

May 14, 2020

Jonathan Thomas, Ph.D., J.D., Chair of ICOC  
Maria Millan, M.D., President and CEO of CIRM

**Extraordinary petition for DISC2COVID19-11813**  
**Combating COVID-19 using human PSC-derived NK cells**

Dear Drs. Thomas, Millan, and Distinguished members of the ICOC:

My proposal “Combating COVID-19 using human PSC-derived NK cells” received a score of 78, which is 7 points below the initial funding line, and was not recommended for funding. I am writing this petition to ask you to reconsider my proposal for funding for three main reasons.

1. Today, as we know, there are no approved prophylactic or therapeutic options for COVID-19, and, more importantly, it is likely that COVID19 will be with us for the foreseeable future. Even with a future vaccine, patients who are severely affected by this disease will continue to appear. Therefore, it is critical to promptly develop effective strategies for the treatment of COVID-19. We propose to develop a stem cell-based NK cell therapy to treat COVID-19. We will use human pluripotent stem cells to make NK cells with enhanced killing effect and unlimited supply, which could lead to the creation of effective NK cell banks available to COVID-19 patients with immediate and vast demand. The significance and impact of this proposal has been acknowledged by vast majority (12 out of 14) of the reviewers.

2. While multiple reviewers agree that the rationale of the proposed research is strong, there was a concern about whether there is a causative relationship between NK depletion/exhaustion and disease progression. Extensive studies have shown that NK cells play an important role in regulating the defense against virally infected cells and tumor cells. Depletion and exhaustion of cytotoxic lymphocytes, such as NK cells, have been shown to be causal for disease progression and poor clinical outcome associated with viral infection and cancer. In this regard, immense advancement has been made in cell-based immunotherapy to enhance patient’s immune system through adoptive transfer of cytotoxic lymphocytes in recent years.

3. The reviewers acknowledged that this project is straightforward and streamlined, and if successful, could be moved to patients quickly. One potential concern was that an NK treatment could be toxic, but to date NK therapy for cancer has had minimal toxicity. An added advantage of NK-based immunotherapy is that NK cells don’t have the side effects often associated with T cell-based immunotherapy, such as cytokine storm or GVHD. Multiple clinical trials using NK cells have demonstrated that NK cells are safe.

The human stem cell approach proposed in this study will allow us to generate NK cells with enhanced killing effect for unlimited doses. These cells will be used to treat COVID-19 patients with immediate and vast demand.

Thank you for considering this petition for funding.

Sincerely,  
Yanhong Shi, Ph.D.  
Herbert Horvitz Professor in Neuroscience