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July 12, 2016

**Re: DISC2-08990 Consideration for funding**

Dear ICOC Members:

I am writing this letter to request enthusiastic ICOC support for moving my proposal entitled "Human heart-on-a-chip for disease modeling and developing new strategies to treat cardiac diseases," to the recommended for funding category. The grant received a score of 83 with a standard deviation of 6, indicating it was statistically within the score of 85 required for funding.

The proposal will develop patient specific 'heart-on-a-chip' diagnostics that will have a significant impact on the early screening of drugs used to manage hypertrophic cardiomyopathy. Currently, there are no drugs that target specific disease alleles of hypertrophic cardiomyopathy. Therefore, this is a unique proposal in the CIRM portfolio that leverages existing investment in the CIRM funded iPSC Bank. If successful, our patient specific 'heart-on-a-chip' diagnostics could significantly reduce the cost and time of bringing a new drug candidate to market while improving safety and efficacy, improving the lives of Californians with heart disease.

The main criticism of my grant was in the level of maturity of the cardiomyocytes proposed in the study. I respectfully point out the following:

- We use the same protocol to differentiate cardiomyocytes as a number of currently funded CIRM investigators, including Disease Team grantees. The criticism of maturity of cardiomyocytes did not prevent funding of those applications.
- The maturity issue is germane to all cardiomyocytes differentiated from hiPS or hES cells and we have observed increased maturity in our organ chip models compared to standard culture conditions.
- Using these cells, we can predict drug response on par with large scale animal models and slice cultures of human hearts, indicating advanced maturity.

Collectively, these points suggest we are significantly ahead of the field in addressing the cardiomyocyte maturity issue with our advanced heart chip technology and our project will have a significant impact on the health of Californians.

Sincerely,

A handwritten signature in blue ink that reads "Kevin E. Healy".

Kevin E. Healy  
Jan Fandrianto Distinguished Professor in Engineering  
Professor of Bioengineering  
Professor of Materials Science and Engineering