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To the CIRM Independent Citizens Oversight Committee (ICOC):

Dear Ms. Bonneville,

I am writing regarding the funding decision related to the project DISC-09095 entitled "**A human platform to model microcephaly caused by the Zika virus**".

The goal of the project was to set up a human stem cell platform to measure the impact of the Zika virus in the nervous system and to screen potential drugs to alleviate the neurological problems associated with the infection. Our work aims to fill fundamental gaps on an urgent unmet medical need.

The Brazilian Zika virus is now established as the causal agent of the congenital birth defects epidemic in South America. The work proving causation was actually performed by my team and recently published in the journal *Nature* (Cugola *et al*, 2016). Cases of infection were already reported in US (including California) and will increase over the summer due to mosquito spreading and sexual transmission. There is no other support on this subject in CIRM disease portfolio. Thus, this proposal is within CIRM mission and priorities.

Since the proposal application, we have learnt that Zika is not only responsible for microcephaly in babies, but can also impact the health of infected adults. Cases of paralysis and death were already reported in Brazil and in other countries. Based on our own data, we anticipate a spectrum of neurological problems, such as developmental delay and motor neuron defects, even in non-microcephalic babies. The extension of the neurological damage is currently unknown - it is just too premature to completely realize the consequences of the Zika infection. Fundamental and translational

approaches at this early stage are essential to understand how the virus works and to create therapeutic opportunities.

I never debated over a grant fund decision before. However, in this case I fell I have the responsibility to alert the ICOC about neglecting studies on what we call now the “Zika virus syndrome”. I can tell by personal experience dealing with this virus in my own lab that this is one of the most dangerous infectious agent I ever seen – one can witness the virus killing brain cells in less than a day. This is a nasty virus that needs to be studied and controlled as soon as possible. I strongly believe it will be beneficial for California to take the lead on such a novel syndrome for health and security reasons.

Thus, I would like to request the ICOC to reconsider the CIRM Review Office’s funding decision on this application. I can make myself available to further discuss this issue with the ICOC and answer any other concerns from the committee members.

Sincerely,

Alysson R. Muotri, PhD

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