SCRIPPS RESEARCH INSTITUTE

Wind-down of stem-cell institute leaves a void

Funds paved the way for rigorous tests of therapies, but unintentionally boosted a market for potentially dangerous fakes, says **Jeanne F. Loring**.

For the past dozen or so years, stem-cell researchers in California have been the envy of the world. In 2004, as a rebuke to the restrictions put in place in the United States by then-president George W. Bush on funding for human embryonic stem-cell research, Californians approved US$3 billion in taxpayer funds to support regenerative medicine. That essentially guaranteed that the state would become the centre of innovation in the field.

Since then, almost all of my research funding has come from the California Institute for Regenerative Medicine (CIRM). But not for much longer.

In June, CIRM announced that it was no longer accepting new grant applications. Its money is running out, leaving researchers with fewer resources to develop stem-cell-based therapies. That same month, several of us stem-cell scientists were featured in a documentary series that promoted unproven stem-cell treatments and was partially funded by a for-profit clinic facing federal charges. We learnt about the nature of the series after that clinic sent mass e-mails promoting it. The film-makers removed interview footage at our request.

This coincidence demonstrates the double-edged sword that is CIRM's legacy. The agency has enabled fundamental science and helped to establish know-how for rigorous assessment of stem-cell therapies. Earlier this year, my colleagues and I started a biotechnology company, Aspen Neuroscience in La Jolla, California, and are raising funds for a clinical trial of a neuron-replacement therapy for Parkinson's disease. Without the work that CIRM has done to educate investors and researchers, this would have been very difficult.

But the agency's work has inadvertently helped to boost unregulated, for-profit 'clinics' claiming, without sound evidence, that cells derived from fat, bone marrow, placenta and other tissues can cure any disease.

Although its intentions were laudable, CIRM raised the hopes of the public too high. It needed catchy advertising to gain voters' support. One of its campaign slogans was "Save lives with stem cells". Effective advertisements often focus on a promise and downplay shortcomings, such as the time and resources required to advance a stem-cell therapy through clinical trials to market approval. No CIRM-supported therapy has been approved by the US Food and Drug Administration (FDA), resulting in dashed expectations. (In fact, the FDA has so far approved only one stem-cell therapy, which uses blood-forming stem cells to treat blood diseases.) Still, fulfilment of the campaign promise is under way. CIRM has granted funding for 56 stem-cell-based clinical trials.

Unfortunately, others are taking advantage of the publicity. More than 700 businesses offer what they call stem-cell therapies for many maladies, including neurological conditions, such as autism spectrum disorder, Parkinson's disease, Alzheimer's disease and stroke. They often charge thousands of dollars. An analysis this year (W. Fu *et al. J. Am. Med. Assoc.* **321**, 2463–2464; 2019) found that fewer than half of these places employ physicians who are trained in all of the conditions that they purport to treat. There are multiple reports of unapproved, unregulated therapies leaving some people blind and others with harmful tumours on their spines.

CIRM has regularly denounced these clinics, which existed before the institute's creation and will persist as long as they can make money. Still, it is easy to understand how public enthusiasm would spill over to those offering quackery.

My colleagues and I are horrified that we might be lumped with these bad actors. They exploit people and put them at risk. They confuse people by pretending to be in the scientific community and are why the term 'stem cell' has become synonymous with 'snake oil'.

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This conflation is, in my view, one reason that, just as stem-cell researchers have advanced projects to the point of launching expensive clinical trials, financial support is ebbing away.

CIRM's founders have announced plans to approach voters in 2020 for another influx of funds. The likelihood of stem-cell treatments being approved is much closer to reality than it was 15 years ago, in large part because of the agency's support. But any future advertising must emphasize the necessity of rigorous scientific evidence alongside the potential of the cells.

We must strike a balance between future potential and current reality when we talk to the public. Researchers should emphasize that even when therapies show promise in mice, they often fail to work in humans. The only way to find out — and to check for safety — is rigorous scientific testing in clinical trials. I often talk to community groups about stem cells, but I think the best way I convey the message is talking with Uber drivers on my way to airports. If they understand what stem cells are and what it takes to develop therapies that will be safe and effective, maybe future passengers will learn the story and pass it on.

I am heartened that the Medical Board of California will take up the topic of unregulated 'stem-cell treatments' this month. The FDA is gaining momentum in its efforts to close places offering bogus therapies, several of which are also being sued for harming patients. I have confidence that, when the FDA approves stem-cell-based therapies, the good work will outcompete the bad. People will receive effective therapies and have them covered by their health insurance. But that is still in the future. In the meantime, we need to temper public hope. ■

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