



M E M O R A N D U M

TO: BOB KLEIN & FINANCE SUBCOMITTEE

FROM: ALAN TROUNSON

SUBJECT: ONLINE JOURNAL

DATE: OCTOBER 4, 2010

One of CIRM's strengths is the way we take on obstacles that impede progress towards our mission. The determination that Bob Klein showed in passing Prop 71 is an ingrained part of how we think.

For some time, it has been apparent to me that the exchange of scientific ideas, in the areas most important to all of us, has been hampered by the absence of an appropriate journal for the publication of research in the translational aspects of stem cell science. There are fine journals devoted to stem cells, but they tend to focus on basic research. Some relatively new journals focus on translational research, but their broad focus will limit their coverage of stem cell research.

I have no doubt that if we wait long enough, we will see journals emerge to focus on this area. I do not think we have the luxury of waiting. I would like to see a journal for stem cell translational research operating within the year, but I do not think that will happen without a kick-start from CIRM.

New journals tend to require a subsidy from a committed publisher during their early years, as they move toward self-sufficiency. With seed funding from CIRM, I believe that we could entice a publisher to enter the stem cell translation field sooner than they might otherwise in the current economic climate

CIRM will seek a highly qualified and established publisher to create an on-line, open access journal for translational aspects of stem cell research. We will expect the publisher to exercise editorial independence and thorough peer review. We will also seek

a commitment to publish negative data quickly. This data on the experience of translational research is generally hard to get published anywhere, yet rapid notification of negative results can avoid wasted replication, and accelerate work on alternative approaches. Publication of industry experience in translation is desirable and currently difficult in the more academic orientated stem cell journals. There is also a need for more room for the rapidly increasing stem cell contributions in discovery and clinical application.

To move this forward, I propose to put out a Request for Proposals (RFP) from qualified publishers. CIRM would offer limited seed funding (up to \$200,000 per year) for up to three years. To be considered, a publisher would be required to submit a business plan showing a reasonable likelihood the journal can be self-sustaining within three years. One publisher would be selected through a competitive process.

I have queried some publishers to see if there is interest. There are three established publishers with existing or proposed offices in San Francisco who have the capacity to create a robust and respected journal in this field. One has expressed interest in submitting a proposal and another has requested to review the RFP when it is issued. We would welcome proposals from any qualified publisher. I have attached relevant sections from a draft RFP. (Appendix 3)

I have also asked leaders in the stem cell field for their views, and found strong interest among academic and industry researchers in California. I have attached sample of the responses. (Appendix 1 & 2)

Comments from Scientists & Industry on need for Translational Stem Cell Journal

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| <p>Catriona Jamieson, MD, PhD</p> | <p>Moore's UCSD Cancer Center, University of California, San Diego</p> | <p>As a field, regenerative medicine provides novel insights into the cell type and context specificity of molecular regulatory networks governing essential stem cell properties such as multi-lineage differentiation, survival, homing and self-renewal. These properties are frequently co-opted in cancer resulting in resistance to standard therapies and relapse - the leading cause of death from cancer. Stem cell research, funded by CIRM, has greatly shortened the timeline of discovery delivery to the bedside but now we find ourselves in a more nuanced area of going back to the bench to understand why some patients respond to stem cell targeted therapy and others do not. This is what Sam Rapaport did when he discovered most of the clotting factors and he alludes to this process in a number of medically important discoveries in the appendix of his book "Hyman Rapaport His Life and Times", which is a tribute to his father, an overworked physician who died of a heart attack.</p> <p>We need to be able to publish the good, the bad and the ugly of the process of translational regenerative medical research and I think that a Journal focusing on this would help to expedite potential cures.</p> |
| <p>Clive Svendsen, PhD</p> | <p>Director, Cedars-Sinai Regenerative Medicine Institute</p> | <p>I think this is a very good idea. The journal should have an academic editorial board and support only high quality, well controlled and relevant studies in translational science. Translational Cell would be a great choice (or Nature Translation).</p> <p>It should also support the publication of "negative" data where good studies that do not cure the disease but eliminate the attempted approach are also published. This will reduce the current problem of high profile translational papers with dramatic results that never get reproduced.</p> |
| <p>David Schaffer, Ph.D.</p> | <p>University of California, Berkeley</p> | <p>This sounds like a very intriguing and promising idea. My modest feedback is that it would be great from the outset to have such a journal distinguish itself from others in the field, as there are many a stem cell journal cropping up these days. A clear affiliation with CIRM would go a long ways in this direction, but it would also be good to work with an organization such as PLoS to add additional immediate credibility. Many of us also like the open access model of a PLoS, as compared to the business models of some other publishers.</p> |

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| Dennis Clegg, PhD | University of California, Santa Barbara, University of Southern California | I think this is an excellent idea for the reasons you mention. One concern I have heard from postdocs and grad students funded by our disease team grant is that the work they are doing might not be that publishable, and they seek basic science angles as a result. Publishing in translational journals might very much help their careers and would be a welcome development. Another thought off the top of my head is that CIRM may wish to be careful to maintain some distance from the resulting enterprise so its not viewed as the "journal of CIRM" |
| Dennis A. Carson, M.D. | Moores UCSD Cancer Center, University of California, San Diego | I agree completely with your analysis. The problem is that appointments and promotions at universities are linked to publications in journals of high impact. Hence, CIRM needs to have a business plan that will maximize the impact of the new journal through press releases, Google citations, and other marketing criteria. Perhaps it would be useful to bring in a consultant who can advise you regarding the best strategy. |
| Eduardo Marbán, M.D., Ph.D. | Cedars-Sinai Heart Institute | <ol style="list-style-type: none"> 1) With CIRM support, I would limit the scope of this proposed journal to translational studies of biological therapies. 2) The case studies format is unlikely to be particularly apt for this journal. 3) I'd suggest that High Wire Press (http://highwire.stanford.edu/) be targeted among candidate vendors. They host the online version of the American Heart Association journals, and I got to know them well in my 10-year tenure as Editor in Chief of Circulation Research. They were very creative, responsive, overall good partners. |
| Hal Sternberg, PhD. | BioTime, Inc. | I'm very enthusiastic about this initiative. I expect so long as the guidelines related to rapid publication of negative results holds, and scientists themselves are not reluctant to publish their negative results, this would a valuable and important step in expediting translational research and development. |
| Irvin S. Y. Chen, PhD | UCLA AIDS Institute, University of California, Los Angeles | I think this is an excellent idea and should greatly broaden the knowledge and facilitate the translation of stem cell research. |

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| Jane Lebkowski, PhD | Geron Corporation | Thanks for the opportunity to give my input to CIRM’s proposal. I think the open access journal would be an extremely valuable tool for the stem cell community. I especially like the “case study” format. As you very appropriately state, it is almost impossible to get “translational” studies published. These studies may involve negative data, however, they may involve good data regarding procedures or endpoints which are viewed as too focused or mundane for some mainstream journals. I think both industry and academic translational professionals will submit studies for publication. I would strongly recommend that the editorial board be scientists/physicians/engineers etc that have experience in translational science/medicine. This leadership will be critical to prevent drift of the journal contents to a basic biology theme. |
| John A. Zaia, M.D. | Beckman Research Institute of The City Of Hope | I support this attempt whole-heartedly. It is really difficult to get early preclinical and even initial pilot clinical trial data published in high impact journals. In our recent experience, despite our trial being the first use of siRNA encoded in lentivirus-transduced blood progenitor cells for AIDS, we were not able to convince Nature, Nature Med, or Blood that this was a worthy publication. But asking for a journal to be “the official journal of CIRM” is clearly a much more difficult road to travel fiscally. My suggestion would be to develop a relationship to a new journal that is likely to have long-term success and partner in it to reach its (and CIRM’s) goals. |
| Larry A. Couture, Ph.D | Beckman Research Institute of The City Of Hope | I’m not certain what feedback you are looking for, but I think this is a great idea and I would look forward to reading, and hopefully contributing, to the journal. |
| Mahendra Rao, M.D., Ph.D. | LifeTechnologies | I think this is a great idea but I would caution against automatically considering a new journal rather than perhaps an addition to an existing journal. Journal of clinical investigation and Stem cells research and Therapy and Journal of Translational Medicine already exist. I would think that the FDA will not contribute too often. My experience is no one likes to write and CIRM case studies may not provide a sustaining number of articles. If one can figure out these issues then I think this would be a really good idea for the entire community. |
| Mark S. Humayun, M.D., Ph.D. | University of Southern California | Sent Letter of Support (See attached Appendix 2). |

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| Martin Pera, Ph.D. | University of Southern California | I think a journal of this nature would probably fill an unmet need in the field and I support the concept. Just a couple of thoughts. I think it would be helpful to specify more precisely what translational research means in this context-maybe by listing the subject areas of potential coverage. The brief includes other aspects of regenerative medicine and cancer stem cells, and translational research can cover a lot of ground, so I think the niche needs to be clarified. |
| Mitchel S. Berger, M.D. | University of California, San Francisco | I think this is a very good idea and has a definite place in the field. |
| Pek Lum, Ph.D. | iPierian | We applaud CIRM’s effort to spearhead an online, open-access journal for translational aspects of stem cell research. We believe that this will be very useful for the stem cell research and patient communities at large. A peer-reviewed open-access journal is important. To date, most of the stem cell work has been published in non-open access journals, making access difficult for many people, scientists or otherwise. In addition to open access, a mandate to publish negative results quickly as well as positive results is critical, especially in a young field like this. Transparency will help move the field forward faster. This will also encourage publications comparing different iPSC lines and their differentiation propensities from independent laboratories. In addition, a journal that covers more clinical and drug discovery aspects of stem cell research will address the current shortcomings of other journals. We strongly support this initiative. |
| Karen S. Aboody, M.D. | City of Hope National Medical Center & Beckman Research Institute | There has been such a great increase in stem cell journals over the past several years, already achieving high impact factors and a solid stem cell researcher following. As you know, these include Cell Stem Cell, Stem Cells, and Stem Cells and Development, among many others. Science Translational Medicine is emerging as a lead translational journal, although as you state – not focused on stem cell therapies. If you do pursue this, I think it should be more broad - encompassing more than “Case Studies of Translation from CIRM”. Not everyone is aware of CIRM outside of CA. Do you plan to accept all translational stem cell research papers? What about stem cell trials already underway? I think contributions from the FDA on stem cell therapy issues is an excellent idea. I also think that if you can truly succeed in motivating researchers to publish negative as well as positive results – it could be a very beneficial source of information – accelerating progress. One problem is that a lot of translational stem cell research is driven by industry, who are not apt to publish details early on, and much useful data is kept confidential. |

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| | | <p>Are you planning to publish pre-clinical studies that don't succeed in IND approval – or only studies that have already been approved for clinical trial? Will it be focused on translational pre-clinical research and clinical trials? Will you include articles on manufacturing and GMP production?</p> |
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Department of
Ophthalmology

January 20, 2010

Mark S. Humayun, M.D., Ph.D.
Cormelius J. Pings Chair in
Biomedical Science
Professor of Ophthalmology,
Biomedical Engineering and
Cell & Neurobiology

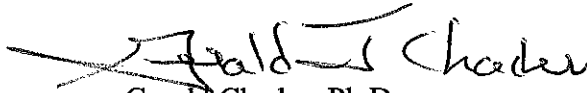
Dear Dr. Trounson,

We are writing in response to your request for an opinion as to the merits of starting a new stem cell journal aimed at clinical translation under the auspices of CIRM. In short, I think this is a great idea. Nevertheless, while there are clear merits of having such a journal, the scale of the project and the associated foreseeable start-up costs do warrant careful consideration.


Stem cell research allows for examination of basic cellular mechanism in ways that were not previously possible. However, it behooves all researchers involved to relate his or her work to the treatment and cure of disease. Certainly, this larger goal would be very well served by having such a translational journal available to investigators. Given the commitment of taxpayers and the State, providing a means for expedited dissemination of both positive and negative results becomes a moral imperative. Carefully chosen and peer-reviewed published work could save much time and effort, and engage both the FDA and industrial and commercial interests. In our experience, the outreach effort made by the Agency over these past few years is unprecedented and extremely encouraging to researchers. It is our hope to move basic research to clinical trials as quickly as possible, and this is not possible without the active input and cooperation of both government agencies and corporate partners.

I feel that the short timeline a publisher will have for achieving financial autonomy will be balanced by the great opportunity of bringing a highly visible journal to an interested and vested public. The offered startup funding will provide a rare opportunity for a publisher starting a new venture. Another inducement might be to get a high profile investigator to agree to be Editor. In any event, the idea is excellent and well worthwhile investigating with publishers around San Francisco, and even well beyond.

Sincerely,



Gerald Chader, Ph.D.
Chief Scientific Officer
Doheny Retina Institute



Ashish K. Ahuja, Ph.D
Executive Director of Operations
The California Project to Cure Blindness



Mark S. Humayun, M.D. Ph.D.
Cornelius J. Pings Chair in Biomedical Sciences
Professor of Ophthalmology, Biomedical Engineering and Cell & Neurobiology
Director, NSF BioMimetic Microelectronic Systems Engineering Research Center
Director, DOE Artificial Retina Project



REQUEST FOR PROPOSALS

XXXX XX, 2010

Partner for Translational Research Journal

1. Introduction

1.1. CIRM

The California Institute for Regenerative Medicine (CIRM) was established in early 2005 following the passage of Proposition 71, the California Stem Cell Research and Cures Initiative. The statewide ballot measure, which provided \$3 billion in funding for stem cell research at California universities and research institutions, was approved by California voters on November 2, 2004, and called for the establishment of a new state agency to make grants and provide loans for stem cell research, research facilities and other vital research opportunities.

The mission of CIRM is to support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury.

To date, the CIRM governing board has approved 345 research, training and facility grants totaling more than \$1 billion, making CIRM the largest source of funding for human embryonic stem cell research in the world. Estimates suggest that these grants already awarded will generate tens of thousands of job-years of employment in the state. For more information please see www.cirm.ca.gov.

1.2. Goals for this Contract

The agency believes that translational science, moving discoveries from the laboratory to the clinic, as it relates to cell therapies and other aspect of regenerative medicine, will have many unique aspects not reflected in other avenues to therapeutic development and not likely to be given sufficient and cohesive coverage in other research journals. Raising these issues in priority to where they become the main mission of a journal will foster the acceleration of the entire field as knowledge is aggregated and shared more readily. Given the urgency of its mission, and the role an online journal could play in advancing the field, CIRM

wants to accelerate the creation and publication of a journal that will accomplish this goal. To that end, CIRM is offering to subsidize start up costs of a new online journal. CIRM is requesting proposals from firms that can show an ability to produce a peer-reviewed, open access, on-line journal.

2. Scope of Services Required

CIRM will subsidize startup costs for publication of an online journal focusing on translational stem cell science and other aspects of regenerative medicine and cancer stem cell investigation. The publisher must be able to solicit, review and publish important manuscripts in the field, and also provide for rapid review and dissemination of negative data. The journal should include a regular column, to be prepared with input from CIRM, discussing case studies in translational science, analogous to the Case Studies from Massachusetts General in the New England Journal of Medicine. Other than this case-based column, the editorial content shall be completely independent from CIRM. The business plan should show an ability to be self-sustaining within three years via advertising, page charges, or other means. (If that business plan requires that the online journal be supplemented with a paid print version, CIRM will consider including that in the contract.) The online journal's first issue date should be within six months of the commencement of this contract.