



# CELLULAR DIVIDE

**Y**ou may not have realized it, but if you were among the 59.1 percent of people who voted for Proposition 71 last November, you helped to put California at the center of a minor revolution in medical research.

The proposition's official text asked whether the California Institute for Regenerative Medicine should be established to regulate and fund stem cell research (with a constitutional right to conduct such research and with an oversight committee), while prohibiting funding of human reproductive cloning research.

Daniel Kiefer realized the implications of his vote. The Los Angeles resident has Parkinson's Disease, an affliction of the nervous system that impairs victims' motor functions causing, among other things, a characteristic shaking in the extremities. (Michael J. Fox is the disease's most famous victim and an advocate for a cure.) Parkinson's is caused by the death or impairment of certain brain cells; why those cells die in some people is not well understood, but they cannot be regenerated. For that reason, there is currently no cure; doctors focus instead on alleviating progressively more intense symptoms.

When his symptoms appeared in 1997, Kiefer was a 35-year-old corporate attorney and a runner. Now he's 42, a new father, and due to Parkinson's, he can't type or

The passage of Prop. 71 puts California in the middle of a controversial medical debate, pitting ethics against the benefits of stem cell research. State funding is threatened and everyone from Parkinson's patients to pundits are weighing in.

**By Lorelei Laird**

write neatly. Unable to perform the basic functions of his profession, Kiefer is on disability. He finds himself taking five medications to control the symptoms of the degenerative disease. Trouble is, the medications come with their own side effects, such as involuntary movements.

Research on embryonic stem cells offers a chance at a cure, for Kiefer and millions of other Californians who have one of 70 diseases identified as potential benefi-

aries of the research. That includes diabetes, cancer, multiple sclerosis and cystic fibrosis — all diseases common enough to help explain why Californians approved Proposition 71 last November. The measure authorized embryonic stem cell research through the state's constitution, allowed the state to purchase \$3 billion in bonds to fund the research and established an independent citizens oversight committee to dole out the funds — which it plans to start doing in May.

Scientists are excited about stem cell research because it could be the key to actually farming new organs and tissues from a patient's own DNA. The reason is that stem cells — unlike every other kind of cell in your body which is designated for a specific organ at creation — can become almost anything. This lack of differentiation makes stem cells extremely valuable to medical researchers, who can manipulate them into the differentiated cell type of their choosing. This gives scientists the potential ability to treat any disease or injury caused by dead and irreplaceable tissue, such as Parkinson's.

Scientists are just beginning to understand how these treatments could work; it could be 10 years before a viable therapy for, say, diabetes is developed. But in theory, organ transplant patients could use their own stem cells to grow new organs without facing the huge hurdles of finding a matching donor and then risking rejection of the donated organ; patients with diabetes could grow functioning pancreatic cells to generate their own insulin; and Parkinson's Disease patients could eventually grow back their dead brain cells.



Within California, metropolitan areas are vying for the chance to house the California Institute of Regenerative Medicine, the organization created by Prop 71 to dole out the \$3 billion in research grants. The institute is expected to be a huge boon to the economy of whatever city gets it, largely because of the life science research companies it's expected to attract. For that reason, at least six California cities — San Francisco, Sacramento, San Jose, Emeryville, Los Angeles and San Diego — submitted proposals March 16 that were thick with incentives like free rent and free or discounted hotel rooms and conference facilities.

Los Angeles' proposal offers four years of free office space in the City National Plaza downtown (with parking); \$1 million in foundation grants; free space at the Los Angeles Convention Center for large meetings; and free flights in a corporate jet. As big as that might sound, it's dwarfed by the incentives offered by some of the other cities; Councilman Antonio Villaraigosa recently criticized Mayor Jim Hahn for "playing catch-up" with more aggressive proposals from other cities. Savvy observers expect a site in the Bay Area or San Diego, both of which have large technology or life sciences economies already. The oversight committee will choose a site May 6.

Meanwhile, Kieffer continues to take his medications two and three times a day. He says the involuntary movements, or dyskinesia, he experiences as a result are actually a sign that his medication is working to combat the stiffness caused by Parkinson's, but overcompensating.

"It's sort of a balancing that everybody goes through," he says. "It means the [drugs are doing their] job, but it's hard for your body to regulate. Right now, Parkinson's is an incurable degenerative disease, which means the question is not whether you're going to keep getting worse, it's at what rate you're going to keep getting worse," he said. "And that's not acceptable for me and for other people who have this awful disease."

Embryos aren't the only source of human stem cells — they exist in smaller amounts in adult cells, and some are present in the blood of the umbilical cord. When Kieffer's daughter Lucy was born in late March, he and his wife saved the stem cells in the blood in the baby's umbilical cord through a private business, the Cord Blood Registry.

And with baby Lucy in the picture, Kieffer is concerned about how much he'll be able to help out with the hands-on parenting. "I don't want the burden to fall too much on my wife, but at the same time I want to be realistic about my own limitations," he said, adding, "anything that takes your mind off the disease is good. In a selfish way, the baby's going to be good for me. [But] I can't even count

the number of ways [Parkinson's] changed my lifestyle."

Kieffer says that aside from being unable to work these days, he can't drive and his voice has changed, becoming softer and hoarser. He has all the classic symptoms of Parkinson's: stiffness of gait and rigidity, slowness generally, tremors that have spread from the left side of his body to the right.

While Kieffer says that organizations like the Cord Blood Registry are becoming increasingly common, it's unknown what function—if any—the stored stem cells from his daughter's birth will serve in his family's life. "Who knows, maybe they'll help me someday," Kieffer says.

Of all the types of stem cells, embryonic stem cells have potential to develop into the widest variety of types of cells. They also have the longest life in the laboratory; the National Institutes of Health call them "essentially immortal."

Embryonic stem cell research is controversial. Because the cells come from human embryos in early stages of development, they must be obtained either from embryos that would otherwise be discarded (extras created during in vitro fertility treatments) or from somatic cell nuclear transfer, in which DNA is implanted into a human egg cell and grown into stem cells in a lab. To some, that means embryonic stem cells are a product of abortion or cloning—neither of which are acceptable to many Americans.

However, an independent poll of 1,045 American adults taken March 2005 showed

that 59 percent of voters supported embryonic stem cell research, and 33 percent opposed it; after the respondent heard a description of the research, support jumped to 68 percent and opposition fell to 28 percent. The poll's margin of error was plus or minus 3 percent.

Because of these ethical considerations, the Bush Administration has limited researchers who wish to use federal funding on embryonic stem cell research to the 22 basic stem cell lines created before the president set his policies on August 9, 2001. (Stem cell lines are groups of stem cells that scientists have cultivated to become endlessly self-replicating, reliable sources of cells.) However, the Salk Institute at UCSD has since found that all of these lines are contaminated with a nonhuman molecule, throwing their safety into doubt.

Private industry is still welcome to develop new embryonic stem cell lines, although the prohibitive cost of scientific

research means only a few companies are likely to do so. And individual states may still fund stem cell research — which is exactly what California set out to do with Proposition 71.

And if this all sounds like an expensive, if noble, proposition for our state, think again. An economic study by research firm The Analysis Group, with Stanford University health policy professor Laurence Baker, found that Prop. 71 will not only pay for itself, but will likely turn a profit for California. The study, commissioned by the Yes on 71 campaign, found that while payback and interest on the bonds will cost California \$5.4 billion through 2039, it will also generate direct income of at least \$2.5 billion; savings to the state health care budget of at least \$3.4 billion; at least \$9.2 billion in savings to private health care providers; and revenues to the state of at least \$547 million, from the royalties generated by whatever new tech-

handling out money in May, both challenges were filed directly with the State Supreme Court, skipping the trial and appellate court process. (Lawyers for the groups say they're not working together, although they've consulted one another and consider their suits complementary.) The high court on March 23 dismissed the two petitions, but did so without prejudice, allowing the groups to refile the claims in lower courts — something at least two of them say they plan to do.

Those groups, People's Advocate and the National Tax Limitation Foundation, take issue with the fact that the ICOC is independent from the state — something they say is unconstitutional because it allows the committee to spend taxpayer money without accountability to officials elected by the people. Dana Cody, the Sacramento attorney for the groups, said they will refile, although as of press time they're still deciding



Photo by Jasmin Persch

Left: The Kieffer family.

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**— DANIEL KIEFFER, PARKINSON'S SUFFERER**

where and how.

The attorney in the other claim, David Llewellyn of Sacramento-area law firm Llewellyn Spann, couldn't be reached by press time but told Reuters a lower-court challenge is highly likely. His client is a newly created organization named Californians for Public Accountability and Ethical Science — which counts among its friends Vincent Fortanasce, head of last fall's No on 71 campaign. The group's challenge said Prop 71 violates conflict-of-interest laws because it requires members of the ICOC to come from a university, research foundation or advocacy group that has an interest in where the money goes. The filing also said the initiative violated California law requiring only one subject for propositions.

Llewellyn says individual members of his group may or may not have ethical issues with embryonic stem cell research, but that's not what the chal-



lenge was about.

"The text of Prop. 71 created exemptions to pretty much every conflict of interests statute in the state," he said. "It's not well known. But when you read it, you discover that the nature of the people who must be appointed to the government body are by definition people who have conflicts of interests. Under the laws that govern every other state official, they wouldn't hold office because of these conflicts."

And that, he said, puts California at risk of having Prop. 71 money misdirected. Llewellyn's not only concerned about committee members who stand to profit monetarily, but by people with an emotional interest in stem cell research,



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which might limit their objectivity about where the money could do the most good. He cited his experience as the son of a multiple sclerosis sufferer bound to a wheelchair for much of her life.

"Would it be reasonable to think if a proposal came up... that I could disinterestedly vote, and basically say 'I'm sorry, Mom, but you're not going to get money?'" he asked. "It's too much to ask of anybody. And that's why we have conflict of interest laws."

That said, Llewellyn also described members of his group as "...people who are concerned about medical research and bioethics." One thing that might illustrate his group's position, he said, is its objection to what he sees as misleading wording in the law. The language bans reproductive human cloning, but

allows "therapeutic cloning" or somatic cell nuclear transfer, which uses the same process to grow cells not intended to become a person.

"If you don't have a scientific education, you don't realize that somatic cell nuclear transfer is cloning," he said. "Prop. 71 actually authorizes and creates a right to clone human beings.... We think people should have a clear idea of what they should be voting on."

Furthermore, Llewellyn said, some members of Californians for Public Accountability and Ethical Science have doubts about the viability of embryonic stem cell research as a technology. Where adult stem cell research has already produced over 80 cures, he said, tests of embryonic stem cell research in animals have shown to be ineffective or outright harmful.

Those are doubts shared by Cody, who in addition to being an attorney is the executive director of the Life Legal Defense Foundation, an organization active in pro-life issues including abortion and euthanasia. That group isn't a plaintiff, but it's financing the suit.

While her clients' challenge to Prop. 71 was brought based on the ICOC's lack of accountability to taxpayers, Cody said the group's objections go beyond that.

"We don't want to see taxpayer money going to fund research that is not really proven," said Cody. "There have been advances in adult stem cell research... that's a proven research method. We think that embryonic stem cell research, whether [or not] it's from discarded embryos, is unethical and it's not a proven research method."

"If embryonic stem cell research were a promising research, you can bet venture capitalists would be funding it," she added. "But they're not. I believe this is a money grab against taxpayers."

Unlike Llewellyn's group, Cody says her clients explicitly have moral problems with embryonic stem cell research.

"We're trying to stop them from operating on taxpayer money," she said. "Admittedly, [that's] because of our moral objections. But this lawsuit focuses on trying to stop funding because it is unconstitutional."

**S**okeswoman Julie Buckner for the California Institute for Regenerative Medicine said the architects of Prop. 71 specified that the ICOC should include scientists and patient advocates for a very good reason: they wanted to "make sure stakeholders had a significant seat at the table."

Buckner dismissed the idea that committee members are in danger of voting against California's best interests. Not only are committee members well-respected scientists and individuals, she said, but they've all filed California Form 700, a financial disclosure form required of public servants. And the committee fully intends to adopt its own ethics rules.

"Thirdly, and our opponents know this, the board is committed and dedicated to and has every intention of adopting strict conflicts of interest policies for itself, its senior staff and its administrative staff," she added. "They will be discussed publicly. And there'll be full public input as the board moves forward with its work."

Kiefer, for one, doesn't see the threat in the conflicts the groups allge.

"Generally I don't think there's necessarily a conflict of interests when you have scientists and experts in the field on the committee," he said. "And there are some safeguards set up in Prop. 71 itself. I don't believe that hypothetical Mr. Smith is going to be in a position to vote to approve a research grant to Mr. Smith's lab. That's not going to happen." And if there are conflicts, he said, so what?

"I'm not sure who these critics would rather have on the oversight committee, but you have to have people who are knowledgeable in the field, but you have to have patient advocates as well," he said. "I think the point of the proposition is to make a difference in the lives of these people, and it only makes sense that people who are going to be most directly affected by this should have some voice in how the money is spent."

**K**iefer came late to Prop. 71 advocacy; he said he followed it before and after November's election, but only got involved when it looked like politics were gumming up the works. That involvement led him to speak before the ICOC in January about the importance of embryonic stem cell research.

"It sounded like the ICOC was getting bogged down, not necessarily through any fault of their own, but at least in part because they were getting attacked... for some procedural issues like lack of sufficient notice and maybe potential issues with the open meeting laws," he said. "And I don't want to minimize those things or say they're not important, but ... I wanted to take a step back and say 'Wait a minute, let's think about what the committee is here to do.'"

"And let's not lose sight of the fact that they're here to hopefully... accelerate treatments and cures for people like me and people who have other incurable diseases."

As with many people who are diagnosed with Parkinson's Disease at a relatively young age, it took a while for Kiefer to find a doctor who correctly identified his symptoms.

"The first symptoms I noticed were about 1997, August or September," he said. "I was a runner and I noticed on my longer runs, at a certain point my left leg would stiffen up."

That was dystonia, he said, a classic indication of Parkinson's. But the first neurologist he saw specifically ruled out the disease because of Kiefer's youth, so he sought treatment for a running injury

and then for stress before seeing a second neurologist, who identified the disease with a few motor skills tests.

"The day I was diagnosed, it was around Thanksgiving of 1998," Kiefer said. "I remember walking out of the doctor's office, going to my car and sitting in my car, and I just sat there and started crying."

But then Kiefer turned on his car radio. As luck would have it, this was around the same time that Michael J. Fox had gone public with the news of his own diagnosis with Parkinson's Disease, and there was a news story about it.

"I thought that was ironic," said Kiefer. "He's almost the same age as I."

Kiefer eventually rallied, and these days — like Fox — he's turned some of his energy to advocacy for Parkinson's patients.

"Michael J. Fox said he thought if he had it to do all over again, he would choose to get Parkinson's," said Kiefer. "I would choose not to get Parkinson's, but having said that, and getting involved in the Parkinson's advocacy work and the stem cell research has [been good]. So in that sense I guess I'm fortunate."

**I**r. Andrew M. Yeager is a professor of medicine and pediatrics at the University of Pittsburgh, and a member of the University of Pittsburgh Cancer Institute/Stem Cell Transplant Program. He and his team work with adult stem cells, looking for a way to rebuild certain cells in the body as a way to fight cancer. As such, the team doesn't stand to benefit from Prop. 71; indeed, Yeager said, embryonic stem cells aren't even useful for the kind of work the team is doing.

Responding to the scientific claims Llewellyn and Cody's groups make, Yeager is happy to agree that embryonic stem cell research isn't proven yet — because of a lack in research.

"It takes time to get these things under way," he said. "One unfortunately starts from not knowing whether things work. That's why you do the careful, thoughtful, well-controlled experiments."

"As with so many things, and in a relatively early stage of this type of research, conflicting reports in biomedical literature are not uncommon," he added. "I would think a thorough critical review of the literature would acknowledge that nothing is proven or disproven; otherwise, why go any further?"

But Yeager praised Californians for even trying. "The idea of having a statewide initiative for embryonic stem cell research — and in a Republican administration, no less — is very refreshing," he said. "Clearly, in a state that has excellence in research in its public and private universities, a populous state, this is courage and leadership."