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Stuart Leavenworth: Truth behind stem cell 'miracles'

By Stuart Leavenworth -- Associate Editor
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Scientists are normally a cautious bunch, nervous about making bold predictions or being accused of unprofessional hype. Yet those cautions flew out the window last year, when supporters of Proposition 71 dangled $3 billion in stem cell research money before scientists and California voters.

A Nobel Prize winner went on TV to tout Proposition 71. Other top-flight scientists joined Dustin Hoffman and other Hollywood stars for a "Countdown to Cures" event in Los Angeles. Promoters sent out press releases claiming that therapies developed by Proposition 71 "could save the lives of millions of California children and adults."

Nothing was mentioned about the embryonic state of embryonic stem cell research.

Now that the initiative is law, Proposition 71 supporters face a daunting challenge - how to manage lofty public expectations.

Partly because of the P.R. campaign, many patient advocates and California taxpayers believe that medical miracles are imminent. In reality, most scientists say it will take years, and possibly decades, before embryonic stem cell treatments are proven and made widely available.

"No one knows if you can control embryonic stem cells," said Arthur Caplan, a University of Pennsylvania bioethicist and supporter of stem cell research. "It is like trying to argue right after the Orville and Wilbur Wright flight whether we could have a Mars mission."

Denis Baylor, a neurobiologist and member of the National Academy of Sciences, says much more must be learned about basic human biology before embryonic cells can be transplanted into suitable test subjects.

"It's a mistake to think that anything earth shattering is going to happen in a year or two," says Baylor, senior scientific officer for the Howard Hughes Medical Institute in Chevy Chase, Md. "The foundation has to be built properly, and that's going to definitely take some time."

This is not to suggest that embryonic stem cells don't have impressive potential. Scientists I've talked to - both in California and elsewhere - generally agree the field is ripe with promise and deserving of public investment. The problem is, California taxpayers didn't vote for Proposition 71 so they could help build a foundation of general biological knowledge. They were sold on the idea of quickly funding cures, a prospect that may be wildly optimistic.

Stem cells, as the name suggests, are biological twigs, ones that can grow into many different branches of tissue. In fact, some studies have found that, when implanted in a diseased animal, stem cells can actually

seek out the injured tissue and start to repair it.

Until now, scientists have mainly worked with adult stem cells - such as those found in bone marrow - to investigate cures for spinal cord injuries and other maladies. Such stem cells are relatively easy to extract and transplant in the same patient. Unfortunately, adult stem cells may not be able to cure all kinds of diseases, and since they are relatively advanced in age, their staying power is uncertain.

Embryonic cells, on the other hand, are young and robust. Perhaps too robust. In animal studies, embryonic stem cells proliferate so much they can cause tumors. It also becomes difficult to coax embryonic cells into say, separate heart cells or brain neurons. If not fully separated, the clinical results can be tragic.

In her book, "The Proteus Effect," author Ann B. Parson describes a middle-aged Parkinson's patient who traveled to China in 1989 for an experimental stem cell therapy. At that time, scientists had not isolated embryonic stem cells, but they knew that stem cells existed in fetal tissues and young embryos.

In this man's case, an American doctor implanted fragments of fetal tissue into part of the patient's brain and also placed infused cells derived from an embryo into his ventricular system. According to Parson, the man's condition improved, but then several months later, he suddenly died. An autopsy was ordered.

In performing the procedure, Boston pathologist Rebecca Folkerth was stunned to find some very un-brain-like material in the man's ventricles.

"It was bizarre. I could see hair shafts, cartilage and connective tissues," Folkerth is quoted as saying in the book. She later wrote a paper about the autopsy. She suspects the man's doctor accidentally implanted non-neural tissue that grew and fatally compressed the patient's brain.

Such a cautionary tale provides ammunition for people on both sides of the stem cell debate. In the eyes of detractors, new-age Dr. Frankensteins are clumsily experimenting with life-creating forces. Supporters, on the other hand, note that terminally ill patients are desperate for help. Better to engage in controlled experiments in California, they argue, than uncontrolled experiments elsewhere.

Sadly, the emotions surrounding stem cell research make it difficult to have a rational discussion about its potential.

During the Proposition 71 campaign, "critics kept talking about the slaughter of babies and the deaths of innocents to save lives," says Caplan. At the same time, supporters were engaged in their own campaign of hype.

Running up to the election, University of California, Irvine researcher Hans Keirstead went around the state showing a heart-tugging video of a rat with spinal cord injuries. After being injected with embryonic stem cells, the rat reappears on the video and is able to use its hind legs.

Some scientists complain that Keirstead was raising false hopes by hyping a single animal experiment, one that hadn't been published in a peer-reviewed journal. Typically, scientists want their research fully vetted - and even duplicated by other scientists - before making public pronouncements.

Keirstead, however, is unapologetic. "You've got a patient community out there that is in desperate need," Keirstead told the New York Times earlier this year. "If the treatment is safe, let's get it out there and try it."

Zach Hall, interim president of California's new Institute for Regenerative Medicine, acknowledges there is enormous pressure on his agency to find cures fast. People with diseases, he says, sometimes come up to him and volunteer for experimental therapies.

"I've had people say to me, 'We don't care what the risks are, that is for us to decide. If I have a disease, I should be able to decide I'm willing to take that risk or not,' " says Hall.

Those comments worry many scientists, partly because of the experience of gene therapy. Up until six years ago, gene therapy was on the miracle fast track. Clinicians thought that by inserting fresh genes into ill patients, they could cure diseases with genetic components, such as cystic fibrosis and cancer.

Proponents, however, underestimated how difficult it would be to deliver genes to thousands of target cells. Then came Jesse Gelsinger, an 18-year-old boy who underwent gene therapy in Pennsylvania in 1999 for a rare metabolic disorder. Four days later he was dead.

"The Gelsinger case was a huge setback," says Hall. "It did a field a disservice. ... Many more lines of experiments were cut off because of the reaction to that."

To ensure it doesn't repeat the Gelsinger tragedy, California's stem cell institute plans to adopt a number of safeguards and protocols. One of these will seek to ensure that embryonic cells aren't contaminated by fetal calf serum or other agents used to grow cells in the lab.

"You have to be sure the cells you put in are the highest possible quality," Hall says. "You can do animal experiments with some kind of cells, but anything you put into a patient has to be pure."

On this front, the stem cell institute will be helped by the National Academy of Sciences, which handed down new guidelines Tuesday on stem cell research. Among other things, the academy recommended "a standard set of requirements for deriving, storing and using embryonic stem cell lines."

With a smart education campaign - regular public conferences, newsletters and a Web site - institute leaders can probably introduce some reality into this crusade. But to do so, they need to be more candid, especially with a well-organized patient-advocate community that holds impressive sway over this agency.

At meetings of the institute's oversight board, patient advocates provide presentations on various diseases that could be helped by stem cell research, such as Lou Gehrig's disease and cystic fibrosis. Rarely do these presentations explore the multiple challenges ahead, particularly with diseases that afflict that most complex of organs, the human brain.

Greater scientific candor will help this institute in innumerable ways. In five short years, the stem cell program will start tapping general fund money to pay off the $3 billion in bonds approved by Proposition 71. If lawmakers and taxpayers have unmet expectations at that point -Cures! Royalties! A biotech bonanza! -they may be tempted to scuttle this ambitious venture.

Hurdles for research

Proposition 71, which will fund $3 billion in embryonic stem cell research studies over 10 years, was sold on the claim it could treat or find cures for 70 different medical conditions. Yet there are high hurdles in this race for cures, including:

* Scientists must create hundreds of new stem cell lines. Donors will be needed to donate embryos for these lines. The new cells must be free of viruses and other contaminants that lurk in the serums used to grow the cells.

* Scientists must learn how to coax embryonic stem cells into becoming, say, heart cells or brain neurons.

Although such cells have the potential to grow into any kind of tissue, the "coaxing" process is a young science.

* Before any cell therapies are tested in humans, they must first be tested in animals. A typical protocol is to test them in mice, then monkeys. Therapies must be peer-reviewed and duplicated by other scientists before tried on human test subjects.

* If a clinical trial is successful, the therapy must be licensed. The cost and availability of these therapies will depend on licensing agreements set by the California Institute for Regenerative Medicine.

* Along with transplant therapies, scientists will use embryonic stem cells to explore the origins of diseases. For example, they plan to take an embryonic stem cell, and replace its nucleus with the DNA of someone who has a particular inherited disease. As it develops into a diseased organ or tissue, this cell may provide clues for creating cures.

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