***Brain Research Through Advancing Innovative Neurotechnologies*® (BRAIN)**
Multi-Council Working Group (MCWG) Meeting
May 16th, 2022

On May 16, 2022, the National Institutes of Health (NIH) *Brain Research Through Advancing Innovative Neurotechnologies*® (BRAIN) Initiative Multi-Council Working Group (MCWG) met virtually to discuss the current state of the NIH BRAIN Initiative and learn about new chemical and synthetic biology technologies from a new MCWG member.

In opening remarks, John Ngai, PhD, Director of the NIH BRAIN Initiative and chair of the MCWG, welcomed a new federal *ex officio* working group member, Kristen Jordan, PhD, from the Defense Advanced Research Projects Agency (DARPA), and thanked Dr. Al Emondi for his service. Next, he overviewed the BRAIN budget through fiscal year (FY) 2026, noting the $620M budget for FY2022 and an anticipated increase in funding for FY2023. Dr. Ngai summarized recent events, including the Brain Behavior Quantification and Synchronization workshop, which brought together experts in neuroscience, engineering, and computer science to identify technological gaps in studying and understanding behavior, and the Brain Across the Lifespan workshop. Dr. Ngai also promoted the 8th Annual BRAIN Initiative Meeting and mentioned two activities, the BRAIN Initiative Challenge: "Ethical Considerations of Brain Technologies" essay and video contest for U.S. high school students and the annual BRAIN Initiative Show Us Your BRAINs! Photo & Video Contest. Then, Dr. Ngai discussed findings from a demographics analysis of BRAIN investigators from FY14 – FY21. The evaluation found that NIH BRAIN Initiative funding rates for women and/or underrepresented groups were lower compared to the NIH overall, while funding rates for R1 institutions and those located in coastal states were higher than lower resourced institutions. Early- and mid-career applicants had favorable funding rates compared to later stage career applicants. He also emphasized new efforts to assess race, ethnicity, and gender in the research participant pool. Dr. Ngai discussed how BRAIN is promoting scientific excellence by enhancing diversity, equity, and inclusion capacity building awards at minority-serving institutions, incorporating the Plan for Enhancing Diverse Perspectives (PEDP) into the grant application process, and other efforts. He mentioned planned communications efforts, such as market research to better understand applicant perspectives. Lastly, Dr. Ngai updated the group on recent BRAIN-funded scientific advancements, including a *Nature Neuroscience* study that used single-cell genomics to identify a specific population of dopamine neurons that degenerate in Parkinson's disease[1], progress towards personalized deep brain stimulation for treating depression[2], and other research outcomes.

The meeting proceeded with an update on Neuroethics Working Group (NEWG) activities by Hank Greely, JD, Director of Law and Biosciences at Stanford University and co-chair of the NEWG. Dr. Greely mentioned a NEWG workshop on continuing trial responsibilities on May 24-25, 2022, which focused on research-related care needs for participants in clinical trials involving implanted neural devices. He also reminded the group about the neuroethics consultation service for BRAIN grantees and program staff. Lastly, Dr. Greely announced that Caroline Montojo, PhD, President of the Dana Foundation, will join the NEWG in August 2022, and he thanked Steve Hyman, MD, for his service. The group considered ways to incorporate patient and research participant perspectives into BRAIN working groups.

[1] Kamath, T., Abdulraouf, A., Burris, S. J., Langlieb, J., Gazestani, V., Nadaf, N. M., ... & Macosko, E. Z. (2022). Single-cell genomic profiling of human dopamine neurons identifies a population that selectively degenerates in Parkinson's disease. Nature neuroscience, 1-8.
[2] Scangos, K. W., Khambhati, A. N., Daly, P. M., Makhoul, G. S., Sugrue, L. P., Zamanian, H., ... & Chang, E. F. (2021). Closed-loop neuromodulation in an individual with treatment-resistant depression. Nature medicine, 27(10), 1696-1700.

After the NEWG update, Bryan Roth, MD, PhD, at the University of North Carolina, Chapel Hill, gave a presentation on his research on novel chemical and synthetic biology technologies. Dr. Roth described his quest to identify new promising therapeutics by examining the hundreds of understudied, untargeted G protein-coupled receptors (GPCRs) in the human genome. He talked about research collaborations between his lab and others that led to solving the structure of various GPCRs, including opioid, nociception, serotonin, and dopamine receptors. Once resolved, researchers can use these structures for drug discovery and structure-guided optimization. For example, Dr. Roth and his collaborators are now using a powerful computational approach to predict receptor binding. Atypical antipsychotics and many other drugs commonly used to treat mental health disorders have serious side effects due to off-target activity. This approach may inform the development of more selective drugs that have less side effects. Next, Dr. Roth discussed how he is using these new synthetic biology technologies to validate novel therapeutics. For example, lysergic acid diethylamide has recently shown great potential as a safe therapy for anxiety and depression. Understanding the drug's binding properties could lead to the development of non-psychedelic therapies for neuropsychiatric conditions. Meeting participants discussed ways to ensure that new drugs cross the blood-brain barrier, developing novel radioligands, and the importance of looking at downstream molecular signaling pathways.

The meeting proceeded with a closed session of the MCWG members and federal staff to discuss funding plans for several FY2022 awards. The next MCWG meeting will be held on Wednesday, August 24, 2022, and a videocast will be available for live viewing and archived.