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SANTA BARBARA • SANTA CRUZ

DEPARTMENT OF BIOMEDICAL ENGINEERING
UNIVERSITY OF CALIFORNIA, DAVIS
ONE SHIELDS AVENUE
DAVIS, CA 95616

TELEPHONE: (530) 754-9149
FAX: (530) 754-5739
EMAIL: jkleach@ucdavis.edu

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Independent Citizens Oversight Committee (ICOC)
California Institute of Regenerative Medicine

Re: Comments regarding RT3-07981 (PI: Leach) in response to Tools and Technologies III (RFA 13-05)

To the Committee,

I write to briefly address the Committee about my recent proposal entitled *"Multimodal technology for non-destructive characterization of bioengineered tissues"*. In the ensuing paragraphs, I will provide more details indicating that **this proposal should be funded** for the following reasons:

1) This is the **only proposal** within the Tools and Technologies grants under consideration that considers musculoskeletal tissue engineering or the development of a non-destructive method to characterize engineered replacement musculoskeletal tissues.
2) The technology proposed here will create an expedient means of assessing dynamic changes in the extracellular matrix arising during the formation of engineered bone and cartilage. This is considered to be a **major hurdle in regenerative medicine** of the musculoskeletal system and impairs the inherent personalized medicine component of stem cell-based methods.
3) The team that we have assembled to develop this technology is arguably **the most qualified team in the nation to conduct these studies**. The research team capitalizes on the combined engineering, medical, and veterinary expertise from UC Davis to test these tissues, further increasing its probability of having a profound and lasting impact on the field.

This innovative proposal is submitted by a collaborative team of bioengineers (Leach, Marcu, and Athanasiou) who seek to tackle the significant bottleneck of variability in manufacturing engineered musculoskeletal tissues using imaging-based tools. The proposal scored 72 (ranked 4th in the Tier 2 grouping), **receiving the same score as another proposal recommended for funding** and recommended by 9 reviewers for Tier 1. Presently, the funding recommendation from CIRM is DO NOT FUND. The stated highlights include three impactful aspects of the work and one concern of overlapping leadership and the development of the same imaging technology in another application.

The co-PI (Dr. Marcu) of this proposal is also PI on RT3-07879, which is focused on assessing stem cell repopulation and remodeling of engineered vascular tissue constructs. However, the use of this technology for monitoring the maturation of engineered bone and cartilage, tissues composed of dense matrix reflective of the differentiation of contributing stem cell populations, is ***substantially different*** from cardiovascular applications. Of course, both applications involve instrumentation based on optical spectroscopy and ultrasound principles, but the implementation and subsequent commercial hurdles for this technology is very different.

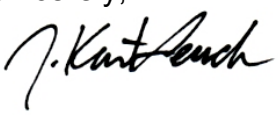
Current methods to assess the properties of engineered tissues suffer bottlenecks between stem cell isolation and their clinical implantation. A non-destructive solution to monitor tissue composition, microstructure, and function during the optimization of stem cell protocols will greatly accelerate their development. Over the last 4 years, this research team has worked closely to demonstrate the promise of individual and related aspects of this technology for characterizing engineered bone and cartilage. However, there is no single tool that correlates matrix composition with construct mechanical properties to nondestructively determine tissue maturation and signify when an engineered tissue is ready for implantation. ***The proposed multi-modal tissue diagnostic tool offers such a solution.***

This application seeks to develop a tool to resolve bottlenecks in engineering replacement bone and cartilage to address an immense clinical need in our population. The medical costs associated with musculoskeletal trauma and disease represents an ***untold financial burden on Californians*** and Americans alike. The successful development of this multimodal imaging technology will be invaluable to **numerous biotechnology companies in our state**, thereby increasing the impact of CIRM investment on improving the health of our citizens, expanding its economic impact, and raising the translational potential to a palpable level. Moreover, the application of this tool will provide new insight into the biology of bone and cartilage formation and remodeling, further increasing our understanding of how tissues regenerate and key indicators at which time intervention is best applied.

The proposed strategy represents a critical first step to develop and validate technologies to test the maturation of engineered tissues for implantation – particularly those which result from stem cell-based manufacturing with inherent patient variability. This proposal leverages unique expertise in biomaterials and the isolation and application of a promising stem cell source from skin to generate replacement bone and cartilage. **The successful development and application of this tool for engineered bone and cartilage is dependent upon funding from CIRM now** to advance beyond its current status. Moreover, if awarded, the result of the proposed work will have a broad-reaching effect on the translation of previous CIRM-funded projects seeking solutions to address tissue loss due to trauma, disease, or malformations.

Thank you for considering these comments. I am hopeful you will fund this proposal.

Sincerely,



J. Kent Leach, Ph.D.
Associate Professor
Departments of Biomedical Engineering and Orthopaedic Surgery
University of California, Davis