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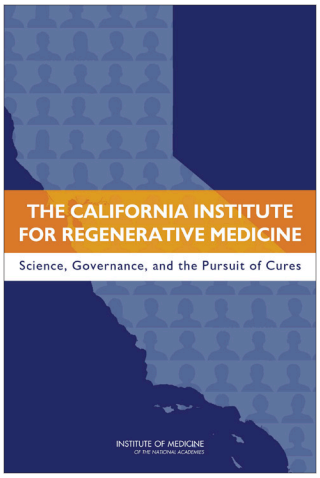
The California Institute for Regenerative Medicine

Science, Governance, and the Pursuit of Cures



At a time when federal funding was uncertain for research in a new and very promising aspect of regenerative medicine that used human embryonic stem cells, California voters agreed to establish the California Institute for Regenerative Medicine (CIRM) and to provide it with up to $3 billion in state funds allocated for stem cell research.

Created in 2005, CIRM has carried out its unique mission at an ambitious pace, successfully and thoughtfully providing more than $1.3 billion in awards to 59 institutions. Given the rapid scientific advances in stem cell science as well as CIRM's own development, CIRM now faces the challenge of transitioning its scientific program and the nature of its partnerships toward bringing the science closer to actual treatments. Central to that challenge is how to restructure its priorities in order to help speed the transformation of promising stem cell therapies into actual medicines available to patients.

At the request of CIRM, the Institute of Medicine (IOM) convened an expert committee to independently review its programs, operations, and strategies thus far. Its report, *The California Institute for Regenerative Medicine: Science, Governance, and the Pursuit of Cures*, offers recommendations aimed at assisting CIRM as it develops its plans to realize the clinical benefits of regenerative medicine and build a sustainability platform that takes the greatest advantage of its many achievements.

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The Promise of Stem Cell Research and the Creation of CIRM

Stem cell research is an important area of biomedical innovation since these cells have great potential to yield new, more effective treatments for a wide variety of diseases. The ability of different types of stem cells to self-renew and differentiate into a myriad of cell types is the foundation of the regenerative medicine field, providing hope for patients who suffer from a spectrum of currently intractable ailments.

A broad coalition of citizens, California-based scientists, higher education leaders, and patient advocates were behind the campaign to create CIRM, and their efforts guaranteed a new, stable source of public funding for regenerative medicine for 10 years. The institute is financed through issuance of long-term general obligation bonds of the state of California, supplementing more traditional sources of biomedical research funding and bolstering the state's already vibrant biotechnology industry.

At the time the legislation was passed, stem cell research faced considerable political opposition at the federal level, and domestic research in the field was lagging. Deriving embryonic stem cells involves destruction of human embryos, raising ethical questions about whether such research is morally acceptable and, if so, whether state or federal governments should fund it. The tension between the unsettled ethical controversy and the perceived potential of this new type of research is reflected in the fact that Presidents Clinton, Bush, and Obama found it necessary to clarify their differing views on these matters through a series of policy guidelines regarding use of federal funding for research creating or using human embryonic stem cells, the committee notes.

Separating Operations from Oversight

The authorizing legislation, Proposition 71, established a 29-member Independent Citizens Oversight Committee (ICOC) to govern the institute. Delegating management roles to a large board of diverse stakeholders, and centralizing a great deal of authority in the chair, provided the requisite expertise and energy for the startup phase and insulated CIRM from potentially hostile political oversight. While this structure may have been appropriate in CIRM's early existence and did contribute to its success, the committee concludes that it could detract from future effectiveness.

Currently, the ICOC functions both as an executor and as an overseer—competing duties that compromise the ICOC's critical role of providing independent oversight and strategic direction. The IOM committee recommends that CIRM's operations be separated from its oversight. The board should delegate more authority and responsibility for day-to-day affairs to the president and senior management, and the ICOC's three working groups should report to senior management within CIRM, rather than to the ICOC. The moves would permit the board to better focus its energy and collective talent on strategic planning, overseeing financial performance, ensuring legal compliance, assessing the president's performance, and devising a plan for preserving and expanding its considerable assets to permit the institute to continue its important work after the bond measures end.

Ensuring Public Confidence

The committee also recommends changes to the board's composition. Far too many board members represent organizations that receive CIRM funding or benefit from that funding. These competing personal and professional interests compromise the perceived independence of the ICOC, introduce potential bias into the board's decision making, and threaten to undermine confidence in the board. Neither the board chair nor board members should serve on any working group. The board itself should include representatives of the diverse constituencies that have an interest in

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stem cell research, but no institution or organization should be guaranteed a seat.

The problematic perception of conflicts of interest has persisted for as long as CIRM has existed. The IOM committee would be less concerned about individual board members with actual or perceived conflicts of interest if the board membership included more truly independent members. The majority of board members should be independent, with no competing or conflicting personal or professional interest. Broader representation from a wider variety of stakeholders will inject new perspectives into the panel and will help to dispel the perception of conflicts of interest.

CIRM also should revise its conflict of interest definitions to include non-financial interests, such as the potential for personal conflicts of interest to arise from one's own affliction with a disease or personal advocacy on behalf of that disease. CIRM policies for managing conflicts of interest should apply to that broader definition.

Enhancing the Scientific Program

The first wave of grants that CIRM issued focused on infrastructure, developing appropriate laboratory facilities for stem cell research, funding basic research in stem cell biology, investing in programs already researching a broad range of diseases, and establishing a stable foundation on which California's leadership in stem cell research could continue to grow. Collaborations have attracted tens of millions of dollars in matching funds, expanding the reach of CIRM's grants.

Next, CIRM broadened its grant portfolio, requesting applications from multidisciplinary teams that seek to translate basic research into therapies, research technologies, and cures that would alleviate patients' suffering. CIRM issued 22 disease team awards totaling $360 million.

While the latest round of awards challenge teams to have filed a request to begin clinical trials or to have completed early-stage trials in patients within four years, the committee feels these ambitious goals are unrealistic. New therapies take more time to progress to federal approval, and early-stage clinical trials are beset by a staggeringly high failure rate. Rather than judging success by simply tallying the number of active clinical trials, the IOM committee suggests that CIRM also continue its focus on underlying biological mechanisms that drive the success or failure of a promising therapy and on careful design of clinical trials. Advances in these areas will help the entire field progress, even if a specific drug candidate is not approved.

To this end, the committee recommends that CIRM establish a single Scientific Advisory Board, comprising people who have expertise in the scientific, clinical, industry, and regulatory facets of stem cell biology and cell-based therapies. This external board would help to ensure CIRM is appropriately funding the best science, provide invaluable input about which discoveries should progress to trials in patients, and outline how best to engage industry partners in costly, time-consuming drug development. The majority of members of this new board should come from outside of California, and they should be appointed by and

report to the CIRM president. The board's reports and the president's responses to them should be discussed in sessions that are open to the public.

Conclusion

Improvements to CIRM's governance structure, scientific program, and policies are critical to better serving California taxpayers who elected to devote funding to promote stem cell research in the state. The necessary changes outlined by the IOM committee, if enacted by the state and/or the institute, would help to instill confidence among the scientific community and California residents in the vital work that CIRM is accomplishing.

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