

Dear Science Subcommittee Members,

Below are thoughts I'd like to share with you in advance of tomorrow's meeting - regarding the work of the Neuro Task Force. I look forward to hearing your thoughts at that meeting."

Charge to the CIRM task force on neuroscience and neuromedicine: The goal of the CIRM Task Force on Neuroscience and Medicine is to ***generate a general plan for the \$1.5 billion set aside*** for neuroscience and related medicine as specified in Proposition 14. In addition to generating a general plan for Neuroscience and related medicine, the task force will aim to ***identify unusual opportunities for high impact in these areas for enhanced investment***. The task force will work in public meetings with the community in California and beyond to identify potentially high impact opportunities in basic neuroscience, neurodegenerative disease, neuropsychiatric disease, neurodevelopment, and normal brain aging. The task force will be composed of a mix of ICOC members with scientific or patient advocacy backgrounds who will work with the CIRM team. A series of open meetings will be held with the external community to gather information and to hear recommendations. The goal of the task force is to provide final recommendations to CIRM and the ICOC within six months of inception.

Summary of neuroscience and neuromedicine task force planning progress thus far: In keeping with our charge and with a deliberative approach, we began our work by conducting a brief overview of the current CIRM grant portfolio. This initial evaluation demonstrated that grant spending and commitments currently met the 27% fraction mandated by Proposition 14 ($1.5/5.5=27\%$) and was expected to continue at this rate. We also learned that neuropsychiatric disease, which is newly tractable with stem cell technologies, was underrepresented in the CIRM portfolio with zero grants and a very high index of disability adjusted life year (DALY) burden. In keeping with the task force charge to identify high impact opportunities, we launched a review of the neuropsychiatric area. To ensure that we adequately understood the current state of neuropsychiatric disorder research, we heard from a number of eminent scientists who told us that genetic analyses had identified appropriate variants to model in stem cell derived neurons and glia, that phenotyping methods were adequate to the evaluation of neurons and glia carrying neuropsychiatric susceptibility variants, and that one example already from Tom Sudhof had used genetic and stem cell technologies to track down the nature of a genetic variant causing schizophrenia. Owing to the demonstration that technology was newly available to evaluate neuropsychiatric disorders using stem cell and genetic technologies, an agreement was reached to develop a concept plan that would have some unique features promoting interdisciplinary collaboration necessary for evaluating neuropsychiatric disease in stem cell derived neurons and glia. It was also agreed that we should ensure that a proposed new concept plan dictated grants of adequate size and term to attract applications from neuropsychiatric disease researchers. This concept plan was discussed by members of the task force and then was voted to advance to the science subcommittee.

Proposed next steps: Proposed next steps for the task force are to continue and to complete an evaluation and plan for neuro diseases other than neuropsychiatric disease, and to create an overall plan for the proposition 14 mandate to fund at least \$1.5 billion of neuroscience and neuromedicine projects. As part of developing such a plan, it is important that the task force make progress on answering the question of how much of the \$1.5 billion should be programmed by the task force and the ICOC as opposed to using the Grants Working Group to define and identify the most appropriate projects submitted for funding. Answering this question will require further deliberation and an evaluation of the current CIRM funding portfolio including projects in at least two obvious areas analogous to the umbrella term neuropsychiatric disease. These areas for further review are neurodegenerative disease and neuroinjuries (Pat Levitt suggested this useful grouping). To complete an appropriate review of these two areas and to make decisions about the creation of new grant programs, simply using DALY as a measure of disease burden and prevalence may be inadequate and some other metrics need to be identified. An important next step is to hear from health care economists about different ways of thinking about disease burden that will be useful to the efforts of the task force. Thus, the next meeting of the task force will include a group of health care economists. Another activity of the task force will be to develop a system for tracking the ongoing neuro grant portfolio to ensure that it stays on track to ultimately sum to 1.5 billion or 27% of the CIRM portfolio of the \$5.5 billion established by proposition 14. Thus, the work of the task force will continue with the potential identification of high impact opportunities in areas of neuroscience and neuromedicine other than neuropsychiatric disease and to ensure that the spending rate and allocation for neuroscience and neuromedicine continues to be consistent with the 27% minimum directive in Proposition 14.