



STEM CELL POLITICS

California Debates Whether to Become Stem Cell Heavyweight

President George W. Bush may end up doing California stem cell researchers a huge favor. Spurred by the Bush Administration's restrictions on funding for human embryonic stem (ES) cells, patient advocates, venture capitalists, and research leaders have launched a campaign to persuade California voters to pass an unprecedented ballot proposal, called Proposition 71, that would allocate \$3 billion for the field over the next 10 years.

If the measure passes in November—and early polls say it's still too close to call (*Science*, 27 August, p. 1225)—California would spend nearly \$300 million a year on human ES cell research, almost 50% more than the \$214 million the National Institutes of Health (NIH) spent on all human stem

diseases, cut health care costs, and boost California's economic recovery.

But some skeptics, including supporters of public funding for human ES cell research, say the plan is too expensive for a state facing multibillion-dollar budget deficits. A group called Doctors, Patients and Taxpayers for Fiscal Responsibility has led opposition to

Proposition 71 at a Glance

- Establishes constitutional right to create and work with pluripotent stem cells, including those created by nuclear transfer.
- Allocates \$3 billion in bond proceeds to stem cell research that NIH is not allowed to fund.
- Establishes California Institute for Regenerative Medicine to administer grants averaging \$300 million per year for 10 years.



Stem cell swing vote? Governor Arnold Schwarzenegger has stayed silent on the state's Proposition 71, which would fund human embryonic stem cell research.

cell research—both embryonic and non-embryonic—in 2003. “It will change the landscape of where this work is done,” says Douglas Melton of Harvard University, who because of the White House's restrictions has had to set up a privately funded lab to derive new human ES cell lines. “California will become a hotbed of stem cell research.”

Supporters of Proposition 71 have raised more than \$11 million from donors such as Microsoft's Bill Gates and eBay founder Pierre Omidyar and his wife, Pamela. In the coming weeks, they plan to make their case for the measure with television, radio, and newspaper ads arguing that the investment will speed discovery of cures for dozens of

the measure, objecting to its cost as well as its focus on embryo-derived cells.

While Proposition 71 proponents say the opportunity for citizens to vote directly for science funding is an unprecedented chance for outreach, others worry that the political slogans could mislead voters and raise unrealistic expectations for miracle cures. “The argument that they use is that it's going to save lives. That's a good argument, politically, but in

reality that's nuts,” says George Annas, a bioethicist at Boston University. “Someday, hopefully, that's going to happen, but not in the next year or 2 or 10.”

Proposition 71 is the brainchild of real estate developer Robert Klein II, whose son with juvenile diabetes and mother with Alzheimer's disease inspired his support for stem cell research. Following the decision that NIH funding for human ES cell research would be limited to cell lines created before 9 August 2001, California, like several other states, passed a bill explicitly allowing the derivation and use of new ES cell lines. But proponents soon realized that the measure meant little without any funding attached, says cell

biologist Lawrence Goldstein of the University of California, San Diego.

Going further than the previous law, Proposition 71 would change the state's constitution, giving researchers the explicit right to conduct research with pluripotent stem cells, including cells created from embryos generated by couples undergoing fertility treatments or by somatic-cell nuclear transfer (SCNT). It would also authorize the state to issue \$3 billion in bonds to establish the California Institute for Regenerative Medicine, a funding body that would disburse grants for buildings and research projects—an average of \$300 million per year for 10 years.

The money would go to stem cell research that NIH cannot fund—namely, deriving or studying new human ES cell lines and working on human SCNT. It would potentially boost medical research funding in the state by 10% a year. (California scientists received about \$3 billion from NIH last year, according to Goldstein.)

“I know these numbers seem immense,” says Irving Weissman, a stem cell biologist at Stanford University and one of the initiative's main backers. “I'll just say that it shocked me” on first hearing, he says. But building buildings and conducting clinical trials—two of the tasks spelled out in the Proposition 71 proposal—can quickly consume tens of millions of dollars a year, he says. “Now it doesn't shock me at all.”

The sums still stun some observers. “I think [\$3 billion] is excessive in a state that is broke and cutting health services for their poor,” says Annas, who notes that he nonetheless wholeheartedly supports federal funding for such research.

With respect to Annas's concern that the potential of stem cells is being oversold to voters, Weissman agrees that the nuances of the complicated field can get lost when distilled into a political slogan. “I say it all the time: ‘Don't expect any cures from this in the next 5 years,’ ” he says. “Every time a public relations sort of person tries to talk about cures, I tell them you can't say that without qualifications. It's just not right.”

What most excites scientists is hard to sell in a 30-second ad spot, says Fred Gage of the Salk Institute for Biological Studies in La Jolla. Although transplant therapies aren't likely to be ready within a decade, he says, stem cells will provide insights into many diseases. “Stem cell biology, and particularly human embryonic stem cells, will be a tool that every lab interested in biological sciences in the ▶

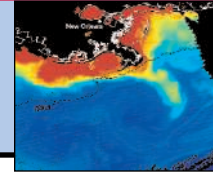
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world will have to have” to test whether animal-based observations are true for human cells, says Gage. “We are asking the public of California to recognize the value that basic scientific discovery has on their lives. That’s pretty ‘out there.’ We are giving the Californian voter credit for being smart enough to understand this.”

Proponents of Proposition 71 also tout the potential economic boost the funding could give the economy. Cures for chronic diseases such as juvenile diabetes would save \$1 billion a year in health care costs in the state, Goldstein says. And he and others argue that tax revenues and royalties from companies spun off from new discoveries will help offset the \$6 billion it will cost to pay off the bonds over 30 years. “You could think of it as an in-

tellectual stimulus package,” Gage says.

But even if scientists develop a stem cell-based cure for diabetes, counters Annas, it would likely be so expensive that overall savings would be minimal.

The potential involvement of industry worries other observers. Richard Hayes of the Center for Genetics and Society in Oakland says that his group is concerned about the prominent role that industry representatives may have on the Institute for Regenerative Medicine’s Independent Citizen’s Oversight Committee. According to the proposition, the panel will include representatives from patient advocacy groups, universities, research institutes, and at least three biotech companies. “We’re pro-science, pro-choice, and support public funding for stem cell re-

search,” he says. “But we’re concerned that Prop 71 gives interested parties enormous power over a huge sum of public funds and restricts public accountability.”

Whether voters will really understand such details before the election is far from clear, says Annas: “My guess would be that no one who is not directly involved will have read this initiative, and not more than a tiny percentage of voters really understand what this is about.”

One wildcard is California’s governor, Arnold Schwarzenegger. The state Republican party has come out against Proposition 71, but the pro-choice Republican governor has stayed quiet. The governor’s support of either camp could decide the race, Weissman predicts.

—GRETCHEN VOGEL

AIDS VACCINES

HIV Dodges One-Two Punch

In what has become a depressingly familiar story line, a leading AIDS vaccine strategy has failed to live up to expectations in human studies.

An international team led by Andrew McMichael, an immunologist at Oxford University in the U.K., reported last week at an AIDS vaccine meeting in Lausanne, Switzerland, that only 20% of 205 participants in the study had had the critical immune response the researchers had hoped to elicit. Like many who attended the meeting, Anthony Fauci, head of the National Institute of Allergy and Infectious Diseases (NIAID), says the meager response surprised him. “It was dreadfully low,” says Fauci.

The 4-year-old study, funded by the New York City-based International AIDS Vaccine Initiative (IAVI), is taking place in five countries, but these preliminary results are from the United Kingdom, Kenya, and Uganda. Although many AIDS vaccines have focused on triggering production of antibodies that prevent HIV from infecting cells, this trial tested whether two vaccines in combination could stimulate the so-called cellular arm of the immune system, which clears cells that the virus manages to infect. The study built on provocative evidence from HIV-exposed but uninfected sex workers in Nairobi and the Gambia. McMichael and other researchers found that these subjects had developed cellular immune responses to the virus (*Science*, 23 June 2000, p. 2165).

The closely followed study has broad implications because several other research groups are pursuing similar approaches. Both vaccines rely on harmless vectors to shuttle an HIV gene (*gag*) and other small pieces of the virus into the body. The “priming” vaccine splices the viral components into a ring of bacterial DNA, and the researchers follow it with a “boost” that delivers the same HIV ingredients by means of an experimental smallpox vaccine called modified vaccinia Ankara (MVA).

The McMichael team measured the ability of the prime-boost vaccination to turn up production of the biochemical messenger interferon γ in response to HIV, an indicator that the immune system has launched a cellular attack against the virus. The negative, preliminary results led IAVI to scotch plans to expand the MVA/DNA trials to other countries, but the researchers will complete those that are under way.

McMichael says their results may be disappointing in part because the team was very



Clinical study. Research in this Nairobi clinic found that HIV-exposed but uninfected sex workers had developed cellular immune responses to the virus. The vaccine failed to produce that response.

stringent in how it defined a positive interferon γ response. But he also suspects that the DNA prime, which works well in mouse experiments, didn’t do its job. “I think DNA is a poor primer in humans,” says McMichael, who notes that it has performed badly in other human studies. Yet there’s no denying the new data call into question the worth of MVA. “Is this the death knell for all MVAs?” asks Cornell University’s John Moore, a member of NIAID’s AIDS Vaccine Research Working Group. “If other MVAs are no more immunogenic than McMichael’s, this has major strategic impact.”