



VIA Email

November 14, 2008

Stuart Drown  
Executive Director  
Little Hoover Commission  
9325 L. Street, Suite 805  
Sacramento, CA 95814

Dear Mr. Drown,

Thank you for your letter and for the invitation to appear in front of the Little Hoover Commission. In your letter, it was explained that the Commission is studying the governance, accountability and transparency characteristics of the California Institute of Regenerative Medicine (CIRM) from several perspectives. As such, the Commission requested from us an assessment of the impact of Proposition 71 upon the Buck Institute for Age Research and our impressions of the conduct of the CIRM and its governing body, the Independent Citizens Oversight Committee. As the Vice President of Facilities and Planning for the Buck Institute for Age Research, I participated in the planning and preparation of our organization's application(s) for grant funding to support our efforts in the development and use of stem cell technology to further the mission of the Buck Institute, and from that vantage point, can respond to the Commission's request. In response, I will provide a brief background of the Buck Institute. I will then go on to directly address each of the Commission's general areas of interest in the Buck Institute's experiences with the CIRM as it implemented the provisions of Proposition 71.

The Buck Institute for Age Research came out of the ideas and ideals of philanthropists Leonard and Beryl Buck whose charitable trust provided the seminal funding for the Buck Institute and for continuing financial support of the Institute which bears their family name. The Buck Institute was organized as an independent, free standing research organization and as such, we are not a university and receive no services or direct financial support from a university. Although the Buck Trust does provide continuing financial support (approximately 20% of our annual budget), we have no revenue stream from tuition and/or alumni and rely on grants, gifts, subcontracts and other sponsored research to sustain us, and as a young Institute, we also lack the sizable endowments of older, larger universities.

We are situated on 417 acres of privately owned land and currently occupy approximately 185,000 square feet of space in two buildings. The existing facility is a portion of an approved master development plan for a total of 355,000 square feet in five buildings. The master development plan includes a housing element of 130 units of housing which remains in the planning stage.

The entire facility master plan, and the organizational and operating structures of the Buck Institute were established to foster and promote research into aging and age associated disease in a collaborative environment of interdisciplinary research free of the multiple, and sometimes competing interests, typically in place in an academic environment.

The Buck Institute began its research operations in August of 1999 which are directed towards understanding the mechanisms of aging and its role as a primary risk factor in a range of neurodegenerative diseases (Alzheimer's, Parkinson's, Lou Gehrig's/ALS, Huntington's) and other age related diseases like cardiovascular disease, diabetes, stroke and cancer. Our desire is to extend "healthspan" in contrast to "lifespan".

From the commencement of research operations, the Buck Institute has steadily grown from an idea to a well established center of research in the field of aging. The growth of the Buck Institute was, and is, driven by the quality of science and the ability of our cadre of investigators to attract funding to support their work. It is incumbent upon us to be aware of grant opportunities to fund our ongoing research operations and to understand trends in our research program areas in order that we may identify relevant emerging technologies that will further the mission of the Buck Institute: to extend the healthy productive years of life through biomedical research. The development of stem cell technology certainly affected the planning of our future research efforts and the emergence of Proposition 71 as a funding opportunity for infrastructure development and research grants created a novel combination of circumstances.

As we tracked and supported the development of Proposition 71, we noted our focus on research into aging and age related disease has a natural connection to understanding the role of stem cells in aging and in the pathogenesis, diagnosis and treatment of age related disease. Furthermore, our research included well established programs in eight of the twelve diseases specifically mentioned in Proposition 71 as targets for stem cell therapies. These eight diseases have a common risk factor, age, and include Alzheimer's, Parkinson's, Huntington's, ALS (Lou Gehrig's), diabetes, stroke and cancer. The passage of Proposition 71 signaled a shift in our scientific strategic planning to emphasize the role stem cell technology would play in our research efforts and the future of the Buck Institute.

The following material presents our perspective of the impact of Proposition 71 from the vantage point of the three areas of interest identified by the Commission.

- **Bullet Point 1: An overview of new facilities, staffing and research at the Buck Institute that resulted from CIRM grants.**

The broad view of the impact of Proposition 71 upon the Buck Institute draws attention to the similarities in the missions of the CIRM and the Buck Institute. As previously mentioned, the Buck Institute had well established research programs in eight of the twelve diseases specifically mentioned as targets for stem cell research at the time of the passage of Proposition 71 by the voters of California. The truly unique opportunity to compete for funding for development of facilities and for program funding was the catalyst for a transformation of the Institute's approach to the fight against age associated disease through full integration of stem cell and stem cell technologies into the design of individual and collective research programs at the Institute. The opportunities created by Proposition 71 and the creation of the CIRM invited the Buck Institute to move past *consideration* of the use of stem cell technology in the design of our research programs to include and apply stem cell technology as an essential and permanent element of our approach to research in aging.

Concomitantly, the opportunities created by CIRM have influenced the scientific strategic plans for the future of the Institute.

In regards to new facilities, the CIRM offered facility grants in two Requests for Applications (RFA); one to quickly create space for hESC work through development of small shared research labs and training facilities (RFA 07-01) and major facilities grants in three categories (RFA 07-03). The Buck Institute responded to each RFA and garnered a grant award under each RFA.

- RFA 07-01. An award of \$4,000,000 to build out approximately 5,300 sf of shared research and support facilities for continuing hESC and related stem cell work and classroom and training space for the conduct of 4 stem cell culture and techniques courses per year. The project partially funded the North Bay CIRM Shared Research Laboratory and Stem Cell Training Facility. This facility offers bench space, equipment and support facilities for as many as 36 stem cell scientists. It also has classroom and training facilities for instruction in stem cell culture techniques for 12 students at a time in classes offered four times per year. This facility opened in July of this year.
- RFA 07-03. Approved for an award of \$20,500,000 to partially fund a new 65,000 square foot building to house a CIRM Center of Excellence in stem cell research. The estimated completion date is in June of 2010.

In regards to staffing, the first addition to our cadre of principal investigators after the passage of Proposition 71 was an hESC specialist, Dr. Xianmin Zeng. While at the NIH, Dr. Zeng helped develop the hESC lines approved by the federal government. She was recruited to join our existing program in adult stem cell research conducted by Dr. David Greenberg. Since the completion of the shared laboratory facility, Dr. Mahendra Rao has joined our research team and our continuing PI recruitment efforts seek stem cell talent wherever it can be found.

In addition to the general impacts of Proposition 71, other effects it had on the Buck Institute include:

- Creation of a safe harbor for human embryonic stem cell research outside federal restrictions
- Additional space for non-embryonic stem cell and related research
- Expose established PI's to stem cell technology and allow them to work in the field without undue burden or jeopardy to their federally funded research
- Expose young investigators to stem cell technology and provide opportunities to attract new talent to the use of stem cells in the field of age related research
- Optimize our existing organizational structure and facilities to include the special needs of stem cell initiatives
- Expose our talented colleagues and collaborators outside California to join our competition for research grants offered by CIRM and to consider relocation to the Institute
- Optimize and expand stem cell culture training facilities and courses at the Buck Institute to prepare the workforce needed by the industry being created by the CIRM
- Increase the PI capacity at our site for new PI's working in stem cells and aging
- Allow us to accommodate visiting scientists and host non-affiliated but compatible stem cell researchers at our facilities
- Provide space for a large scale biospecimen/biorepository storage facility for our use and create capacity for use by others. Such facilities would be created and operated

in compliance with national and international best practices and rules and regulations applicable to biospecimen and biorepository facilities. The startup nature of a large scale facility will provide the opportunity to establish CIRM standards for the collection, processing, indexing, cataloging, storage, reproduction, distribution and accounting of the sources of materials from which CIRM cell lines are derived and used. Moreover, establishment of a central repository for CIRM can assist the creation of a bioinformatics system to manage materials and establish libraries for materials to be shared by CIRM sponsored research.

- **Bullet Point 2: The level of stem cell research at the Buck Institute would be performing if not for Proposition 71.**

At the time of the passage of Proposition 71, the Buck Institute was conducting research in adult neuronal stem cell development and we were exploring how to include hESC technology into our research efforts. However, like many others, the potential to expand our stem cell research was affected by federal limits on the use of stem cells, low availability of grant funds for stem cell work and the perceived risks to federal funding associated with stem cell work outside the federal limits. As an independent research institution conducting basic research, our primary source of research funding is from federal research grants.

We are fortunate that the federal government has chosen to emphasize areas of research around diseases associated with aging over time. However, if the federal government chooses to restrict and/or de-emphasize funding in any area of research, it affects the depth and breadth of the research at the Buck Institute. Proposition 71 created an entirely new opportunity for us, and others, to participate in the development of an important emerging technology and creation of an entirely new industry in the State of California. Absent Proposition 71, we would be performing the level of stem cell research we could afford rather than what we could imagine.

The outcomes of the passage of Proposition 71 are still revealing themselves to California but in the case of the Buck Institute, it enabled the near term changes in our facilities, staffing and research described in Bullet Point 1.

- **Bullet Point 3: The process used by the Buck Institute to apply for and receive CIRM grants, in comparison to other grant-making bodies, such as the National Institutes for Health.**

Generally speaking, a comparison of the grant process for infrastructure development funds between the grant making bodies of the CIRM and the National Institutes of Health reveal many similarities and a key difference. Our experiences with the CIRM process differed from the NIH in areas that can be seen in the contrast between the maturity and depth of the NIH against the comparative youth and inexperience of the CIRM. In that sense, the comparison between the NIH process and the CIRM process is not really a fair comparison. The NIH process does not include the level of public scrutiny and oversight applied to all of the CIRM's activities. Furthermore, the direct influence of the ICOC, patient advocates and the public upon the process added layers of intensity to the CIRM infrastructure development activities absent from the NIH facility grant application process. Unlike the NIH, the CIRM was charged with the discreet task to create an entirely new organization to seek, review, judge and rank applications for bricks and mortar according to scientific merit and then to determine if the facility will properly support the research programs contemplated for the

facility. All of this was done under the watchful eye of both proponents and opponents to Proposition 71.

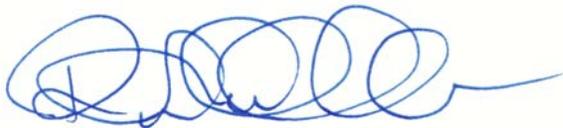
When Proposition 71 was passed in November of 2004, we were hopeful that our combination of well established programs in eight of the twelve targets for CIRM sponsored research and ability to deliver large scale facilities within the two year time frame established in Proposition 71 would put us in a good position to compete for CIRM funding. We watched the process of establishment of ICOC and the Facilities Working Group (FWG) with great interest and developed concerns that smaller and relatively young research organizations would not be strong contenders for funding for infrastructure development given the makeup of the ICOC.

We attended almost every meeting of the FWG as it addressed the enormous task of establishment of methods to distribute approximately \$300,000,000 for creation of a distributed infrastructure to house the research programs to be funded by the CIRM. It became clear to us that the members of the FWG and the staff of the CIRM adopted transparency and fairness as guiding principles for the discharge of their task. The FWG and the CIRM staff went to great lengths to solicit public comment throughout the proceedings of the meetings. We also felt that the FWG and the CIRM staff wanted to clearly define the criteria by which each application would be judged and ultimately did so.

All things considered, we believe the FWG and the CIRM staff created a process that was clearly defined, fair and consistent with the provisions of Proposition 71. We believe we would hold the same opinions had we not been awarded an infrastructure development grant from the CIRM.

We hope our comments and observations provide the desired insight into our experiences with the CIRM and the impact of Proposition 71 has had upon the Buck Institute.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Ralph A. O'Rear', with a long horizontal flourish extending to the right.

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