The California Institute for Regenerative Medicine: A Model for Driving Medical Intellectual Capital

By Robert N. Klein II

California's Proposition 71 has made possible the development of a new model for government funding of stem cell research and therapy development. The $3 Billion California Model proposes that with world-class scientific talent and facilities, the funding source redefines the scope, complexity, and time frames for medical discoveries, and the application of the medical technologies discovered and developed. The funding must be protected from pressures and distortions to the scientific discovery process. Long-term funding commitments are critical to provide adequate assurance to attract the best scientific talent. Stable funding is critical to assure those taking on long-term scientific challenges of the capacity to carry the best discoveries through the development process to patients. The capital source must provide sufficient financial scale so critical mass can be achieved in the field, with a broad portfolio of potential therapies and treatments. Resource allocation must be based on objective scientific criteria, allowing research to be funded across an integrated pipeline from basic research through Phase II human clinical trials for proof of efficacy.

Introduction

The California Institute for Regenerative Medicine (CIRM) is the California state agency created by the passage of Proposition 71, the California Stem Cell Research and Cures Initiative, on November 2, 2004. The Initiative, approved by 59% of California voters (7 million votes in support), provided $3 billion in funding for stem cell research, facilities and other vital research; and called for the establishment of a new state agency to make grants and provide loans to California universities, companies, and research institutions. The agency's Governing Board, the Independent Citizens Oversight Committee, is a 29-member body representing expertise from California's leading public and private universities, non-profit hospitals and research institutions, patient advocacy organizations and the biotech industry. The detailed selection criteria for Board members serve to separate expertise and mission commitment from politically driven appointments.

When stem cell research in the United States was being held back by ideological positions in Washington DC, California took the lead with Proposition 71 to provide funding for a substitute publicly funded program. A recent study by the National Science Foundation (NSF) summarized Proposition 71 and CIRM's impact to date as follows: "In its short history, the CIRM has taken on a vigorous life of its own. It is apparent that the shift of a major focus for stem cell research to California will have a significant effect into the future on the geographic distribution of biological science and biotechnology infrastructure in the United States; on the location of university, biotechnology and pharmaceutical research and start-up firms; and on the investment of venture capital. Evidence for this is the $300 million the CIRM has invested in stem cell facilities, already leveraged to more than to more than $1 billion in linked donations."[1]

Proposition 71 and CIRM have provided a promising new model for government funding of stem cell research and therapy development. CIRM funding can carry discoveries from basic scientific research all the way through to Phase IIB human efficacy trials. CIRM's broad, integrated funding pipeline and its stable funding derived from bonds, as well as its vigorous, world-class peer review system and high medical and ethical standards, have made the agency both the driving force for California's global leadership in stem cell research, as well as an attractive collaborative partner for other nations and states. Partnering with seven nations and three US states, to date, has allowed CIRM to deliver on its goal of building and sustaining global momentum for California's scientists, and to build teams and dissolve barriers for the benefit of the global medical research effort to reduce human suffering and save lives.

CIRM Highlights to Date

The Stem Cell Revolution is Launched…

- 5 .5 years, 286 weeks, 1,250 hours of public meetings of Proposition 71's Governing Board and Subcommittees;
- State Supreme Court and Federal court victories validating the Initiative and the vision of 7 million voters;
- $1.1 billion of medical research and facilities authorized;
- $1.2 billion in donor and institutional matching funds; no other state agency in the history of California matches this record;
- 12 World Class Research Institutes and Centers of Excellence, and Special Programs, funded;
- Bi-lateral funding agreements with seven nations and three states
- FDA approved clinical trials in process…Lives saved;
- Over 500 new research discoveries published;
- 14 Disease Teams aim for Human Trial approvals within 48 months from all cell types-embryonic to iPS cells---for cancer, diabetes, stroke, sickle cell disease, HIV/AIDS, blindness from retinal disease, heart disease;
- Over 100,000 job years from funding to date; and
- Over $100 million of new, net positive state revenue.
- Proposition 71's progress honors the Initiative Mandate of the People of California.
- The California Stem Cell Revolution…Promises kept!

The Prop 71/CIRM model is groundbreaking in three fundamental ways:

1) stem cell research is treated as an intellectual capital infrastructure investment of the society funded by general obligation bonds: a long term capital asset financing mechanism designed to amortize capital costs over the benefiting generations;
2) the portfolio scale of the research pipeline funded by a single state agency; and
3) the long term, integrated structure of the funding program permitting a more rapid advancement from discovery to human trials.

The stable funding provided by the Prop 71 bond financial structure makes the broad CIRM funding spectrum possible, all through one state government agency. The long-term, stable funding stream provides the predictability to build collaboration among non-profit research institutions and for-profit companies in California, and among Californian scientists and scientists in nations across the globe. All of this leads to teams of the best scientists and clinicians working on a global basis in order to protect and improve human health and lessen the enormous governmental healthcare cost burdens.

Public Funding for Medical Research

Medical research produces the *intellectual capital* needed to provide the best healthcare possible and reduce human suffering, allowing individuals to live the healthiest lives they can. The existing systems for public sector funding of medical research are based on the industrial capital system. The problem is that the industrial capital system does not meet the needs of the development of medically-focused intellectual capital. The industrial capital system demands direct financial returns, and does not provide a system to internalize the value of societal benefits, e.g. quality of life, or even reduced healthcare costs. These are returns, but they are benefits to the society and its individual members that cannot be captured by the private (industrial) capital system.

The majority of funds for medical research in the United States have always come from the public sector, largely through the National Institutes of Health, augmented by US military funding and other government organization resources. The largest share of this funding has come through the federal government's appropriations process, and the states have used the same process. The appropriation process leads to major swings in funding, particularly for medical research. These fluctuations in funding cause instability and uncertainty in funding for medical research in this country. We have entered a time in which it is highly likely that funding increases for medical research, in the face of federal deficits and global economic challenges, will be erratic, if available at all. It is important to ask the following questions with respect to medical research:

- Is a government appropriation the best approach to future medical research funding?
- Should and can the burden of medical research funding be carried by current taxpayers?
- Should medical research compete for funding against critical, current needs for operating costs of public clinics and hospitals or medical reimbursements under Medicare or other national systems?
- Is medical research an operating cost of the country or society?

The answers to these questions should be contrasted with the philosophy and outcomes associated with the California, Prop 71 funding model. This funding model is built on a political-economic philosophy that characterizes medical research funding as an investment in the intellectual capital infrastructure of the society. It is not viewed as an operating cost to be funded solely by the current taxpayers.

Intellectual Capital: Capital vs. Costs

Intellectual capital infrastructures, including the medical research intellectual capital infrastructure, will be the driving force behind economic and social prosperity during this century, much like the investment in the physical infrastructures of roads, bridges and railways, in the last century drove prosperity for the nations and states that heavily invested in those fundamental infrastructure elements. If

we do not fund medical research at a level and with a system that allow us to remain competitive in the medical research arena, the US will fall farther and farther behind, and our global leadership in biotechnology company and product development will fade away.

Funding for the development of intellectual capital cannot be treated as an annual expense. Medical research funding, given that it drives the creation of our intellectual capital infrastructure for the healthcare system, must be viewed as a capital investment. Medical research funding should not compete against crucial current healthcare costs funded by the federal and state governments each year. The funding for medical research is an investment in our future and in a long-term capital asset that will deliver returns to society for years to come.

Benefit Groups Should All Pay Their Share

Given that investment in medical research is a long-term capital asset, it should not be entirely paid for by current taxpayers in any given nation or state. The American people, and indeed, people around the world, have benefited over the years from discoveries leading to the development of cures and therapies including the polio vaccine, flu vaccines, artificial human insulin that keeps diabetics alive, HIV/AIDS treatments and many others. Such vaccines, cures and treatments continue to benefit the global society, and will do so for years to come.

In order to align the cost of research that leads to decades of benefits for the actual benefit group, rather than having current taxpayers bear the whole burden, long-term capital funding bonds should be used to fund medical research. This allows the funding to be paid for over a number of years, spreading the cost across more than one generation of payers. The broad intergenerational base of taxpayers spread the burden across a medical benefit group that is so diverse that virtually the entire society receives benefits at the individual or family level.

Changing the Political Landscape for Medical Research Funding

When long-term capital bonds are used for funding medical research, hospitals and medical professionals no longer have to view the cost of medical research as competition for their own funding needs in order to keep our critical healthcare system in place. As demonstrated by Proposition 71, healthcare constituencies can align themselves together to fight for the approval of bond funding for medical research. It is in the interest of the healthcare constituencies to have voters approve bonds to fund medical research, so the demand for medical research funding is separately satisfied, leaving more funds for annual appropriations to cover current healthcare costs.

How California's Effort Promotes Leadership While Complementing Federal Programs

California's Proposition 71 funding model was not created as either an interim or long-term replacement for NIH funding. The NIH is one of Proposition 71's anticipated long-term funding partners for CIRM. Proposition 71 did bridge the gap, at least in California, for stem cell research funding during the eight years such funding was limited at the federal level, and CIRM continues to fund human embryonic stem cell research that is still outside the funding authority of the NIH. However, one of the core purposes of the CIRM is to create a global funding network and system that is governed and funded by US states and foreign nations via collaborative funding agreements. This network will allow the California funding agency to meet its goal of driving discoveries from basic stem cell research to the clinic - undertaken as a critical stem cell research supplement to NIH funding.

CIRM As Driver For Global Collaboration

A major facet of Proposition 71 and CIRM's mission is to build teams globally and dissolve barriers between nations, states, academic departments, rival institutions and academic-biotech collaboration. CIRM grant programs are designed to knock down the funding-driven walls blocking scientific collaboration between research institutions and between departments in those institutions. Proposition 71 drives the building of collaborative scientific teams, rewarding partnerships between the best scientists at a given institution and those at their "competitor" institutions; the best teams will prevail in CIRM's world class peer review of their applications. CIRM drives global collaborations through its collaborative funding agreements with seven nations and three US states, to date, allowing California scientists to form teams with scientists from around the country and around the world, again putting forth the best teams possible. Collaboration between research institutions and biotech companies is driven by CIRM's ability to provide grants and loans directly to companies, as well as to teams that include scientists from both research institutions and companies. One example of this is CIRM's Disease Team Research Awards, which reward the formation of teams uniting the finest public and private sector scientists, enhancing the grant or loan applicant teams' opportunity to be successful in peer review and receive CIRM funds for their collaborative work.

Government Funding, Private Capital and Leverage

In order for government funding to optimize its impact on stem cell research and regenerative medicine, it must create a funding framework that drives the recruitment of private capital to share some of the risk at the earliest possible point on the research pipeline. Private capital does not normally fund early stage, basic stem cell research. However, for cellular therapies specifically, it is possible to attract private capital participation in early stage preclinical research if there is credible, stable government capital committed to the same projects. The government capital permits private capital to leverage its assets and diversify its risk, with less private capital required for each investment. In a system of mutually beneficial leverage, the entire development cost does not need to be carried at venture capital internal rates of return, which means projects that will take years to complete, like many biotech development projects, do not have to be cut off from private capital.

Engaging Biotech

To drive discoveries all the way through the pipeline, from preclinical development through phase III clinical trials, the biotechnology industry must be engaged as a fundamental part of the overall California Model. The experience of biotech industry personnel in managing products through the FDA process, and ultimately commercialization, will be crucial to the effort to deliver therapies to patients.

The Future

The future of the California model will ultimately be judged by the medical research progress it achieves. Over 580 articles have been published to date based upon Proposition 71 funding. One FDA-approved phase I clinical trial has been concluded with preliminary evidence of surprisingly high levels of efficacy; and another phase I trial is underway. Ultimately, the California Model will be distinguished from other funding models by the medical results achieved for patients, comparing time and resources against other models. At this point, the progress milestones are highly positive, but the final medical outcomes funded by the votes of 7,000,000 Californians will determine the future of this model.

Robert N. Klein

Robert Klein's commitment to advancing medical research originated with his son's diagnosis of Juvenile Diabetes in 2001. Bob served as the author and campaign chairman of California's Proposition 71, the $6 billion "California Stem Cell Research and Cures" ballot initiative. Bob serves as the Chairman of the governing board of the California stem cell research funding agency, the CA Institute of Regenerative Medicine (CIRM), established by Proposition 71.

Time *Magazine honored Bob as one of the "World's 100 Most Influential People of the Year" for 2005. Soon after,* Scientific American *named Bob one of "The Scientific American 50" as a leader shaping the future of science. Most recently, Bob was honored by Research! America with their national "Gordon and Llura Gund Leadership Award" for patient advocates and the Biotechnology Industry Organization (BIO) recognized him with their "2010 Biotech Humanitarian Award."*

References

1. Adelson, JW, and Weinberg, JK. (2010) The California Stem Cell Initiative: Persuasion, Politics, and Public Science. *Am J Public Health.* 100(3):446-51. 2010 Mar; Epub 2010 Jan 14.