



## Transgenic and Chimeric Neuroscience Research: Exploring the Scientific Opportunities Afforded by New Nonhuman Primate Models—A Workshop

October 4, 2018

Keck Center of the National Academies  
500 Fifth Street, NW | Washington, DC

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### Background:

The translational disconnect from preclinical studies with predominantly rodent animal models to human clinical trials remains a key challenge associated with lagging development of therapies for brain disorders. Since 2012, the Forum has hosted a series of workshops examining different aspects of this challenge, including maximizing the translation of effective therapies from animal models to clinical practice and exploring the evidence needed to bring compounds that appear to be safe into human efficacy trials. While no animal model will fully recapitulate human nervous system disorders, nonhuman primates—such as marmosets and macaques—have shown promise in their ability to serve as models for complex brain disorders, given the phylogenetic proximity and genetic similarity to humans, similarity of neuroanatomical organization (e.g., a well-developed prefrontal cortex) and associated cognitive and behavioral functions, social cognition, and the ability to study developmental phenotypes and prodromal disease states.

### Workshop Objectives:

This one-day public workshop will bring together experts and key stakeholders from academia, government, industry, and non-profit organizations to examine the scientific opportunities and challenges, as well as bioethical considerations, of genetically engineered nonhuman primate models for neuroscience research.

Invited presentations and discussions will be designed to:

- Discuss the state of the science of transgenic and chimeric neuroscience research and emerging models for nervous system disorders, and explore the potential usefulness of such models to enhance understanding of behavior and higher cortical function, and advance therapeutic development.
- Examine current tools and technologies used in rodent models (e.g., transgenesis, chimera, AAVs [adeno-associated viruses], gene therapy, etc.) and explore how they would need to be modified for use in other animal models, such as nonhuman primates.
- Consider bioethical principles and issues related to genetic engineering of animal models for nervous system disorders, and discuss potential metrics for determining the models' readiness for nonhuman primate research.
- Discuss policies and infrastructure needed to advance research in this domain including, for example, training, recruitment of early career scientists, and the potential development of specialized research centers and international collaborations.

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8:30 a.m.      Welcome and Overview of Workshop  
FRANCES JENSEN, University of Pennsylvania, Perelman School of Medicine (Chair)

**Session I: Emerging Transgenic and Chimeric Nonhuman Primate Models for Neuroscience Research and Therapeutic Development for Nervous System Disorders**

Objective:

- Discuss the state of the science of transgenic and chimeric nonhuman primate models for nervous system disorders, and explore the potential usefulness of such models to enhance understanding of behavior and higher cortical function, and in translational science to advance therapeutic development.

8:45 a.m.      Session Overview  
                     SARAH CADDICK, Thalamic (Moderator)

8:55 a.m.      Speakers  
                     GUOPING FENG, Massachusetts Institute of Technology  
                     HIDEYUKI OKANO, Keio University School of Medicine; RIKEN Brain  
                             Science Institute  
                     YOLAND SMITH, Yerkes National Primate Research Center; Emory University  
                     ANGELA ROBERTS, University of Cambridge

9:55 a.m.      Discussion  
                     Discussant:     WILLIAM NEWSOME, Stanford University

10:30 a.m.     BREAK

**Session II: Technology, Research Methodology, and Assessment Tools For Transgenic and Chimeric Nonhuman Primate Models**

Objectives:

- Examine how current tools and technologies developed in rodent models (e.g., transgenesis, chimera, AAVs [adeno-associated viruses], gene therapy, in vitro fertilization, etc.) through the BRAIN Initiative and elsewhere, and might be modified for use in nonhuman primates.
- Consider potential logistical and feasibility issues unique to nonhuman primate models (e.g., cost).

10:45 a.m.     Session Overview  
                     ROBERT WURTZ, National Eye Institute, Scientist Emeritus (Moderator)

11:00 a.m.     Speakers  
                     MU-MING POO, Chinese Academy of Sciences  
                     BEN DEVERMAN, Broad Institute of MIT and Harvard University  
                     JEAN BENNETT, University of Pennsylvania  
                     KAREN PARKER, Stanford University

12:00 p.m.     Discussion

- Why and how do you make that leap from rodents to NHPs technically?
- What are the logistical and feasibility issues in using genetic and chimeric technologies in NHP models for neuroscience research (e.g., cost)?
- What tools and technologies are currently being used or needed to create these models?
- What measures and assessment tools are needed (i.e., behavioral assessments)?

                    Discussants:     DAVID AMARAL, University of California, Davis  
                                     ROBERT DESIMONE, Massachusetts Institute of Technology

12:30 p.m.     LUNCH



- 3:25 p.m.      Keynote  
                   MU-MING POO, Chinese Academy of Sciences
- 3:40 p.m.      Panel Discussion  
                   JOHN MORRISON, California National Primate Research Center, University of California,  
                   Davis  
                   HIDEYUKI OKANO, Keio University School of Medicine; RIKEN Brain Science Institute  
                   JOSHUA GORDON, National Institute of Mental Health  
                   MARK FRASIER, Michael J. Fox Foundation for Parkinson’s Research  
                   JOHN SPIRO, Simons Foundation Autism Research Initiative  
                   LISA STANEK, Sanofi
- 4:25 p.m.      Discussion
- 5:15 p.m.      Closing Remarks  
                   STEVEN HYMAN, Broad Institute of MIT and Harvard University
- 5:30 p.m.      Adjourn Workshop

#### **Workshop Planning Committee**

**Frances Jensen (Chair)**, University of Pennsylvania, Perelman School of Medicine  
**Susan Amara**, National Institute of Mental Health  
**Sarah Caddick**, THALAMIC  
**Marina Emborg**, Wisconsin National Primate Research Center, University of Wisconsin–Madison  
**Guoping Feng**, Massachusetts Institute of Technology  
**Joshua Gordon**, National Institute of Mental Health  
**Hank Greely**, Stanford University  
**Jeffrey Kahn**, Johns Hopkins University  
**Walter Koroshetz**, National Institute of Neurological Disorders and Stroke  
**John Morrison**, California National Primate Research Center, University of California, Davis  
**William Newsome**, Stanford University  
**Karen Parker**, Stanford University  
**Michael Steinmetz**, National Eye Institute  
**Andrew Welchman**, Wellcome Trust  
**Stevin Zorn**, MindImmune Therapeutics, Inc.