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RESEARCH PAPER

Citizen-driven innovation: stem cell scientists, patient advocates and financial innovators in the making of the California Institute of Regenerative Medicine (CIRM)

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Our attention in this paper is to the relationship between society and science in science-based innovation processes. We propose that citizens' and scientists' actions are interlaced and that civil society provides a platform on which novel approaches to innovation may be formed. The empirical focus is set on stem cells and regenerative medicine in California, and the emergence of the California Institute for Regenerative Medicine (CIRM). In an effort to advance the area, a coalition of actors went beyond conventional roles and ventured into a broader realm of 'innovation in innovation', creating a new financial and organizational model. This has played out in a number of interesting and fruitful ways, and implications can be drawn for innovation policy and practice.

Introduction

Something novel happened in California in 2004–2005. A coalition of citizens and scientists in 'bottom-up' fashion created an innovative research and development (R&D) system in response to the anti-abortion movement's successful campaign to restrict federal government support of stem cell research. With normal channels of research support blocked by the Bush administration, a Stanford stem cell scientist and his colleagues – highly motivated to remove political impediments to the performance of innovative experiments to advance the field – converged with patient advocates and their organizations seeking cures for diseases. Together, they went beyond conventional scientists lobbying for research support and citizens lobbying for increased funding for a particular disease area; they created a new model for advancing the practice of innovation.

As research opens new areas to change that had once seemed immutable, the drivers, benefits and consequences of innovation become ever more salient. This paper concerns itself with the role of civil society in science-based innovation and associated product and service advance and economic growth. We suggest that civil society provides a platform on which novel approaches to innovation are constructed in a variety of settings (for example, in contemporary California and in Depression-era Oregon), with hitherto esoteric controversies becoming public debates (Etzkowitz, 2014). As an illustration of these arguments, we have dug deep into the case of stem cells and regenerative medicine in California, and the emergence of the organization and 'movement' of the California Institute for Regenerative Medicine (CIRM).

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This paper explores an overlapping of roles as scientists act as citizens, and a subset of citizenry (patient advocates) become increasingly scientifically sophisticated in the pursuit of their objectives, redrawing the traditional boundaries between science and society. We will argue that the attitudes and actions of citizens and scientists are inherently intertwined, and that this interlacing has been augmented lately in the California case of stem cells and regenerative medicine. The paper is structured in the following manner: after a brief methodological note, we discuss the transformation of the scientist–citizen relationship in developing a novel funding model for citizen-driven innovation. This is followed by an analysis of the developments around the creation of CIRM, the development towards citizen-driven innovation, their policy implications and the emergence of a California innovation system uniting the seemingly disparate worlds of social and political activism with scientific and technological innovation.

On our research approach

A 'new' mode and the puzzle at hand

Scientist citizens and citizen scientists, individually and collectively, may join together to utilize popular democratic processes. The science–society relationship is thus transformed from an ancillary activity, enacted through appointed science advisors and public education outreach activities, into a collaborative process in which a previously distant and even adversarial interaction is transformed by coalitions of scientifically informed citizens and citizenship-infused scientists uniting to pursue common objectives. Several recent movements exemplify these different scientist/citizen relationships and trajectories. The scientist/citizen relationship expands as a broader range of organizations and individuals become involved, on both the scientist and the citizen sides. The interaction is illustrated in Figure 1. From the public citizen side, this involves enhanced expertise and political pressure tactics to put science to use. The other pressure is from the scientists' side, extending from engagement with political elites to broader coalitions.

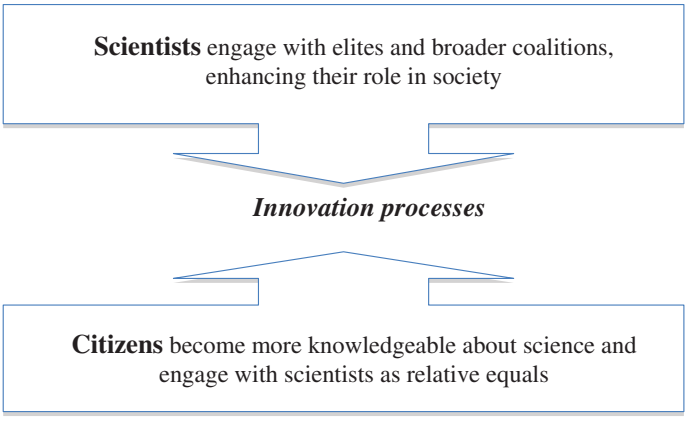

Figure 1. The interaction between citizens and scientists
Note: The authors wish to acknowledge Alice Zhou for her assistance with the illustration.

In the literature there are several models aiming to grasp the entwined interactions of various actor groups in modern innovation processes. The innovation system approach (Carlsson and Stankiewicz, 1991; Bergek *et al.*, 2008) and the triple helix approach (Etzkowitz, 2008) are two of them. Whereas scientific communities as well as civil society in general, and citizens in particular, are part of both these models, their detailed interactions are seldom scrutinized. Admittedly, some observers have suggested that civil society be included in an expanded triple helix model (as a fourth helix, recognizing its role in the innovation process). However, such a format would vitiate the creative triadic properties of the model, and underplay civil society's vital role as the very platform of innovation processes. Rather than focusing on the role of selected civil society elements (such as non-governmental organizations, or NGOs, as partners), we see it as the source of new initiatives between scientists and citizens.

Methodology and data collection

The study has as its foundation the authors' longitudinal analysis of the global sector of stem cells and regenerative medicine. The focal point is the development of CIRM, based on several sets of data. First, an analysis of secondary documentation of the process of forming Proposition 71 provided the basic blueprint for the historical process of stem cell development, the emergence of CIRM. Second, we have met with CIRM management as well as with members of its governing board. Third, a set of interviews with firms in California that have received funding from CIRM gave an appreciation of how these actors saw the possibilities and challenges of Proposition 71. Fourth, to capture time dynamics, we conducted in-depth interviews over several years (2010–2015) with scientists at universities and research institutes. We followed a purposive sampling strategy. Our sample of respondents is consciously biased towards star scientists who have made a scientific breakthrough, are highly cited or have secured large-scale financing. We carried out a total of 40 interviews. These various actors came together in an 'innovation space' that opened up at the intersection of the two California worlds of scientific and technological advance, and political, cultural and social activism.

Organizing for an innovative society

Innovation in innovation

Innovation is based on the potential for creating novelty, but what are the conditions under which novelty is best produced? This is the realm of innovation in innovation: the analysis and creation of conditions that enhance the likelihood of innovation in the conventional sense of product or process innovation (Etzkowitz, 2003). Two sources of innovation in innovation have been identified: the expansion of sources that may be drawn upon for ideas, and the creative synthesis that may result from bringing together different perspectives on a problem. Meta innovation refers to the shift from a single-sourced innovation model (proceeding from government, industry or university) to a multi-faceted approach, drawing upon multiple sources of ideas that arise top down, bottom up and laterally.

For example, early nineteenth century Connecticut farmers, realizing that they were individually unable systematically to apply scientific knowledge to improve

farming practice, lobbied their state government to found an experiment station and college, collectively accomplishing this objective (Rossiter, 1975). This bottom-up model of citizen-driven innovation, with bi-directional links between users and researchers, was replicated nationally by the Morill Act of 1862, establishing the land grant university system (Nevins, 1962). William Barton Rogers, a visionary academic from the University of Virginia with family ties to Boston, extrapolated the agricultural model of science-based innovation to industry, and with the assistance of the city's business and political elites directed one third of the Massachusetts land grant to support the founding of Massachusetts Institute of Technology (MIT) (Etzkowitz, 2002).

Hybridization (the intercalation of elements of previous organizational formats into a new configuration) often occurs at the intersection of multiple perspectives (e.g., university–industry–government), creating new innovation venues, such as the venture capital firm Technopole, and science parks. A free and open civil society encourages meta innovation and hybridization as they are the source of the capacity to produce and integrate diverse perspectives, and the right of citizens to discuss freely, meet and form new organizations. This occurs without special permission of government within a general legal framework that narrowly excludes such activities as use of force and fomenting of hate as organizing tools (Cohen and Arato, 1992). Civil society is both a product and a process of individuals and groups creating organizations and movements that may cut across institutional categories.

Civil society is the underpinning of an institutional order that facilitates enhancement of the conditions that foster innovation. The ability to seek remedies as citizens cooperating with each other, without having to seek authorization to collaborate, is the premise of an innovative society. Solzhenitsyn's novel *The First Circle* (2009) depicts product innovation in Stalin's gulag, where incarcerated scientists worked, or pretended to work, on an encrypted telephone. The Soviet Union collapsed in the transition from an industrial to a knowledge-based society. Lacking all but a rudimentary underground civil society, it failed to produce novel organizational formats, such as the start-up firm. Nevertheless, a gray area emerged of 'fixers' who helped overcome some of the disjuncture and gaps in the Soviet innovation regime.

In the transition from an industrial to a knowledge-based society, the knowledge superstructure is turned on its head to become the infrastructural base of society. From an epiphenomenon resting on the production of economic surplus, science becomes a productive capacity. The shift of science – and virtually all intellectual and artistic fields and their practitioners – from a dependent status as a beneficiary of various forms of public and private patronage to a generator of wealth that produces its own support is exemplified by recent donations to Stanford University from technology entrepreneurs to support research programs in artificial intelligence and allergies. Buildings at MIT have long been named for the entrepreneurial researchers who funded them.

While munificent government support is still the key to thriving innovation outcomes, it is increasingly supplemented by subventions from scientific entrepreneurs who have built significant enterprises, often based on that very state support. Indeed, this is one of the specific objectives of the CIRM initiative, and public support was, in part, generated on that basis as well as curing disease. Analysis of its creation may be useful to those faced with analogous problems of blockage to creation of new interdisciplinary fields and entrepreneurial ecosystems.

Science and society

The received view is that the actors in the citizen–scientist relationship stay in their separate spheres and interact with each other across well-defined boundaries, typically through intermediary translators in a principal agent format (Guston and Kenniston, 1994). In this model, the primary interest of scientists in relation to citizens is to improve the understanding and appreciation of their work in the expectation that knowledgeable citizens will increase their support for science. From the 1920s, individual journalists (such as Waldemar Kaempffert, the first science editor of the *New York Times*, who was invited to witness the atomic bomb test in the New Mexico desert) have grown in prominence. Science journalism as a whole has expanded into special newspaper sections and specialized media, such as *New Scientist*, designed to mediate between science and the public in a rather one-way, linear mode. In this paper, we take the position that this one-way mode has actually become a deficit model.

Indeed, this view no longer accurately reflects reality, if it ever did. Certainly, in the early development of modern science, there was close interaction between scientists and citizenry. In fact, the very term 'scientist', denoting a professional role, is a relatively recent invention (Whewell, 1847). Scientists, such as Lavoisier and Darwin, practiced their crafts largely at home and (if not supported by wealthy patrons and very occasional state patronage) self supported their investigations with private means. Although membership-only formats emerged early on (such as the Lincei Academy and the Royal Society), much interaction among researchers and between scientists and a broader public took place in the informal setting of coffee houses where lectures and demonstrations were offered, 'making the secrets of nature accessible to artisans …bridg[ing] the gap between the London public and the colleges of Cambridge' (Stewart, 1992, pp.145–46).

An ideological distance was created in the late nineteenth century by academic scientists who posited separate spheres of basic and applied research, distancing the university from industry, with the notable exception of the US land grant and European polytechnic schools (Artz, 1966). A wartime and post-war era of large-scale government-funded science allowed additional distance to emerge between scientists and a broader public.

The scientists' viewpoint

The politicization of scientists has occurred both in terms of funding science to meet national needs, and of addressing the consequences of science. A significant number of physical scientists, fearful for the future of civilization, became involved in movements to eliminate atomic weapons. The concern extended to biological scientists, who understood the harmful effects of radiation on human health (Bohr, 1945; Brown, 1971; Horowitz, 1998). The novel political activities of scientists coalesced with the concerns of citizens about the effects of science in the context of fallout from atomic bomb testing in the years immediately after World War II. Sharing common concerns, women's groups with civic organizing expertise made common cause with scientists who had been politically active within such organizations as the American Association for the Advancement of Science, involved with policy from an educational and an advisory standpoint.

Barry Commoner (a biologist who later became famous as an environmentalist), together with anti-nuclear test activists, helped organize a public campaign to collect

baby teeth. Parents would send in their children's teeth and the laboratory would analyze them to see the different levels of radiation that were appearing from nuclear fallout from atomic testing in different parts of the world. This was a very creative way of using research as a political tool to raise political consciousness and to support a scientific goal that was also a political goal. To engage simultaneously in social and political movements and organizations while reaffirming their role as disinterested analysts, scientists raised the neutral concept of information to a higher level by infusing it with humane values, combining the authority of scientific knowledge with political organizing skills in a hybrid format (Commoner, 1966).

In recent years, we have seen a return to an earlier era of closer, informal interaction through joint scientist/citizen projects in support of scientific research and dissemination. From the scientists' side, this intertwining has been ongoing since at least World War II. Indeed, the emerging tradition of the political engagement of scientists surfaced during the 1930s Depression, gained strength in response to the Second World War and took new directions in response to the military uses of sciences after the war.

Wartime science policy arrangements persisted in the post-war era, albeit in a more attenuated format, encouraged by a legitimating document produced by the head of the office of scientific research and development, Vannevar Bush (1945). This agency had produced innovations that led to several successful weapons, and Bush proposed to translate the process into solving peacetime problems across the spectrum of societal needs, from housing to military R&D. This was to be done without the wartime integration of industry, academia or users, and was thus a linear model of science driving innovation without apparent 'need' for intermediary organizations. The political process eventually accepted a set of military research agencies, a greatly expanded health research program, and a basic research agency focused mainly on the physical sciences with modest inclusion of the social sciences. These efforts culminated in providing a science policy advisor to the president and the founding of the Defense Advanced Research Projects Agency with a broad remit, restoring some of the war's integrated triple helix model in response to the Sputnik crisis.

The citizens' standpoint

A pronounced change in scientist–citizen relations occurred during the AIDS crisis of the 1980s as citizens shifted from providing a support structure for scientists' political actions in the anti-nuclear testing movement to taking a more direct leadership role. AIDS advocates achieved a measure of success in gaining input to the medical R&D system through a multi-pronged strategy of public protests, providing research funds and acquiring knowledge to engage with scientists as specialized experts: 'the … "AIDS movement" … is more than just a "disease constituency" pressuring the government for more funding, but is in fact an alternative basis of expertise' (Epstein, 1996, p.8). Thus, the scientist/citizen relationship shifted as patient advocates increased their power through highly visible protests that attracted media attention. Also, a subset of lay advocates became capable of discussing the science involved on relatively equal terms with scientific interlocutors. This dual strategy paid off in achieving access and influence within the decision-making bodies of scientific regulation.

Activists, knowledgeable about available and potentially available treatments, organized pressure groups to encourage governmental authorities and the medical scientific community to move clinical trials forward at a quicker rate. This experience changed the relationship between scientist and citizen. Scientists eventually took account of the new citizen movement and negotiated a new cooperative and collaborative relationship with groups that had been formed to be their adversaries. The following section shows how the successor stem cell controversy played out in California, a global hub of research, product development and entrepreneurship.

The Californian creation of a stem cell community

The stem cell controversy

Our case partly has its origin in the collision course between the anti-abortion movement and proponents of human embryonic stem cells. Ever since the legalization of abortion and the introduction of in vitro fertilization (IVF) treatments in the 1970s, there has been concern about the treatment of unused fertilized eggs. Abortion opponents had defined the earliest stages of cell division as constituting human life, justifying earlier restrictions on abortion procedures. The controversy over abortion spilled over into basic research on cells because of the use of discarded clusters of embryonic cells that had been stored to aid reproduction. The cells no longer needed for the purpose of reproduction were put to use as research tools. After a heated scientific and ethical debate, the Clinton administration decided in 1995 that federal funding could not be used for research on human embryos. The identification of stem cells in mice in the early 1980s had led to an increased scientific interest in using stem cells for medical treatment. As federal funding for research on human embryos was precluded, private sources supported the isolation of the human embryonic stem cell in 1998.

This opened up an emerging area of scientific research holding great promise for a broad spectrum of disease cures (Holland *et al*., 2001). However, in 2001, the controversial issue debated by life science ethicists and others – whether human embryonic stem cells should be used for research purposes – landed on the president's desk. Anti-abortion advocates prevailed in extending their definition of life to ever-earlier stages, but with a significant caveat. President Bush's decision in 2001 to limit stem cell researchers to data sources from embryos that had previously been created, but not to allow new ones, was a Solomon-like prescription, 'cutting the baby in half' to satisfy two opposed claimants. The attempt to satisfy irreconcilable opponents satisfied no one – not the anti-abortion advocates who viewed stem cells as a homunculus of a human being and wished all activities in the field cut off, and not the stem cell scientists and their supporters who viewed the science arising from stem cell investigation as inaugurating a new era of disease cures and even reversal of negative biological processes. They termed the emerging field 'regenerative medicine'.

In practice, only about a quarter of the stem cell lines created were available for research, thus severely limiting the availability of research materials. Physicians, patient groups and members of the business community were concerned about lost treatments, cures and business opportunities. Lobbying on the federal level gained some slackening of the strict laws on embryonic stem cells in 2005, and the allocation of funding to research on adult stem cells and umbilical cord blood stem cells.

Nevertheless, the research pathway was virtually blocked through highly restrictive administrative regulations that the stem cell research community feared threatened US centrality in publications and patents. The Californian response consisted of several interlinked components: a political coalition, a policy innovation using bonds, and a new organization.

Setting up CIRM as a solution through political coalition

Arguing that the president's edict was valid only at the federal level, a group of California stem cell scientists and citizens raised the banner of states' rights and posited an alternative approach to stem cell innovation. In the face of federal blockage, the US constitutional system left open a pathway to develop new institutional roles and relationships at the state level that could be pursued in the realm of civil society (Eisinger, 1988). States' rights are historically a concept used to restrain the federal government from action, such as ending slavery in the mid-nineteenth century. At the beginning of the twenty-first century, the doctrine of states' rights was turned on its head and invoked to overcome federal government unwillingness to act. Indeed, the perception was that only establishing an alternative research funding and laboratory complex would overcome this problem, with a new pathway to innovation, independent of federal control.

Stem cell scientists who were concerned that their ability to carry out research was being impeded at the federal level looked to the state level. In 2002, Irving Weissman and his allies at Stanford and at other research organizations were not seeking historical precedent, but sought a way forward. A nascent coalition of academic scientists, patient advocates and venture capitalists had been lobbying the National Institutes of Health (NIH) to expand research funding. Now they were blocked by federal decisions to allow only previous research on lines of stem cells that had been harvested to treat fertility problems, while halting the creation of new stem cell lines, at least with federal funds.

The response was to organize a joint patient advocate/research scientist/financial industry movement aimed at funding the science and moving it into the clinic and to the bedside. Posing the stem cell blockage problem to the patient advocate scene soon led to an introduction of the scientists to the most politically sophisticated patient advocates. It involved organizing a coalition, together with patient advocates, philanthropists willing to fund medical research, politicians and leading scientists. The coalition included the juvenile diabetes research foundation, the Christopher Reeve paralysis foundation, the children's hospital of Los Angeles, former secretary of state George Shultz, the California medical association, dozens of Nobel Prize winners, and governor Arnold Schwarzenegger. The proponents deliberately avoided any involvement with the pharmaceutical industry given what was, in their view, its troubled public image.

A policy innovation: using bonds

Robert Klein is a graduate of Stanford Law School, who had built a real estate firm using the bond-funding mechanism for affordable housing and becoming an expert in developing bonds for this purpose. He joined the patient advocate movement, partly spurred by the fact that his son had type 2 diabetes (a disease that stem cell therapy has the potential to ameliorate or even cure). A precursor move was

lobbying for increased NIH funding for stem cell research. The typical goals of patient advocate movements are increased budgets, or new divisions of NIH. In fact, Klein did take part in the process of increasing the NIH budget by more than a billion dollars for this concern. However, scientists advised him that, while significant, the increase was insufficient to reach his objective: the amounts needed to lead to cures were much larger.

This was one impetus for Klein to become involved in translating his expertise in bonds into a mechanism for supporting scientific research. Scientist and attorney met through the scientist's sister in the movie industry, who was also active in the patient advocate movement, and found common cause in applying the attorney's innovations in bonds to the creation of a novel R&D agency. The idea was a large-scale R&D funding model at the state level. Publicly supported bond issues like those used to pay for physical infrastructure, such as roads and bridges, would be applied to intellectual infrastructure, such as research buildings, basic and translational research-funding programs and student traineeships. Whereas legislative appropriations are subject to yearly changes based on economic and political conditions, the bond issue would lock in funding for a 10-year period, irrespective of economic fluctuations or political opposition, if the initiative survived legal challenges to its validity. Utilizing long-term bonds as a countercyclical strategy was an experiment, transcending the negative effects of business cycle downturn on yearly legislative decision-making for R&D spend. It fills an innovation-financing gap and may be as significant an advance in innovation funding as the venture capital model invented in Boston in the 1930s and 1940s (Etzkowitz, 2002).

A new organization

The organizational innovation of bonds for building research infrastructure was coupled with the fact that California's constitution contains a direct democracy provision that, upon collection of a requisite number of signatures, mandates votes on ballot initiatives. In essence, the pro-stem cell movement took advantage of this direct democracy provision in the California state constitution, allowing citizens to put measures on the ballot as amendments to the state constitution. In effect, citizens could legislate in place of the legislature. For example, the University of California was founded by this procedure in the mid-nineteenth century. More recently, advocates of limited government have used the procedure to reduce property taxes and implement their vision of limited government.

Thus, Proposition 71 was placed on the ballot in 2004 and received a majority after a campaign in which scientists publicly countered the arguments of opponents. They passed a US$3 billion bond issue to establish at least a decade-long stem cell R&D and innovation project favoring embryonic stem cells. A state agency, CIRM, was set up to manage the funds and the innovation process. If the current funding rate of US$200 million per annum is maintained, the agency can continue until 2022.

When a significant delay in accessing funds was created by legal actions from opponents, steps were taken to move the initiative forward. On the one hand, in 2006, Governor Schwarzenegger authorized US$150 million in loans to CIRM, and on the other, six local philanthropies purchased US$14 million in bond anticipation notes. With these monies, a first round of training grants commenced (CIRM, 2007). Bonds, however, are a form of borrowing that must be repaid with interest. Issued

on the credit of the state of California, the state has the ultimate responsibility to pay the purchasers of the bonds as they fall due. The outcomes of medical advances were expected to cover the payback directly through the spillover effects of research, new jobs, firm establishment and growth, increased tax revenues, etc., and indirectly through improved health and reduction in medical costs. The initiative provisions also gave the state of California the right to take equity in firms formed with the assistance of Proposition 71 funding. More immediately, the local purchase of research equipment and the attraction to California of researchers who would bring their existing research funding to the state were among the arguments offered by proponents of Proposition 71.

Towards citizen-driven innovation

CIRM is a government R&D funding agency with several unique features, including a decision-making role for patient advocate citizen activists in the grant decision-making process. Although election primarily relies on peer review, citizen board members have made possible funding for higher risk projects than an essentially conservative academic peer review system would typically support. A citizens' board with the power to reverse negative decisions via an appeal process complements an elite peer review process. Citizen board members have also encouraged CIRM to stick to its disease cure goals, while recognizing the important role of basic science in reaching these goals. Citizen input, along with scientific allies also focused on patient cure, have prevented CIRM from being transformed into just another basic science funding agency.

CIRM has expanded the critical mass of stem cell research in existing centers and created new ones, contributed to the construction of research facilities, sponsored basic research and tool development programs, and dozens of Phase I and Phase II clinical trials conducted by hospitals, universities and firms. CIRM both built upon and made up for the shortfall in federal research funding in this field. Innovation in science and technology policy occurred through this mechanism creating a new funding source for R&D. Some respondents say:

> NIH funding is too small. CIRM has kept people going.

> I wouldn't be able to do the research I'm doing now without CIRM funding.

> The CIRM experiment is very profound and a new way for America to learn how to conduct translational medical research.

In the development of citizen-driven innovation, there are three interlinked processes at play, pertaining to changing roles for the federal government, between organizations, and in positions taken by scientists versus citizens.

Changing roles between federal and state government

In general, the federal government's role in science, technology and innovation is subject to continuing debate over where boundaries should be drawn. The CIRM initiative was intended to evade, if not break down, federal government restrictions on stem cell research. These limits extended beyond which cell lines could be utilized

for research purposes but also affected where research could be done, disallowing stem cell research based on non-approved cell lines from being conducted in university laboratories supported with federal government funds. Thus, new laboratories had to be built and research programs supported to avoid these restrictions. This required an expensive large-scale project that brought state government into a realm that had largely been ceded to the federal government.

Even as federal funding has remained core for most academic research groups, it has become less dominant. CIRM and philanthropic funding have been guiding the field. However, with CIRM shifting its focus to clinical efforts, furthering basic science is no longer its priority. This means that one needs to look elsewhere for financing facilities, equipment and training programs as well as basic science projects. Again, federal agencies, such as NIH, become the locus of attention, but these do not currently have the volume of funds to match what CIRM has provided. California, a state whose technological and agricultural economy has become the world's fifth largest, has demonstrated the capability to carry out government initiatives on the same scale, and even larger than that of many national governments.

Long-term concerns that growing federal powers and resources have vitiated state capacity may be lessened, at least for those few who have both the resources and political will to undertake macroscopic projects. The voters of California made possible a scale-up of funds and activities in stem cells that can potentially be applied to other areas where broad coalitions can be created. In the past, relatively small-scale state funding provided models for larger scale federal extrapolations, such as the Morill Land Grant Act of 1862, creating a nationwide development-oriented university system that had originated with the Connecticut initiative a few decades earlier. Indeed, there has been a long tradition of policy innovations made at the state level later being upgraded to the federal level as national policy. Precursors to various welfare rights instituted during the progressive era in the state of Wisconsin became federal policy during the 1930s New Deal. Although the initial problem addressed by the movement to create CIRM was the inhibitory Bush stem cell regulations, the larger problems that it ended up addressing included the internal gap between basic research and utilization, and the external gap between science and the public.

Changing roles between organizations

CIRM reconfigured triple helix roles and relationships in stem cell innovation in California, extending university capabilities into a gap opened up by big pharma inaction and venture capital reticence. The coalition focused on filling the increasing gap between the federal funding which provides the resources for basic research on the assumption that large corporations will pick up the ball when solutions have been found. But an intermediate period has opened that has come to be known as the 'valley of death', increasingly the focus of CIRM attention. Indeed, the need for a new organizational mechanism can be seen in the deficiencies in existing approaches to long-term financing of an emerging field. There is a place for a range of actors – big pharma, venture capital, etc. – but these cannot be relied upon to carry the development forward. Big pharma cannot be depended upon for long-term stable financing as pharmaceutical companies change their strategies and react to market-related rhythm and rationale. Traditional venture capital funding of start-ups cannot always work well in this area as it tends to come in at later stages than the scientific development, and is not long term. Given the traditional research funding model,

universities can provide only research findings, or possibly 'proof of concept'. Government research funders expected companies to come into play at this point, but the pharmaceutical industry expected research to be carried further forward into the clinic. A start-up firm might accomplish this objective, but many findings were not exploited because the venture capital industry also expected research to be developed before it was willing to invest. The CIRM program filled some of this translational research gap.

NIH focused on hypothesis-driven research and did not until quite recently commit significant resources to what has come to be called 'translational research', bringing research findings to the level of utilization. According to one scientist, 'As a translational-oriented [researcher], you have to team up with experts in other fields. There's no way you can do this whole thing by yourself'. Although NIH has since initiated a translational research-funding program, it is not yet on the scale of the CIRM initiative and, even if it were, the gap to be filled would still persist as it is so enormous.

CIRM has transformed the possibilities for California's universities in this field, allowing them to take a longer term and larger scale approach, solving the problem of who can move stem cell research forward to treatment. CIRM has scaled up the capacities of universities to do things that companies might ordinarily do but are not doing. In consequence, universities now have capabilities to do even the first parts of Phase II clinical trails. In addition to hypothesis-driven research, universities also become involved in moving the research into use in a way they would not ordinarily have done. CIRM also activated philanthropic resources by providing opportunities for participation in CIRM-funded building projects. As a CIRM administrator commented:

> There's new terms out there – 'philanthropic venture capital' and 'venture philanthropy'. It seemed to me it's either a pure investment for money, but there is this concept: What about someone out there investing who cares about cancer and cares about the disease? It's not 100% they want return on their money. They want to move the field. This is a new concept that's come up.

From separate spheres to scientist/citizen and citizen/scientist

In the late 1990s, the two lines of innovation converged, with scientists and citizens each taking on some of the role of the other, thereby changing the character of the relationship. There are two growing collectivities, characterized by the emergent hybrid roles of scientist/citizen and citizen/scientist: the former engaging in direct political activity in support of their science, and the latter increasingly informed about science and taking direct steps to influence the research support system and even the course of research direction. Citizen–scientist relationships are usually thought of as a dichotomy, with scientist and citizen separate, even opposed, categories. What is especially interesting about the CIRM experiment is that it shifts some of this relationship. As scientists take action as citizens, they reach out to the community to speak at public meetings, to convince the voters to vote for the initiative. In taking on the role of citizen, they also act as scientists, explaining the science of stem cells and its validity.

In the inception phase of CIRM, we identify a movement in two directions and on two levels with citizens taking on elements of scientific roles in cooperation and in conflict with scientists, both as subordinates and as equal partners. Scientists engage in political activities as citizens in relationship to political elites and ordinary citizens. Indeed, scientists were involved the campaign for Proposition 71, appearing in television commercials and at public meetings:

> I was part of a group of faculties. Stanford was involved in this. People from all over California were working in stem cell biology. We campaigned for Prop 71. I gave a lot of talks. There were a lot of symposiums. We went down to southern California and there were a lot of events with Bob Klein for the public where we told people about stem cells and stem cell biology. It's the first time I really ever engaged in any significant level with the public on explaining science. It was an extremely interesting experience.

> I knew Bob Klein and he approached me and I ended up giving some of the talks that would get people on board for Prop 71.

Researchers were taken aback by the breadth and depth of interest in their work as people listened intently to detailed explanations of stem cells that dispersed concerns raised by opponents:

> I was astonished by the number of people who would show up, it was amazing! I spoke at ten o'clock one Saturday morning over at a big high school over in East Bay, and my husband took me over there. This was kind of the beginning. I didn't know what to expect and the parking lot was crowded. We couldn't even find a place to park. I said, 'It must be homecoming, I don't know what's going on here!' And so he let me off at the door and I went in there and there were 10,000 people!

At the same time, citizens were involved, especially as patient advocates. These are people who do not fit the 'normal mode'. Surveys of knowledge of science among the citizenry typically show low levels of knowledge (Rainie, 2015). However, as people take on advocacy roles, they are incentivized to raise their knowledge level in order to understand the issues and be effective. In particular, those who have family members with a disease go on the Internet and become knowledgeable about the disease at a much higher level than the average person.

Policy implications

A series of periodic funding crises has made periods of upturn, such as Word War II and the post-war period, appear exceptional, with science subject to the same cyclical behavior as business activity. The 2004 California experiment suggests an alternative path. Californians voted for Proposition 71, an initiative that amended the state constitution to provide US$3 billion in funding for stem cell research to break through the research blockage created by the Bush administration. Facilities have been founded and research programs established by means of a peer review system that includes an appeal stage in which the public can override scientists' decisions.

California stem cell scientists, citizens, firms and patient advocates raised the banner of states' rights and created an alternative science and technology policy at the state level. In the stem cell field, this is larger and more far reaching than any initiative yet taken at the national or supranational level. Several other states, among them New Jersey, New York and Massachusetts, also began stem cell research

programs, but, dependent upon yearly appropriations, these often had to curtail activities in the face of economic stringency. In contrast, CIRM, with its funds locked, has continued its funding programs without respite. Indeed, it has stepped up the pace, providing a significant number of 'disease team' grants of up to US$20 million each to universities and firms.

Shifting roles

As high technology conurbations, such as Boston and Silicon Valley, become stronger economic engines than many nation states, regional innovation initiatives draw upon larger resources, disrupting the conventional hierarchy of nation, region and locality. California's effort is better funded than many national programs. Thus, when a state like California is involved, the fifth largest economy in the world, a regional effort may easily outclass national or even supranational efforts, especially if it is a targeted and focused initiative aimed at 'picking winners' in a specified field rather than an effort to fund science and technology more broadly.

Citizens and scientists have mobilized public support for a new innovation model in which large-scale funds are aggregated by creating public debt secured by the credit of the state. This new model depends on upon broad public belief in the potential for economic and social benefits from scientific research. The California project went well beyond providing a way around federal limitations on sources of stem cells. It also addressed another blockage at the federal level, the relative lack of funds to pursue translational research and bring promising research findings from research bench to patient bedside, from academic laboratory to clinical practice. By filling gaps in the conventional linear model, it was an assisted linear model providing resources to tackle the valley of death problem, the gap in the innovation process that allows projects to linger on the shelf. In the case of stem cells, the intersection of previously parallel trends led to recombining elements of government R&D agency, patient advocate organization, and public venture capital to support translational research and innovation. In addition, the university's role was extended into the domain formerly left to industry where big pharma, viewing risk as too great, had largely abdicated its traditional role.

CIRM arose from a changed relationship between scientist and citizen, in which citizens internalize some of the role of scientist, and scientists become active as citizens. CIRM has also had an effect on this relation. Through CIRM, scientists entered into coalition, as leading actors, with fellow citizens to restructure the relationship among university, industry and government in stem cell research and development. In fact, the very creation of Proposition 71 and CIRM arose from changed relationships between the scientist and citizen: patient advocates attained scientific knowledge, and scientists become active as citizens. The CIRM initiative built upon this restructuring of the scientist/citizen relationship. Scientists exercised their citizen's rights to advance science, thereby bringing into conjunction aspects of their lives that may have been compartmentalized and divergent. Citizens enacted elements of the scientific role without formal training and certification, becoming lay experts in fields of special personal concern, typically taking advantage of knowledge resources freely available on the Internet.

Conclusion: the California model of citizen-driven innovation

The hybridization of scientists and citizens holds great promise. Under certain conditions, scientists may unify their roles as scientists and citizens – aspects of their lives

previously enacted separately – in collaboration with citizens, who are increasingly knowledgeable about the potential of science. In this way, coalitions advance projects with various combinations of scientific, economic and social goals. Scientists and ordinary citizens exercise their rights, individually and collectively, to influence the political process that provides the support base and regulatory framework for a large proportion of scientific R&D. The innovation process, however, is broader than simply introducing a technological solution. Political, social and cultural factors explain why technological advance can be delayed or impeded (Mensch, 1979).

The intersection of technological, political, social and cultural innovation precipitated the CIRM experiment. Both San Francisco and New York were sources of gay activism that extended into citizen scientist initiatives in response to the AIDS crisis. Other areas of biotechnology and stem cell development may be identified in San Diego and Boston. Boston also had a tradition of financial innovation, having originated the venture capital industry in the mid-twentieth century. Patient advocate movements were a nationwide phenomenon, although particularly strong in southern California. California's bottom-up direct democracy initiative is perhaps the most radical form of citizen political participation since the Athenian *polis*.

The unique confluence of these elements in the San Francisco Bay Area provided the necessary conditions for CIRM. As always, the *explanandum* of the sufficient condition can be sought in the person or persons who synthesized these elements into an innovative solution and took the lead in its implementation (e.g., Karl Taylor Compton of MIT and Georges Doriot of the Harvard Business School in the invention of the venture capital firm, and Robert Klein, financial innovator, in the application of bond funding to the valley of death. The state of California has a long history of involvement in technology development, building upon a tradition of addressing large problems, such as moving water from north to south to make a desert-like region habitable (Williams, 1997). From the mid-twentieth century, public pressure to improve air quality and the scientific finding that particulates in smog came mainly from automobile exhaust led California to legislate ever-stricter emission standards, requiring manufacturers to improve automotive technology. From the 1980s, spurred by citizen activists, legislators passed special acts to provide funding to the University of California to conduct research on a variety of topics, typically related to health. Expected failure of an attempt to scale up this appropriation-based model, during a period of budgetary constraint in 2002, inspired the CIRM countercyclical funding model to support long-term technological innovation.

Activists, working though government, typically allied with researchers, working both collaboratively and in opposition to industry, have created a stream of knowledge-based innovation in innovation that may be characterized as the 'California model', a civil society-based triple helix that periodically renews itself in response to new issues. Attempts to replicate this model elsewhere should take into account special local features, such as the direct democracy provisions in California's constitution, and find models appropriate to their own circumstances. Just as Silicon Valley is potentially replicable, but not as an exact duplicate, so is the California innovation system (Etzkowitz and Etzkowitz, 2015).

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