspects and the