State stem cell agency floats idea of $70 million 'Alpha' clinics

Clinical trials networks are nothing new. But a clinical trials network focused around a broad therapeutic platform, rather than a particular disease, disease area or specific type of treatment, would be.

On 25 July, the governing board of the California Institute for Regenerative Medicine (CIRM) will decide whether to fund a $70 million network of so-called 'Alpha' stem cell clinics that, as currently envisioned, would bring together the necessary scientific, technical and medical expertise to host and advise clinical trials for stem cell–based therapies for a range of illnesses. "It would make sense to start building a brain trust of individuals who have that expertise," says CIRM's Natalie DeWitt, special projects officer at the state stem cell agency, which is headquartered in San Francisco.

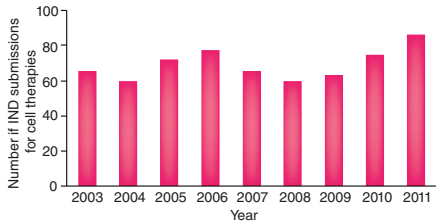
Few stem cell therapies, with the exception of hematopoietic stem cells derived from bone marrow or cord blood, are currently used in routine medical practice. The proponents of the Alpha clinics hope to lay the groundwork for more. "We're kind of doing this in anticipation of this field really growing," DeWitt says.

The Alpha clinic investment represents about 10% of the total money left in CIRM's coffers. Under the proposal, the funding would be spread over five years and would go toward supporting a handful of clinical sites at academic medical centers and a central coordinating and information management center, all based in California. An as-yet-unspecified proportion of the money would additionally be spent on developing education and outreach resources for the general public. The participating sites, which would be decided by a peer-reviewed application process, would receive training in the unique scientific and regulatory challenges of working with cell-based therapies—storage, shipping, administration, manufacturing, cell tracking and more.

It's precisely issues like these that often make it difficult for stem cell biologists with promising translational data to negotiate an investigational new drug application (IND) with the US Food and Drug Administration (FDA), says CIRM medical officer Maria Millan. "There's not a lot of expertise regarding navigating the proper IND-enabling activities—being able to have meaningful discussions with the FDA and crafting the right pathway to bring some of these product candidates to the clinic—and as a consequence there's maybe promising projects that stay in the lab and get held up there."

What happens in California…

Mahendra Rao, director of the Center for Regenerative Medicine at the US National Institutes of Health (NIH) in Bethesda, Maryland, applauds the Alpha clinic model. But he doesn't see the same approach being tried nationally anytime soon, noting that the NIH already supports many networks designed to translate cell therapies into the clinic. For example, the agency's National Heart, Lung and Blood Institute already spends around $12 million per year on the Production Assistance for Cellular Therapies (PACT) program, which goes toward supporting a coordinating center and five cell-processing facilities that provide clinical-grade cell products for investigators across the country. Additional training in bringing therapies forward is available through initiatives such as the Clinical and Translational Science Awards (CTSA) program.



Sci. Transl. Med. **4**, 149fs31 (2012).

Clinical catalyst: CIRM expects requests to start human testing with investigational cell therapies to rise dramatically.

Rao regularly asks researchers hoping to advance promising stem cell therapies whether they require additional clinical infrastructure. "So far, what they've told us is they'll let us know if they need anything more than CTSA and the PACT programs that we have already established," he says.

Elie Dolgin

Tuberculosis trials, already struggling, hit hard by US sequester

The US federal spending cuts imposed by the so-called sequester have made a brutal dent in research spending: the country's National Institutes of Health (NIH) and National Science Foundation are among the agencies that must shed roughly 5% of their budgets this year. That's bad news for research on global killers such as cancer and HIV/AIDS, but the prospects are perhaps even bleaker for fields that are already underfunded, such as research into tuberculosis.

According to the New York–based advocacy organization Treatment Action Group, tuberculosis research received $209 million from the NIH in 2011—a small sum, critics complain, compared with the $3.1 billion the agency invested in HIV/AIDS research. That same year, the tuberculosis pandemic was responsible for 1.4 million deaths, almost as many as attributed to HIV/AIDS.

"Our budget [for tuberculosis research] is very small to begin with. We're a very lean-and-mean operation," says Neil Schluger, who chairs the steering committee of the Tuberculosis Trials Consortium (TBTC), a research nexus based in Atlanta that conducts tuberculosis clinical trials across nine countries in collaboration with the US government, nonprofits and drug companies. "Now, because of sequestration, our consortium is receiving cuts at a time when we have some of the most exciting research results we've ever had."

Over the past three years, the TBTC has seen an approximate 10% drop in its budget, which is determined by the US Centers for Disease Control and Prevention (CDC) and which peaked in 2008 at $10.4 million, according to Schluger. This year, the consortium learned it would be facing dramatic additional reductions as a result of the sequester. Although the cut was initially proposed to be as high as 30%, as *Nature Medicine* went to press members were hoping that it would not exceed 13%. In anticipation, the TBTC has begun shutting down three of its 20 clinical sites. In Durham, North Carolina, Washington, DC, and Rio de Janeiro, Brazil, TBTC clinics have ceased enrolling patients and begun laying off nurses and doctors. Other sites have been reduced, and if the budget cut is increased more sites will probably close.