



UC San Diego

SCHOOL OF MEDICINE

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Ref. CIRM DISC2COVID19-12014 application

Dear CIRM Board Members,

Recent clinical studies have pointed to several neurological problems associated with COVID19, both in adults and newborns. The short and long-term neurological consequences of this condition should not be underestimated.

In the last months, I dramatically re-structured my lab to perform all the necessary experiments to confirm the ability of the SARS-Cov-2 virus to replicate in human brain cells. We now know that the virus can infect neurons, killing cells and reducing the number of connections. Moreover, we tested drugs that could block the viral replication and the loss of synapses. We found one promising candidate, an FDA-approved antiviral for Hepatitis C that can cross the blood-brain-barrier. Our CIRM application requested support to validate these observations, adding evidence to support a clinical trial.

We received a number of fundable scores but the final median score was just below the fund tier. Upon reviewing the comments from reviewers, I was surprised that the discussion was minimally about the scientific merit of the project but converge on the eventual cost of the potential future treatment.

While the candidate drug is currently costly in the US for a Hepatitis C treatment, it is not expensive elsewhere. The drug's reduced price outside the US is a reflection of the negotiation between the different nations and the pharmaceutical (Gilead). Also, the current application is a niche market. It will be of interest of the pharma to make it available with a reasonable price in a worldwide market, and reduce its price in the US for COVID19 treatment.

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I feel this discussion is premature, and negatively impacted the decision to fund this work. This outcome will be unfortunate for California since this technology might end up being licensed by others. It will be a missed opportunity for a pharmacological treatment that blocks viral replication and has excellent penetration in the brain, unlike any other candidate for COVID19.

I wonder if it is possible for the Board to overcome this decision. If so, I would incorporate all the relevant scientific criticisms (for example, adding other antiviral drugs as comparisons), and work with Gilead to seek an agreement plan on accessibility of the drug during the grant period.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Alysson R. Muotri'.

Alysson R. Muotri, Ph.D.