



UNIVERSITY of CALIFORNIA, SAN DIEGO  
SCHOOL OF MEDICINE

August 18, 2021

CIRM Governing Board  
c/o Dr. Maria Bonneville  
MBonneville@cirm.ca.gov

**Re: DISC2-12588**  
**Dear Members of the Board,**

I have submitted the above application to obtain support for development of new therapeutic antibodies that should lead to the killing of pancreatic cancer stem cells as well as differentiated cancer cells. The application received a score of 80, which is just below the fundable score of 85. Our approach to antibody development and use for the therapeutic targeting of pancreatic cancer was judged as technically sound and feasible by 9 out of the 10 reviewers. In the review summary that I received, the only criticism was that the antibody we plan to develop, targeting a protein called SDC1 that is expressed in higher levels in pancreatic cancer stem cells than in differentiated cancer cells, is not stem cell specific. I do not contest this criticism, but I strongly believe that the ability of the antibody to target both cancer stem cells and differentiated cancer cells is an advantage that probably accounted for the ability of a prototypical antibody targeting the mouse SDC1 protein and genetic ablation of SDC1 to cause dramatic, nearly complete, tumor regression. Such durable tumor regression and disappearance of all histologically identifiable cancer cells would have never been achieved if the antibody did not target cancer stem cells.

As you may know, pancreatic cancer is the most lethal of all cancers and its 5-year survival has remained at 10% or less for the past 30 years, despite the development of effective targeted therapies and immunotherapies for other types of cancer. We believe that our approach to target SDC1 in combination with chemical inhibitors of the protein kinase ULK1, which are ineffective on their own, is likely to change this grim picture. Despite the strong focus of CIRM on stem cell biology, I do believe that such a project falls within the realm of CIRM and will be of great benefit to the citizens of California, including underserved groups who are at a high risk of developing pancreatic cancer. It will certainly be a pity if CIRM will not participate in the development of such a promising therapeutic approach to the most lethal of all cancers.

Sincerely,

A handwritten signature in blue ink, appearing to read "Michael Karin", with a large, sweeping flourish at the end.

Dr. Michael Karin  
Distinguished Professor of Pharmacology  
Ben and Wanda Hildyard Chair for Mitochondrial and Metabolic Diseases  
American Cancer Society Research Professor

**DEPARTMENT OF PHARMACOLOGY**

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