STEM CELLS

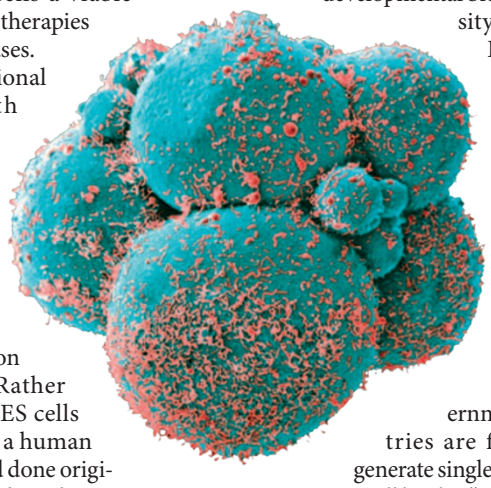
Hidden toll of embryo ethics war

Federal funds continue to be withheld for stem cells derived without destroying embryos.

BY HEIDI LEDFORD

At its heart, the ongoing legal battle to block US federal funding for research on human embryonic stem (ES) cells seeks to protect embryos.

But *Nature* has learned that in a bitter irony, the dispute seems to be holding up research on lines of human ES cells that can be derived without destroying embryos. The delay is also hampering work that researchers say could help to make adult cells a viable source of stem cells for therapies in a wide range of diseases.



Y. NIKAS/SPL

In 2009, the US National Institutes of Health (NIH) unveiled draft guidelines on the human ES cell work that would be eligible for government funds. But public comments on the draft recommended a more precise definition of the eligible cells. Rather than classing human ES cells as those derived from a human embryo, as the NIH had done originally, the agency was advised to restrict the definition to cells derived from a blastocyst — an embryo of more than 100 cells. In making that change, however, the NIH inadvertently excluded a handful of lines that had been derived from a single cell — a blastomere — plucked from an eight-celled human embryo (pictured). Although deriving stem cells from a blastocyst destroys it, extracting a single blastomere — something routinely done to look for defective genes in embryos intended for *in vitro* fertilization — seems to do no harm, leaving a viable embryo that can be frozen.

Last year, the NIH proposed a further change to the ES-cell definition that would make lines derived from embryos younger than blastocysts eligible for funding (see *Nature* doi:10.1038/news.2010.85; 2010). But the agency was overtaken by the court decision in August 2010 that halted NIH support for all research on human ES cells. The court ruled that such research conflicted with prohibitions on using government money to support work that destroys embryos. The judgement was suspended a few weeks later, allowing research to continue until further court rulings are made (see *Nature* **470,** 156–159; 2011).

The NIH has continued to approve new cell lines for federal funding under the original guidelines, but faced with so much uncertainty over the court case, the proposed changes to the definition of human ES cells have fallen by the wayside (see 'Battle lines'). Asked when the NIH would take action on the guidelines, an agency spokesperson declined to comment.

"It's extremely painful," says Susan Fisher, a developmental biologist at the University of California, San Francisco, who submitted ten single-blastomere lines for NIH approval in December 2009. "We have invested so much time and effort to make these cells and now there they sit in virtual purgatory."

In contrast, governments in other countries are funding efforts to generate single-blastomere lines for stem-cell banks. "I think this is the right approach for the field in the future," says Carlos Simón Vallés, who heads the Valencia branch of Spain's national stem-cell bank, and who is creating such lines. "Nobody likes to destroy embryos."

In the United States and the United Kingdom, companies are planning to do similar work with private funding. Advanced Cell Technology (ACT), headquartered in Santa Monica, California, and Roslin Cells in Edinburgh, UK, are in discussions to establish banks of stem cells derived from blastomeres; the embryos themselves will be frozen rather than destroyed after the procedure.

Some researchers say that the restrictions on US federal support for single-blastomere lines could hamper efforts to explore the potential of stem cells generated from adult tissue. Called induced pluripotent stem (iPS) cells, these were once heralded as a potential replacement for ES cells. But recent findings suggest that they differ in some ways from ES cells (see *Nature* **470,** 13; 2011). How those differences affect pluripotency — the ability to develop into many of the body's cell types — remains unclear. "The ultimate question for the field now is what defines pluripotency," says Chad Cowan, a stem-cell researcher at Harvard Medical School in Boston.

Early data from Fisher's lab — from studies funded by the California Institute of Regenerative Medicine — suggest that single-blastomere ES cells are even more malleable than those from blastocysts. "Not having federal funds used on cell lines derived from earlier embryos can stifle our opportunity to understand this pluripotent state," says Cowan.

"Single-blastomere lines are several times more efficient at generating certain replacement cell types than are the dozens of other human embryonic stem-cell lines we've tested," adds Robert Lanza, chief scientific officer at ACT, which has patented the single-blastomere technique.

For ACT, the funding restrictions also threatened to delay a clinical trial. The company had been counting on funding from the Foundation Fighting Blindness, a non-profit organization based in Columbia, Maryland, to back its trial of a therapy for Stargardt's disease, a hereditary cause of blindness in children. But the human ES cells in the therapy were derived from a blastomere, and as the foundation draws its clinical-trial support from the federally funded National Eye Evaluation Research Network, it was barred from contributing to the costs of the trial.

"We're tearing our hair out over here," says Stephen Rose, chief research officer at the Foundation Fighting Blindness. "We really wanted to help fund this trial." Eventually, ACT pulled money from its other research programmes to fund the trial, which is scheduled to begin later this year. ■

BATTLE LINES

Stem cells derived from blastomeres are stuck in regulatory limbo.

Cell lines submitted by	Number of lines	Source	Stage of embryo	NIH status
Various	86	Whole embryo	Blastocyst (> 100 cells)	Approved
George Daley, Children's Hospital, Boston	3	Whole embryo	Morula (~32 cells)	Approved, but now on hold*
Advanced Cell Technology	7	Single blastomere	Eight-cell embryo	Pending review
Susan Fisher, Univ. California, San Francisco	10	Single blastomere	Eight-cell embryo	Pending review

*Approval placed on hold because cells were derived from a pre-blastocyst embryo.

SOURCE: NIH

NATURE.COM
For more on the stem-cell injunction, see:
go.nature.com/ljonzx