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## States vie for stem-cell scientists

BY: CHRISTINE VESTAL, STATELINE.ORG STAFF WRITER

Far from resolving an epic moral quandary, last year's groundbreaking discovery that ordinary skin cells eventually could replace the use of human embryos in stem-cell research actually stoked the fiery debate over the cutting-edge science.

Religious opponents hailed the skin-cell breakthrough as proof that research involving the destruction of embryos is unnecessary and must end. Scientists countered that studies on stem cells harvested from human embryos must continue for at least several more years while the new technique is perfected. And the battle went on.

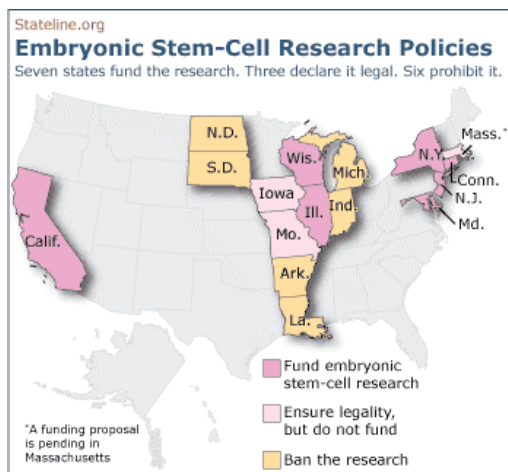
(A subsequent report, published in a scientific journal Jan. 11, revealed that stem cells had been produced from human embryos in a private U.S. lab without destroying the embryos, adding to already mounting enthusiasm for the science.)

Much of that battle is being waged in state capitals.

At the forefront, seven big states are leading the world in political and financial support for embryonic stem-cell research.

Their goal: Attract the best stem-cell scientists from around the globe and become a hub for a multi-billion-dollar bioscience industry. So far, their plan appears to be working.

In the past two years, California, Connecticut, Illinois, Maryland, New Jersey, New York and Wisconsin have awarded some \$230 million in grants — more than three times as much as the federal government spent on embryonic stem-cell studies in that time — and there has been no shortage of scientists seeking the money.



Source: National Conference of State Legislatures, December 2007

But six others — Arkansas, Indiana, Louisiana, Michigan, North Dakota and South Dakota — now ban studies that result in the destruction of human embryos, and Arizona bars state funding for embryonic studies. These states have positions closer to those of Japan and most European countries.

Except in these states, work on embryonic stem cells is free to go on in the United States at places such as universities and private, nonprofit and corporate laboratories — as long as no federal money is involved. But states that want to be players in the nascent stem-cell arena are finding they must ante up with state financing and a science-friendly environment.

Polls indicate a majority of Americans approve of embryonic stem-cell research, which explores special cells in 5-day-old embryos that have the unique ability to transform into cells from any organ tissue in the body. Scientists say these so-called pluripotent cells hold the keys to discovering the causes and cures for many human ailments, including Alzheimer's, Parkinson's and Lou Gehrig's disease, juvenile diabetes, blindness and spinal-cord and brain injuries.

But President George W. Bush, the Catholic Church and right-to-life groups have cited the same moral objections they raise to abortion in demanding that human embryos — which they regard as the beginning of life — not be sacrificed, even in a search for cures to save human lives. Instead, they pressed for research into non-controversial adult stem cells.

The latest discovery satisfies those with moral objections and dramatically tips the balance toward more work on skin cells. But for scientific reasons, embryonic studies won't be abandoned just yet.

Embryonic stem-cell research is still the “gold standard” for scientists, said Jonathan Moreno at the University of Pennsylvania's Center for Bioethics. “Everyone is saying the future is with the new cells. But we're not in the future yet. It's going to take several years to get there.”

(The Jan. 11 news that stem cells had been derived from human embryos without harming them may not hold as much promise as the skin cell method, because it is more difficult to perform, scientists say. In addition, religious leaders strongly objected to early reports of the research in 2006, and administration officials so far have said the federal government is not likely to approve it for funding.)

### **Scramble for scientists**

Among states seeding the fledgling science, California is the bellwether with a \$3 billion fund of taxpayer dollars being spent to build worldclass research labs and lure leading stem-cell scientists to the sunny West Coast. When all seven states' investments are totaled, the commitment comes to nearly \$5 billion over the next 10 years. Massachusetts could add another \$1 billion.

States with a financial and political climate that welcomes embryonic stem-cell work may shift more emphasis to the new techniques, but existing investments in embryonic studies will continue as well.

“States that have chosen to fund the research are in an ideal position,” said Bernard Siegel, founder of the Genetics Policy Institute, a nonprofit stem-cell advocacy group. “Scientists are energized by the new developments, and many of the best and brightest already are flocking to California and other states with generous grants and friendly science policies.”

In fact, Shinya Yamanaka, the scientist who led the research team in Japan that made the November 2007 breakthrough transforming skin cells into stem cells, recently accepted a California grant and in August 2007 began working part-time in a lab in San Francisco to avoid restrictions in his home country. In all, the California Institute of Regenerative Medicine reported it has scored 24 of the world’s top stem-cell scientists, who have relocated to take advantage of the state’s offer.

As Gov. Arnold Schwarzenegger (R) predicted when California voters approved their landmark 2004 ballot measure authorizing the stem-cell investment, the message has gone out to “the world’s scientific elite and aspiring students that, in California, you will find the resources and the freedom to expand the frontiers of science.”

For states not yet in the game, the recent discoveries could open a window for state funding that conservative state politics previously had closed. For example, Moreno cited Florida and Texas, which have major universities and businesses with big stakes in biomedicine but state politics that have prevented investment in the research so far.

“State policies will determine which states become magnets for high-tech research and which will become irradiated zones,” said Daniel Perry of the Alliance for Aging Research, a citizen advocacy group for stem-cell research.

Missouri already has learned that lesson the hard way.

In 2004, when Harvard stem-cell scientist Kevin Eggan was completing a post-doctoral stint, he considered a position at Missouri’s well-funded Stowers Institute for Medical Research. He liked the facilities in Kansas City, the generous grant and prestigious faculty, but after learning about Missouri politics, he declined the offer.

“I couldn’t rationalize the risk of waking up some morning to find that I was a felon because of an action taken in the state Legislature,” he said.

Eggan was the first scientist to turn down an attractive post at Stowers because of Missouri politics, but he was not the last.

At the time, conservative Missouri lawmakers were trying to outlaw the human-cloning techniques used by Eggan and others in stem-cell studies.

While cloning to produce duplicate human beings — or human reproductive cloning — is universally denounced, human cloning to harvest stem cells is key at this time in the search for therapies that one day might allow a patients’ own cells to be used to regenerate diseased or damaged tissues.

Missouri's research ban passed the Legislature in 2005, but Missouri Gov. Matt Blunt (R) — himself a conservative and abortion opponent — vetoed it. The next year, Missouri voters were asked to settle the issue and narrowly approved a constitutional amendment ensuring the legality of the science — a first-of-its-kind measure that the United Nations has since asked all countries to adopt.

Despite the legal assurance, Stowers decided to give \$12 million to Eggen and two other Harvard scientists and let them stay in more liberal Massachusetts. Stowers also moved \$800 million of its \$2 billion private research trust to a separate out-of-state funding organization. According to Stowers chief William Neaves, the move was spurred by continuing instability in Missouri politics.

In 2007, conservative Missouri lawmakers tried to pass a bill repealing the stem-cell amendment. The initiative failed, but they succeeded in blocking bioscience funding for the University of Missouri because they said it might be used for embryonic studies. In addition, grassroots opponents began gathering signatures for a 2008 ballot measure that would outlaw the science.

### **Stem-cell politics in 2008**

Last year, 39 states considered more than 100 bills for and against the research, but only three laws were enacted, according to the National Conference of State Legislatures. New York approved \$650,000 in funding for stem-cell and other biomedical studies. Iowa repealed its 5-year-old ban on the research. And the Illinois Legislature affirmed Democratic Gov. Rod Blagojevich's 2005 executive order creating a \$15 million stem-cell research fund.

On the political scene, the skin-cell breakthrough came after almost all states had ended their 2007 legislative sessions. So its impact will be measured in 2008. The debate is expected to intensify in light of the discovery, said Patrick Kelly, state strategist for the Biotechnology Industry Organization.

Opponents of embryonic studies may rally for more state bans on the research, but they also could call for new investment in non-controversial techniques. Proponents may push for more state funding of embryonic research to speed the necessary parallel studies to determine if the new science works as well.

Massachusetts lawmakers will weigh Democratic Gov. Deval Patrick's proposal to join the pack of states underwriting stem-cell and other biomedical studies by investing \$1 billion.

If the winner of the White House decides to drop Bush's restrictions on stem-cell funding, Congress could press again for federal money. The current policy put in place by Bush allows federal funding only for work on embryonic stem-cell lines created before Aug. 9, 2001, preventing any further destruction of embryos using federal money.

In 2006 and 2007, Bush vetoed bipartisan bills that would have allowed federal funding for the creation of new stem-cell lines using surplus embryos and research on existing cell lines created since Bush's cutoff date. Neither bill included appropriations.

Even if the next Congress and president are willing, the extent of any federal funding is another question.

“With a budget deficit and the war in Iraq, the odds of a major bump in federal stem-cell funding are slim no matter who is elected president,” said James Fossett, a bioethicist with the Rockefeller Institute of Government. “The economic opportunities presented by the research make it unlikely states will diminish their funding efforts.”

On the presidential campaign trail, Democratic candidates uniformly support increased federal funding for the science. U.S. Sen. Hillary Clinton (DN. Y.) has been most outspoken, proposing broad intellectual freedom and support for science in general. Republican presidential candidates, however, vary widely. Former New York Mayor Rudolph Giuliani and U.S. Sen. John McCain of Arizona favor increased federal funding as proposed by Congress, but McCain said he opposes cloning embryos for research, according to data collected by the Pew Forum on Religion & Public Life.

Former Govs. Mike Huckabee of Arkansas and Mitt Romney of Massachusetts fall in line with Bush in support of research only on existing cell lines. Like McCain, they oppose human cloning for research purposes. U.S. Rep. Ron Paul of Texas opposes expanded federal funding but not the research. Actor and former U.S. Sen. Fred Thompson of Tennessee condemns embryonic stem-cell studies, according to the Forum, which, like Stateline.org, is funded by The Pew Charitable Trusts.

### **States take sides**

Most states entered the stem-cell fray in the last six years. But the ethical debate over embryonic research began in the mid-1970s over so-called test tube babies and laid the groundwork for Bush’s 2001 funding decision.

In 1994, President Bill Clinton approved federal funding of research involving surplus embryos — similar to Congress’ 2006 and 2007 bills — but Congress overrode his decision in 1995, enacting an appropriations rider that prevented such funding. Clinton also imposed a five-year moratorium on funding for studies involving cloned embryos, which Bush extended in 2000.

With mounting pressure from scientists and patients, Bush decided to open a small window of funding for the fledgling research. On Aug. 9, 2001, he limited federal money to studies using already-created embryonic stem cells, skirting Congress’ restriction on spending for work involving embryos. He assured his anti-abortion allies that no new embryos would be destroyed.

His decision satisfied neither side. Religious opponents had argued for a federal ban on all of the studies, and scientists complained that most existing cell lines were contaminated and thus unusable for research.

Political positions on the issue didn't neatly divide along partisan lines. While most national Democrats supported embryonic stem-cell research, certain high-profile Republicans — including former first lady Nancy Reagan, who watched her husband succumb to the brain-destroying effects of Alzheimer's disease — parted with Bush and came out in support of the science.

The same divisions were evident in statehouses. Four states — Arkansas (2003), Indiana (2003), North Dakota (2003) and South Dakota (2004) — reinforced existing bans on human reproductive cloning to outlaw embryonic stem-cell research within their borders. Louisiana (2000) banned all research using human embryos created in fertilization clinics. Michigan already had banned research on embryos in 1978 and all forms of cloning in 1998.

Still, Louisiana is investing in other bioscience projects, including noncontroversial gene therapy. And top stem-cell scientists at Michigan's state universities are working around the restrictions, in some cases relying on help from out-of-state scientists for work deemed illegal in Michigan.

With a cap on federal funding, other states saw opportunity.

New Jersey was the first to underwrite research into stem cells, appropriating \$10 million in January 2004 and taking on a role historically held by the federal government's esteemed National Institutes of Health. California came next with its November 2004 voter-approved fund of \$3 billion and immediately outstripped all other investors.

In 2005, Connecticut allotted \$100 million and Illinois \$10 million, adding another \$5 million in 2006. Maryland approved \$15 million in 2006 and \$23 million more in 2007, and New York invested \$650 million in 2007. Wisconsin Gov. Jim Doyle (D) created a \$750 million building fund to construct a stem-cell research laboratory on the campus of the University of Wisconsin, Madison. New Jersey in 2006 appropriated an additional \$15 million in grant money, \$9.5 million for administrative costs and \$270 million to build five new research facilities.

While they didn't pony up dollars, Missouri in 2006 and Iowa last year declared their state open for stem-cell business with measures legalizing work on embryos. Massachusetts lawmakers in 2005 overrode a veto by then-Gov. Mitt Romney to ensure the legality of the research.

However, even in states with firm commitments to the research, the waters remain unsettled.

On Election Day 2007, New Jersey voters defeated Democratic Gov. Jon Corzine's bid to raise an additional \$450 million for new stem-cell grants. Some objected to the proposal on moral grounds, but political analysts said most voters were worried about how the cash-strapped state would repay the loans.

After California voters approved the state's landmark funding initiative in 2004, opponents tied up the money in court battles over copyright and other issues. In 2006, Schwarzenegger approved state loans to jump start the program. Courts have since cleared the way for funding to flow.

In Connecticut, shortly after the state distributed its first grants in 2006, conservative lawmakers attempted to outlaw the studies and repeated their efforts again last year, failing both times.

In job-hungry Michigan, Gov. Jennifer Granholm (D) and a handful of lawmakers have been trying for four years to repeal the state's ban on the research.

### **Science and ethics**

Opponents of embryonic stem-cell research object to two basic scientific techniques: harvesting stem cells from 5-day-old human embryos and cloning human embryos using somatic cell nuclear transfer (SCNT). In both cases, the embryo is ultimately destroyed.

Instead, opponents have maintained scientists should redouble their efforts in other medical research fields, such as non-controversial adult stem-cell studies, and now, the new skin-cell process.

Up to now, scientists argued that adult stem-cell research was no substitute for embryonic studies, because the undifferentiated cells in embryos have unique capacities to develop into pluripotent cells that can make up any organ tissue in the body. In the newly announced research, scientists created what they say appear to be pluripotent cells by coaxing adult skin cells to revert to an embryonic stem-cell-like state referred to as induced pluripotent cells.

Cloning, or SCNT, used in many embryonic stem-cell studies, ultimately may be replaced with the newly developed induced pluripotent cells. SCNT — perfected by the Scottish scientist Ian Wilmut, who produced Dolly the cloned sheep in 1996 — replaces the DNA in an egg with DNA from another organism.

The new skin-cell technique would produce stem cells compatible with the donor, and scientists believe it ultimately will make SCNT unnecessary. In addition to avoiding the ethical controversy over creating and destroying embryos, scientists say the new technique would avoid the cumbersome process of acquiring donated eggs and embryos.

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