

NEWS

US stem-cell chaos felt abroad

Court ruling endangers international partnerships.

"If the ruling stands, our collaboration is severely curtailed," wrote Benoit Bruneau in an e-mail to a UK-based colleague last week. Bruneau is a developmental biologist at the Gladstone Institute of Cardiovascular Disease at the University of California, San Francisco, whose work relies on funds from the US National Institutes of Health (NIH).

He had only recently established a partnership with Roger Pedersen, a human embryonic stem-cell scientist at the University of Cambridge, UK, to study a particular family of genes that has a prominent role in the development of cardiomyocytes — the specialized cells of heart muscle. Their enthusiasm for the project was running high because mutations in the genes have been implicated in congenital heart defects, heart arrhythmias and heart failure.

Bruneau was planning to dip into a large consortium grant from the NIH to fund his part of the planned work. Pedersen would provide him with human embryonic stem cells fluorescently tagged and genetically modified to carry the disease-causing mutations. Bruneau would then analyse how the relevant genes were acting as the cells developed into fully formed heart cells. But an injunction on 23 August by US district judge Royce Lamberth temporarily blocking federal funds allocated for human embryonic stem-cell research has thrown the collaboration's survival into question. If the suspension becomes permanent policy, and the project dies, "it will be a huge missed opportunity", says Bruneau.

"Because Benoit is the world's expert on this gene family, it may impede our ability in the United Kingdom to get funding for this project, to achieve the project's goals and to bring it to the clinic," adds Pedersen.

Pedersen's concerns point to the global repercussions of Lamberth's decision. Overseas collaborations are threatened, foreign postdocs face the prospect of a sudden end to the projects that brought them to the United States, and confidence abroad has been shaken. Although the government is appealing Lamberth's ruling, the likelihood of a future court battle and legislative jousting means that, at the very least, months of uncertainty will hang over the field (see 'Stem-cell bill may need fixing'). "The fact that [US] policy can change every four years or less is a huge deterrent to [human embryonic



Roger Pedersen left California to work on human embryonic stem cells and may now lose a US collaborator.

stem-cell] researchers and to the progression of research," says Pedersen. "That's the hurricane. That's what's doing the damage."

Andrew Elefanty, a stem-cell scientist at Monash University in Melbourne, Australia, says that if the US situation is not speedily resolved it will affect his work. Elefanty is an expert in producing stem-cell lines labelled with fluorescent 'reporter' genes, which are useful for identifying specific cell types as they differentiate *in vitro*. Since 2008, 13 of the 21 international research collaborations that Elefanty and his lab co-chief Ed Stanley have established or are in the process of establishing are with groups in the United States.

"Our concern is that uncertainty in the United States will limit our ability to collaborate, which then has knock-on effects on the quality of work we can put out. We depend on a lot of those collaborators to do really good science," says Elefanty.

The funding freeze may affect some foreign scientists directly; they are eligible to win NIH grants if no American is doing the same work. Andrew Laslett, a stem-cell scientist at the Commonwealth Scientific and Industrial Research Organisation in Melbourne, was paid as a postdoc for three years from a large, collaborative NIH grant to derive kidney progenitor

cells from human embryonic stem cells.

"That grant really set me on my career. It introduced me to the people I am still collaborating with today, and led me to getting my first independent grant," says Laslett. The news of some of those collaborators in the United States now losing funding "made me cringe", he adds.

A further layer of uncertainty hangs over foreign postdocs working in the United States who must now consider whether to remain in the country. "It's kind of all sinking in at the moment," says Adam Goulburn, who earned his PhD in Elefanty's lab and started a postdoc at Weill Cornell Medical College in New York last month. Working in the lab of Stewart Anderson, Goulburn is trying to derive pure populations of interneurons from human embryonic stem cells. The improper migration and function of these cells in the developing brain has been implicated in diseases including autism, epilepsy and schizophrenia. Goulburn's project is not immediately threatened, but the private seed money supporting him today will ultimately require scaling up with NIH funds. Anderson says that if the injunction stands, his ability to fund Goulburn's project in the long run will probably be impaired.

In the future, "highly talented, well-trained stem-cell researchers from abroad, like Adam,

"It's kind of all sinking in at the moment."



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will likely seek further training in other countries”, says Anderson. “The work and growth will continue,” he says, “just not in the United States.”

Some foreign postdocs in the United States are committed to staying the course. Dennis Van Hoof, a Dutch postdoc at the Diabetes Center at the University of California, San Francisco, is supported by private and state grants. A type 1 diabetic himself, Van Hoof

says that the injunction has not changed his plans; he was drawn to the United States by the chance to work on human embryonic stem-cell applications to his disease — an opportunity that was lacking in the Netherlands. Yet, he concedes, the prospect of federal funding for his work now looks “very insecure”.

Pedersen says he is sad for colleagues working in the United States: he decamped from

the University of California to Cambridge in 2001, after George W. Bush was elected and Pedersen’s application for a grant for human embryonic stem-cell work — the first such application to the NIH — was summarily shelved.

Looking back, “I don’t feel vindicated”, says Pedersen. “I feel aggrieved. It’s my country and I think it’s harmed by this.”

Meredith Wadman

SOURCE: US CONGRESS

Stem-cell bill may need fixing

The legal battle over US federal funding for human embryonic stem-cell research could be resolved by an act of Congress, but experts differ on what kind of bill is needed to withstand future challenges. In 2006, Congress passed a bipartisan House bill co-sponsored by Representatives Michael Castle (Republican, Delaware) and Diana DeGette (Democrat, Colorado). Known as the Stem Cell Research Enhancement Act, it was vetoed twice by then-president George W. Bush, whose aim was to restrict funding to a limited number of existing cell lines.

In March, DeGette and Castle reintroduced the bill, which would effectively turn President Barack Obama’s 2009 executive order lifting stem-cell research restrictions into law. But according to judge Royce Lamberth’s 23-August ruling, that order violates the Dickey-Wicker Amendment, a 1996 statute prohibiting funding for work that involves the destruction of human embryos. Until now, Congress has operated on the premise that

research with human embryonic stem cells is distinct from the act of deriving those cells, which requires the destruction of embryos. Lamberth’s opinion asserts that Dickey-Wicker applies to all work involving human embryonic stem cells. This alters the legal landscape around the issue and means that the wording of the DeGette bill will probably need to be modified.

“I think it would have to have some additional language” to deal with the Dickey-Wicker Amendment, says Richard Hynes, a stem-cell researcher at the Massachusetts Institute of Technology in Cambridge who is closely involved in the policy side of the field. “It didn’t have to be before, because nobody thought it was necessary.”

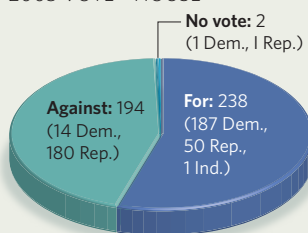
Others have raised concerns that the bill’s current wording could fuel opponents’ arguments against its passage. Louis Guenin, a philosopher of science at Harvard Medical School in Boston, Massachusetts, says that the bill does not specifically exclude funding to derive stem-cell lines, which puts it at odds with the presidential order, and does not restrict the use of stem cells to medical research and therapy. He has proposed a modified version of the bill, which addresses these and other issues.

“I think all of us have been trying to understand what is politically feasible,” says George Daley, a stem-cell researcher at the Children’s Hospital Boston in Massachusetts. A survey by the research advocacy group Research!America in August found that 70% of Americans

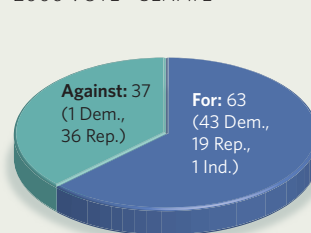
HOW THE VOTES WERE CAST

The US Congress has twice passed a bill to remove funding restrictions on human embryonic stem-cell research. Each time, a minority of Republicans who voted in favour of the legislation was crucial to its passage. President George W. Bush vetoed the bill on both occasions.

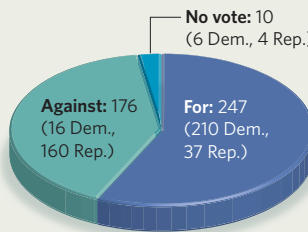
2005 VOTE - HOUSE



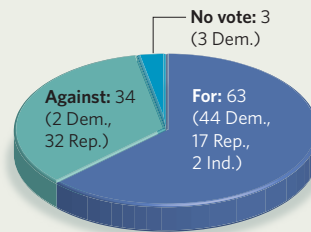
2006 VOTE - SENATE



2007 VOTE - HOUSE



2007 VOTE - SENATE



Dem., Democrat; Ind., Independent; Rep., Republican

support expanded federal funding for embryonic stem-cell research, but political realities suggest that DeGette’s bill could still be in for a rocky ride.

At present, polls indicate that the Democrats may lose their majority in the House of Representatives in mid-term elections this November. A stem-cell bill could pass before then, but it is unclear whether bipartisan support can be mustered to move the legislation forward. During the previous two votes, a small number of Republican ‘yea’ votes were important in getting the bill passed (see ‘How the votes were cast’).

Once the election is over, the current Congress could still pass a bill before it adjourns in 2011. If a House-bill passes, a parallel bill

would then have to be introduced and passed in the Senate. Senator Tom Harkin (Democrat, Iowa), who co-sponsored and introduced stem-cell bills vetoed by Bush, will hold a hearing on 16 September to examine the broad impact of last month’s injunction.

Lawmakers “are still figuring out “what to move forward with, but there’s a sense of urgency”, says Juliet Johnson, a spokeswoman for DeGette’s office. Other supporters in Congress agree. “I believe the recent court ruling only re-energizes the efforts of lawmakers like myself to develop bipartisan legislation that allows us to move forward without delay,” says Representative Mark Kirk (Republican, Illinois).

Alla Katsnelson

J. YOUNG/REUTERS



Diana DeGette will push for the stem-cell bill’s passage this autumn.