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Texas governer Rick Perry has received a stem-cell treatment deemed illegal in the United States.

REGENERATIVE MEDICINE

Texas prepares to fight for stem cells

Enthusiasm for unapproved treatments worries regulators.

BY DAVID CYRANOSKI

There's a showdown brewing in the state of Texas — and it could get ugly. On one side stands the US Food and Drug Administration (FDA), which is clamping down on the proliferation of unapproved stem-cell treatments being offered to Americans. On the other is state governor Rick Perry, who is riding high in the polls as the Republican party's favoured candidate for the 2012 presidential elections — and a staunch advocate of the stem-cell treatments.

At least a dozen companies in the United States offer the treatments, which involve extracting adult stem cells from a patient's tissue, culturing them, then reinjecting the cells. The theory is that the cells will flourish and replace diseased or damaged tissue in a range of conditions from spinal-cord injury to Alzheimer's disease and diabetes.

But no treatment that involves anything more than "minimal manipulation" of adult stem cells outside the body has been approved by the FDA. Although bone-marrow transplantations, for example, involve extraction and reinjection of haematopoietic stem cells, those cells are not cultured or significantly processed.

"Any procedure involving removing cells from the body and manipulating them — even if it's something as simple as centrifuging them or putting them in a plastic tube — and then putting them elsewhere in the body poses risks," says Paul Knoepfler, a stem-cell specialist at the Institute for Regenerative Cures at the University of California, Davis. No clinical trials have shown any evidence of efficacy, he says. "Patient testimonials cited by the people selling the treatments have little if any meaning."

Depending on exactly how the cells are processed and administered, many of these procedures are illegal in the United States. But that didn't stop Perry from being injected with a concoction of his own stem cells in July to treat a back complaint. Perry's procedure was carried out by Stanley Jones, a surgeon based in Houston, Texas, who specializes in cosmetic procedures and who is a friend of the governor.

The previous month, Perry had supported legislation that authorized Texas's health commission to create a stem-cell bank in which patients would be able to deposit their adult stem cells for future use.

PUBLIC INTEREST

Texas has poured millions of dollars into studying and commercializing adult stem-cell treatments through its Emerging Technology Fund, an initiative created at Perry's behest. Perry sees the treatments as both a potential boon to the Texan economy and an alternative to treatments that use embryonic stem cells, which he opposes. In a 25 July letter, he asked the Texas Medical Board (TMB), which regulates the state's physicians and is currently reviewing its policy on stem-cell treatments, to take a lenient view on the procedures. "It is my hope that Texas will become the world's leader in the research and use of adult stem cells," he wrote. "With the right policies in place, we can lead the nation in advancing adult-stem-cell research that will treat diseases, cure cancers and, ultimately, save lives."

Although scientists and physicians in Texas are excited about the funding to develop stem-cell science, many are concerned that treatments will reach the clinic before safety and efficacy are properly established. "I do believe governor Perry is pushing research to the clinic too quickly," says Kirstin Matthews, who researches science and technology policy at Rice University in Houston, and who is a member of the TMB's stakeholder group, which is helping to draft the board's stem-cell policy.

"People should know what they are doing," adds Mari Robinson, executive director of the TMB. "Otherwise they'll try to use it for everything from getting rid of wrinkles to curing cancer."

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Bettie Sue Masters

The TMB's draft stem-cell policy is open for public consultation, and will be finalized in November. In a series of written submissions, scientists have pushed for more patient protection. "As a biomedical researcher, I feel the extremes of regulatory burden every day, but I also feel that we must protect patients from risky treatments advanced by overzealous, even greedy, entrepreneurs," wrote Bettie Sue Masters, a biochemist at the University of Texas Health Science Center in San Antonio.

APPROPRIATE OVERSIGHT

Mary Ellen Weber, vice-president in charge of government affairs and policy at the University of Texas Southwestern Medical Center in Dallas, hopes that patients will be properly informed that any benefits that they experience may not be attributable to the stem-cell treatment, and may not be long-lived. By contrast, she warned in a letter to the TMB, the "risks conferred by stem-cell therapy may be delayed and permanent". Consequently, any adult stem-cell procedures should be looked at by an institutional review board, she wrote.

But state representative Rick Hardcastle, who introduced the legislation to authorize the Texas stem-cell bank, has questioned the need for institutional-review-board consideration of procedures that use adult stem cells. "It was not, and is not, my intent to create onerous and unnecessary regulations to impede the practice and research of physicians in regards to the use of investigational agents," he wrote to the TMB on 23 August.

Although the TMB's forthcoming policy is meant to provide clearer guidance on the use of adult stem cells in the state, physicians and companies are still subject to FDA regulations. And there are growing signs that Perry's ambition is on a collision course with recent efforts by the FDA to flex its regulatory muscle.

For many years, stem-cell clinics have been able to flourish by skirting the FDA regulations. Some clinics recruit patients in the United States and then send them overseas for treatment: the Stem Cell Treatment Institute in San Diego, for example, treats its patients in Mexico. Others invoke a 'compassionate use' exemption to FDA regulations, which allows them to charge patients for experimental therapies if no other treatment options are available. Some argue that the FDA has no jurisdiction over their activities, claiming that adult stem cells are not drugs — merely the patient's own tissue — and therefore not subject to FDA oversight.

"The growth in the number of clinics and companies marketing stem-cell products without approval is explosive," says Doug Sipp, who studies global stem-cell regulation at the RIKEN Center for Developmental Biology in Kobe, Japan. "The United States is becoming one of the most rapidly expanding markets for unregulated stem-cell applications."

The FDA has long pursued a policy of trying to get companies to comply with the regulations, rather than prosecuting them. Recently, however, it has taken stronger steps to crack down. On 15 August, for example, the agency sent a warning letter to Chuck Naparalla, chief executive of TCA Cellular Therapy in Covington, Louisiana, saying that the company had failed to meet safety standards in some of its five FDA-approved clinical trials of its stem-cell therapies. The FDA also accused it of selling treatments to patients "outside of clinical protocols". TCA Cellular Therapy has not responded to *Nature*'s repeated requests for information on its efforts to comply with the FDA's demands.

On 18 August, after an investigation by the FDA and the FBI, Fredda Branyon, former owner of Global Laboratories in Scottsdale, Arizona, was convicted by the US Attorney's office in the Southern District of Texas court of selling unauthorized stem-cell products across state lines.

And in a court case that began last year, the FDA is demanding that Regenerative Sciences of Colorado stop selling its adult stem-cell product Regenexx (see *Nature* **466,** 909; 2010). Christopher Centeno, medical director of Regenerative Sciences, claims that "the Regenexx procedure is the practice of medicine, something Congress and the courts have expressly prohibited the FDA from regulating". The FDA argues that Regenexx falls under its jurisdiction because its is classed as a biological drug under the Code of Federal Regulations 21 on human cells and tissues. That regulation allows the reinjection of a patient's adult stem cells if they have been "minimally manipulated", but the FDA says that the culturing involved in Regenexx is not minimal because "the cells are grown, processed and mixed with drug products outside the body".

While the FDA is busy in court, Texas's enthusiasm for stem-cell treatment is growing fast.

The cells used to treat Perry were cultivated at a recently opened laboratory in Houston that is jointly run by RNL Bio, a stem-cell company headquartered in Seoul, and Celltex Therapeutics, a company established and run by Jones and David Eller, former chairman of the board of Texas A&M University and now a supporter and adviser to Perry. Neither Perry nor Jones responded to *Nature*'s interview requests.

RNL Bio's affiliated clinics in the United States take fat samples from patients and send the cells to Seoul for processing. The manipulated cells are not approved for reinjection in the United States or South Korea, so patients typically travel to China or Japan for the procedure. RNL Bio is now being investigated by the Korean government after two people who underwent this procedure in Japan died (see *Nature* **468,** 485; 2010). Jones himself travelled to Japan last year to receive an injection of cells, prepared by RNL Bio, to treat his arthritis — successfully, he claims.

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Perry's procedure was reportedly carried out in the United States, at Jones's clinic. The FDA declined to discuss any ongoing or future investigations into stem-cell clinics, but a former reviewer at the FDA's Center for Biologics Evaluation and Research, which regulates the clinical use of stem cells, says: "If Perry was treated in the United States, it was clearly in violation" of FDA regulations.

Jones has said that Perry may be prepared to stand up to the FDA over the issue. In a letter to the TMB, Jones wrote: "Please don't make this difficult, as Governor Perry has really gone all out personally to make stem cells available to people in need of them in Texas."

"He is incidentally not against a challenge from any government agency that wants to impede us in Texas," Jones added.

Jones is now set to treat Hardcastle, who has multiple sclerosis. The former FDA reviewer, however, says that after the publicity over Perry's procedure, it would be standard practice for the agency to warn Jones against carrying out further injections. "If you do it a second time, you could be in hot water."

The showdown could be about to begin. ■

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