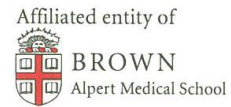


BRETT D. OWENS, M.D.

*Professor
Department of Orthopaedic Surgery
Brown University
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Division of Shoulder & Knee Surgery*

*100 Butler Drive
Providence, RI 02906*

*Patient Office (401) 330-1434
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3/12/2016

To:
Maria Bonneville
Executive Director of the ICOC
mbonneville@cirm.ca.gov

Dear ICOC members,

I am contacting you in order to express my strong support for the grant proposal titled: "Ultrasound-mediated Stem Cell Activation: A Therapy for Tendon and Ligament Injuries" (TRAN1-08527), which I believe you will be discussing during your upcoming meeting on March 16th 2016.

I am an Orthopaedic Surgeon specializing in Sports Medicine who practiced for 12 years in the US Army, recently transitioning to civilian practice. Given the young and active population among the United States Military personnel, Anterior Cruciate Ligament (ACL) tears are common injuries and these injuries represent a significant health issue for our servicemen and servicewomen. In fact, we have demonstrated previously that the rate of ACL injury among active duty personnel is ten times higher than the rate of these injuries among the general population. Given the prolonged recovery from these injuries, this represents a substantial issue from both a direct cost and a force readiness perspective. These issues are compounded by studies reporting that approximately 10% of ACL injury patients whom present to a military healthcare system ultimately are discharged from the military with permanent disability as a result of their ACL injury.

I have reviewed the projects currently funded by CIRM on their website and I am unaware of any currently funded investigations aiming to develop stem cell therapies for tendon and ligament injuries. As patients continue to pursue various "stem cell" therapies both in the U.S and abroad, it is clear that there is a significant interest in this technology. However, this technology should be applied based on scientifically robust investigations such as the proposal mentioned above (TRAN1-08527).

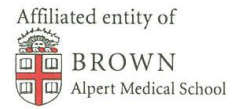
In summary, the proposed project is of extraordinary importance to both our military and civilian populations, as it has the ability to facilitate a much-needed enhanced healing response in the treatment ACL injuries. Additionally, this technology seems applicable to a multitude of other tendon and ligament injuries. I urge CIRM to strongly consider funding this research proposal, as I believe studies such as this are paramount to improving the treatment of these extremely

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common injuries, and this is especially important among our military personnel. I look forward to the day that a technology like this can advance the care of my patients.

Sincerely,

A handwritten signature in black ink, appearing to read "B. Owens", with a stylized flourish at the end.

Brett D. Owens, MD
Professor of Orthopaedic Surgery
Brown Alpert Medical School

Professor, Norman M. Rich Department of Surgery
Uniformed Services University of Health Sciences

3/10/2016

To: Maria Bonneville
Executive Director of the ICOC
mbonneville@cirm.ca.gov

Dear ICOC members,

My name is Jason Lezak and I am a former professional competitive swimmer. I have been a member of the last four United States Olympic Swimming Teams and served as the men's team captain of these teams in both 2008 and 2012. I have won a total of eight Olympic medals including four gold medals. I was also the recipient of an ESPY Award for the "Best Moment" of the 2008 Olympic games in Beijing. I am a current world record holder in the 4x100 meter freestyle relay and previously held the American record in the 100 meter freestyle.

I am writing this letter to convey my strong support for a CIRM grant proposal titled: "Ultrasound-mediated Stem Cell Activation: A Therapy for Tendon and Ligament Injuries" (TRAN1-08527), which will be discussed on March 16th.

I have participated in competitive swimming since the age of 5 years old. During my career, I have known many swimmers as well as other athletes who have suffered greatly from various tendon and ligamentous injuries. In 2012, I myself injured my knee and underwent surgical treatment prior to the 2012 Olympic games in London. I vividly recall that the recovery from this injury which was prolonged and extremely frustrating. As a former professional athlete, I can tell you that the desire to return to your sport is insatiable, and this strong desire to return to sports exists for any individual who enjoys an active lifestyle. As a result, any well studied and safe therapeutic modality that holds the potential to accelerate or improve your recovery from an injury, even if only by a modest margin, would certainly be worth pursuing wholeheartedly. This certainly holds true for injuries that are traditionally associated with a prolonged recovery such as anterior cruciate ligament tears or rotator cuff tendon tears.

I am not personally familiar with stem cell medicine, however, I have been exposed to numerous athletes who seek out and then undergo so-called "stem cell" treatments for tendon and ligament injuries both here in the United States as well as in Europe. In my experience, there is a clear need for further research in this setting with a particular focus on the legitimate science and safety of these treatment strategies. It is my understanding that, currently, the California Institute for Regenerative Medicine does not fund any stem cell research directed at improving the treatment of tendon and ligament injuries. In light of this, it seems that studies such as the one mentioned above (TRAN1-08527) provide a tremendous opportunity to have a significant impact on our physically active population both here in California as well as the rest of our nation. I hope that the ICOC strongly considers funding this proposal, as I am certain that research of this nature will contribute significantly to lives of patients who suffer these injuries.

Sincerely,



Jason Lezak



University of Connecticut Health Center
Institute for Regenerative Engineering

Cato. T. Laurencin, M.D., Ph.D.
University Professor
Albert & Wilda Van Dusen
Distinguished Professor of
Orthopaedic Surgery
Professor of Chemical, Materials,
& Biomolecular Engineering
Director, Institute for
Regenerative Engineering

March 14, 2016

Maria Bonneville, ICOC Executive Director

Dear ICOC Members,

I fully support the grant proposal: "Ultrasound-mediated Stem Cell Activation: A Therapy for Tendon and Ligament Injuries" (TRAN1-08527), which is on the March 16th agenda.

As an orthopaedic surgeon, I am an expert in the treatment of shoulder and knee pathology and have been designated as one of "America's Top Doctors" and "America's Top Surgeons." I am also a tenured Professor of Chemical and Biomolecular Engineering at the University of Connecticut. I serve as Chief Executive Officer of the Connecticut Institute for Clinical and Translational Science, and the director of the Institute for Regenerative Engineering. Furthermore, I am an elected member of the the National Academy of Medicine and the National Academy of Engineering.

As a practicing clinician, I can attest to the great importance of developing new therapeutic modalities to enhance the treatment of ligament and tendon injuries. there are more than 200,000 anterior cruciate ligament (ACL) injuries each year in the United States alone, with approximately 100,000 of these patients being treated with ACL reconstruction annually. Based on census data from 2010, more than 5.5 million people in the United States have a rotator cuff tear. Repair of these tears is one of the most common orthopaedic procedures and perhaps the most common procedure of all shoulder surgeries. It is estimated that, in the United States, between 200,000 and 300,000 rotator cuff tendon repairs are performed each year with a failure rate reported to be from 20% to more than 90%. Currently, one of the main challenges of successful rotator cuff tendon repair is the poor biology of. As a result, these repairs necessitate a prolonged healing time which prevents patients from returning to their usual activities in a timely manner.

As a scientist in the field of regenerative medicine, I strongly support the application of stem cells and gene therapies to augment ligament reconstructions and tendon repairs. The development of these therapies should be based on comprehensive, rigorous and transparent scientific investigations in order to yield the safest and most effective results. We constantly hear of patients receiving all sorts of "stem cell" treatments in clinics both in the U.S. and abroad in order to treat injured ligaments. I believe it is the role of funding agencies, like CIRM, to support scientifically robust research projects, such as the proposal mentioned above, which can translate excellent science into the optimal clinical solution for patients.

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Although CIRM has not yet supported a study investigating stem cell therapies for ligament and tendon repair, the TRAN1-08527 proposal is only two points away from being included in Tier 1 of funding. This seems to me like a marvelous opportunity to support an excellent study with tremendous potential clinical impact on patients in California and throughout the United States.

Sincerely,

A handwritten signature in black ink, appearing to read 'Cato T. Laurencin', with a stylized, cursive script.

Cato T. Laurencin, MD, PhD

University Professor

Albert and Wilda Van Dusen Distinguished Professor of Orthopaedic Surgery

Professor of Chemical and Biomolecular Engineering

Professor of Materials Science and Engineering

Professor of Biomedical Engineering

Director, Raymond and Beverly Sackler Center for Biomedical, Biological, Physical
and Engineering Sciences

Director, Institute for Regenerative Engineering

Chief Executive Officer, Connecticut Institute for Clinical and Translational Science



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John M. Adams, Jr., M.D. Kevin M. Ehrhart, M.D. Michael B. Gerhardt, M.D. Ronald J. Gowey, M.D. Kenton S. Horacek, M.D. Thomas P. Knapp, M.D. Arash Lavian, M.D.
Robert K. Lee, D.P.M. T. Michael Lain, M.D. Bert R. Mandelbaum, M.D. M. Ramin Modabber, M.D. John R. Sellman, M.D. Clint J. Soppe, M.D. Rachel Triche M.D.

Ms. Maria Bonneville
Executive Director of the ICOC
mbonneville@cirm.ca.gov

Dear ICOC members,

My name is Bert Mandelbaum MD and I am an academic Sports Medicine Orthopedic Surgeon in Santa Monica ,California .I am also a leader and work with all types of athletes young, old , elite and those with special needs. I have served as National team physician since 1991 for our US Men's National Soccer team. I have been team doctor at UCLA , Pepperdine University and the LA Galaxy. I have worked to developed the medical network with the U.S. Olympic committee,served as Major League Baseball's director of research and was the Chief Medical Officer for the World Special Olympic Games in Los Angeles in 2015. As a consequence I practice and lead the concept that clinical care drives innovation and innovation and research drives clinical care. As a sports doctor we are always pushing for results that are faster, higher and stronger. In my field there has been an unmet need and a dearth of biological and stem cell innovation in the areas of tendon, cartilage and bone. Without good science and innovation we can not progress in our knowledge, our evidence and our patient care. Tendon tears, Osteoarthritis and bone deficits plague our population causing inactivity and disability. As a field we need to develop preventive, regenerative and reparative strategies to keep us active at all levels.

I am now contacting you in order to express my strongest possible support in a grant proposal titled: "Ultrasound-mediated Stem Cell Activation: A Therapy for Tendon and Ligament Injuries", which I believe you will be discussing during your upcoming meeting in March.



John M. Adams, Jr., M.D. Kevin M. Ehrhart, M.D. Michael B. Gerhardt, M.D. Ronald J. Gowey, M.D. Kenton S. Horacek, M.D. Thomas P. Knapp, M.D. Arash Lavian, M.D.
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Searching the CIRM website and list of funded grants I could not find any support for research trying to develop stem cell therapies for ligament injuries. As you probably know, several American athletes have already received stem cell therapies in different clinics both home and abroad. However, I am not sure how established are these so-called stem cell therapies and I would rather rely on treatments that originate from CIRM-funded research.

With this letter I wish to serve as an advocate in the State of California. I urge you to support this grant proposal in order to bring hope to those who sustain ligament and tendon injuries.

Sincerely,

Bert Mandelbaum MD

Co-Chair of Medical Affairs Kerlan Jobe Institute at Cedars Sinai
Santa Monica Orthopaedic and Sports Medicine Group and Sports Foundation
Chief Medical Officer LA 2015 World Special Olympic Games
Team Physician LA Galaxy, US Soccer, Pepperdine University
Member FIFA and CONCACAF Medical Committee and F-MARC
Assistant Medical Director Major League Soccer

Keck School of Medicine of USC

JAY R. LIEBERMAN, M.D.
Professor and Chairman
Department of Orthopaedic Surgery

March 14, 2016

Maria Bonneville
Executive Director of the ICOC

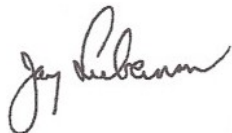
Dear Ms. Bonneville,

I am writing this letter in support of the CIRM grant entitled "Ultrasound-mediated Stem Cell Activation: A Therapy for Tendon and Ligament Injuries." The principal investigator is Dan Gazit, MD, PhD. I am an orthopaedic surgeon and I am presently Chairman of the Department of Orthopaedic Surgery at the Keck School of Medicine of USC. As an orthopaedic surgeon, I can verify that this is an important topic that requires funding. Ligament and tendon injuries have an impact on both athletes and weekend warriors. Dr. Gazit and his research team have developed a novel strategy, using ultrasound based gene delivery, to enhance bony fixation of ligament repairs. This technology could revolutionize the treatment of injuries involving the anterior cruciate ligament in the knee and the rotator cuff in the shoulder. A novel aspect of this potential therapy is the use of ultrasound which is commonly available in many orthopaedic offices at this time.

It is essential that stem cell and gene therapy are expanded to the orthopaedic and musculoskeletal arena. Our patients are now more active than they ever have been and they want to maintain their quality of life. I hope you will seriously consider funding this proposal.

Thank you for your consideration.

Sincerely,



Jay R. Lieberman, M.D.
Professor and Chairman
Department of Orthopaedic Surgery
Keck School of Medicine of **USC**
Professor of Biomedical Engineering
Viterbi School of Engineering of **USC**

