



Forum on Neuroscience and Nervous System Disorders



2017 Annual Report





MESSAGE FROM THE CHAIRS

Steven Hyman and Story Landis

Developing therapies for nervous system disorders—such as Alzheimer's and Parkinson's diseases, schizophrenia, depression, and addictive disorders—remains one of the most important, but challenging frontiers in the quest to improve human health. Despite a critical need for better therapies to address these highly prevalent causes of deep suffering, disability, and significant societal and economic costs, the discovery and development of new treatments have lagged behind other therapeutic areas. The many contributing factors include the complexity and inaccessibility of the human brain, the difficulty of effectively modeling brain disorders in animals, a lack of biomarkers to monitor disease progression and assess intervention efficacy, and the long clinical trials needed to study neurodegenerative disorders.

In the face of these challenges, the research community is at work to develop new technologies and model systems to improve our understanding of the healthy brain and disease mechanisms, and to translate these findings into effective therapies. In addition to continued work on more traditional small molecule drug approaches, individuals and organizations are increasingly working on a host of newer therapeutic strategies, including biologics for the brain, gene therapies, genome engineering, and implantable and noninvasive devices. Efforts are also under way to harness emerging technologies and analytical methods, such as artificial intelligence and machine learning focused on “big data.”

The National Academies of Sciences, Engineering, and Medicine's Forum on Neuroscience and Nervous System Disorders provides an important venue for candid discussions about emerging and critical issues among key stakeholders, including federal agencies that serve as research sponsors and regulators; the private sector; the academic community; and the nonprofit sector, including foundations and disease advocacy groups. The Forum's activities serve to inspire

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new ideas and shape the field, foster relationships and collaboration, develop an improved understanding of each other's perspectives and priorities, and influence policies and programs.

In 2017, the Forum tackled three key topics: identifying and validating biomarkers of neuroinflammation, which is increasingly understood to have an important role in many different brain disorders; improving methods of traversing the blood–brain barrier, which would greatly expand the armamentarium of potential drugs; and building public–private partnerships to advance the development of non-addictive pain medications and therapies for opioid use disorders, which would play an important role in addressing the current opioid crisis.

Looking ahead to 2018, the Forum will address another set of important topics. In March, we will gather to learn about the planning process for the second stage of the BRAIN Initiative and continue to discuss therapeutic development for pain and opioid use disorders. The Forum will also invite members of the legal community, including federal and state judges, to join its members and other scientists in exploring how emerging neurotechnologies will impact the legal system. In June, the Forum will bring interested individuals together to discuss the tremendous promise—and challenges—associated with using mobile technology devices to predict, diagnose, monitor, and develop treatments for brain disorders. And, in the fall, the Forum will turn to transgenic and chimeric neuroscience research, exploring how just-emerging nonhuman primate models may open the door to many scientific and therapeutic opportunities, while also examining the fundamental ethical considerations involved in such research.

We look forward to another engaging and productive year for the Forum.

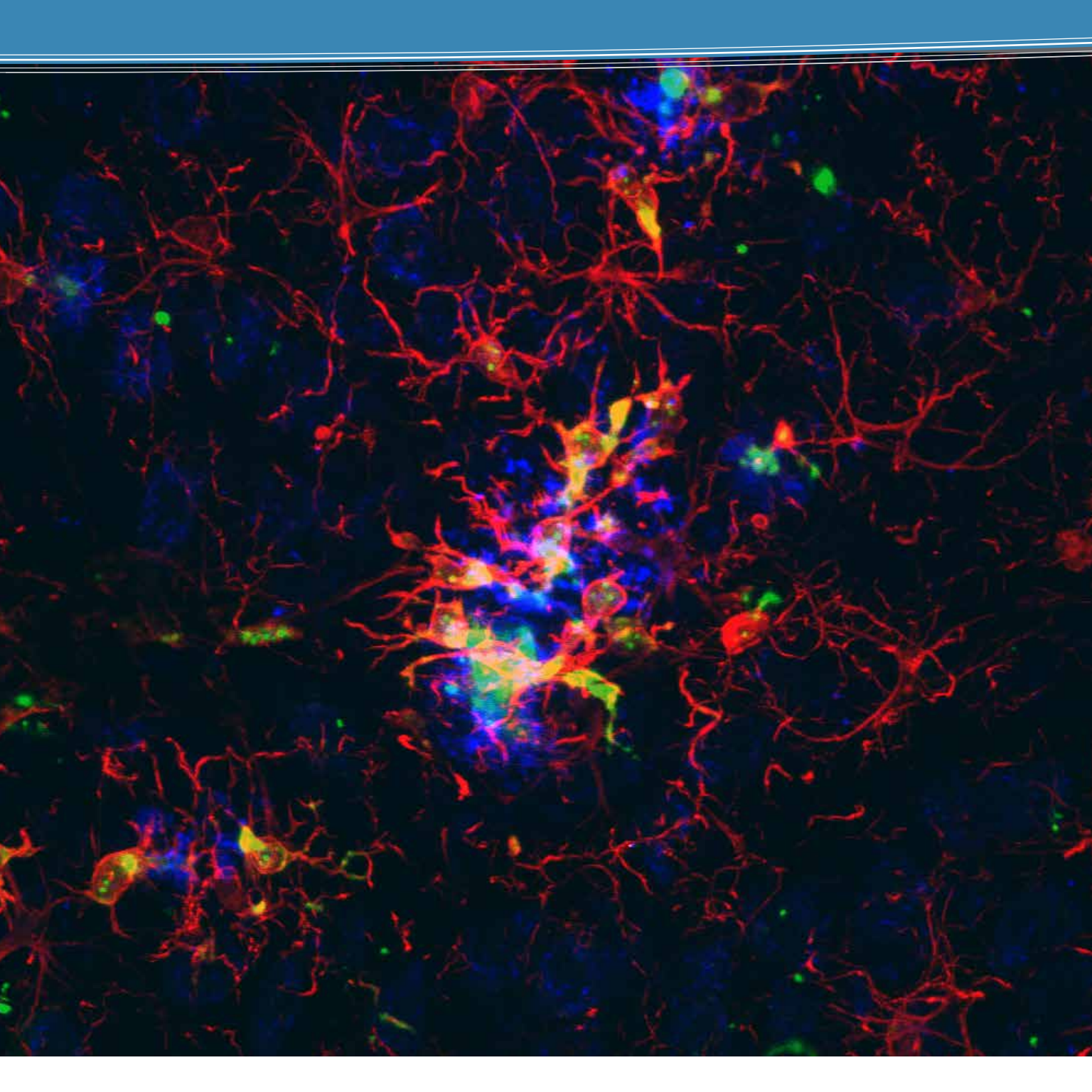
Steven Hyman and Story Landis
Chair and Vice-Chair



Steven Hyman
Chair



Story Landis
Vice-Chair



Reflecting Back: Forum Activities in 2017

Biomarkers of Neuroinflammation

Innate and adaptive immunity have become very important areas of investigation for psychiatric, neurological, and neurodevelopmental disorders, and neurodegeneration resulting from traumatic brain injury. To address gaps in our understanding of mechanisms and how to translate understanding into therapeutics, the Forum convened a workshop bringing together leaders in the field from industry, academia, and governmental agencies to explore the role and mechanisms of neuroinflammation in a variety of central nervous system (CNS) diseases. The workshop also considered strategies to advance the identification and validation of biomarkers of neuroinflammation that could accelerate the development of therapies, bringing much-needed treatments to patients with disorders ranging from neuroinflammatory diseases such as multiple sclerosis to neuropsychiatric disorders such as depression.

Enabling Novel Treatments for Nervous System Disorders by Improving Methods for Traversing the Blood-Brain Barrier

The blood-brain barrier (BBB) presents a special challenge to the development of therapeutics for many CNS disorders. Far from acting simply as a physical barrier, the BBB is a complex dynamic system involving several cell types, passive and active transport mechanisms, and adaptive function to control the exchange of substances between the blood and the CNS. Few therapeutic agents, including most small molecule drugs and the vast majority of large molecules such as proteins, readily traverse the BBB to reach the brain or spinal cord. Several



Left: Micrograph of inflammation-related protein expression in plaque-associated myeloid cells. Image courtesy of Dr. Gary Landreth, Case Western University.

Success in these endeavors would greatly increase the armamentarium of potential drugs for treating psychiatric and neurological disorders.

research groups are exploiting intrinsic BBB transport mechanisms using molecular Trojan horses and exploring technologies, such as chemical modifications and physical disruption, to improve the delivery of therapeutics to the CNS. Success in these endeavors would greatly increase the armamentarium of potential drugs for treating psychiatric and neurological disorders. The Forum hosted a public workshop including key experts from academia, government, the biotechnology and pharmaceutical sector, disease-focused organizations, and other interested stakeholders to explore the current development of novel methods for traversing the BBB to deliver therapeutics for nervous system disorders and to identify potential opportunities for moving the field forward.

Advancing Therapeutic Development for Pain and Opioid Use Disorders Through Public–Private Partnerships

Pain is a leading cause of disability in the United States, affecting more people than cancer, diabetes, and heart disease combined. Many physicians have come to prescribe opioids to their pain patients and pain patients have come to expect such prescriptions. The resulting dramatic increase in opioid prescriptions within the last decade has been a major factor in the opioid epidemic the country currently faces, with alarming rates of misuse, abuse, and overdose deaths. To help address this epidemic, Dr. Francis Collins, Director of the National Institutes of Health (NIH), hosted three small meetings in June and July 2017 focused on creating public–private partnerships to address the urgent public health need associated with opioids and the treatment of chronic pain. NIH joined with private partners in the pharmaceutical industry and the research community to explore a research initiative to cut in half the amount of time required to develop new therapies for (1) safe, more effective strategies for pain management; (2) new and innovative opioid addiction treatments; and (3) overdose reversal interventions. The Forum hosted a public workshop that brought together key stakeholders to advance the discussions that emerged from the three NIH meetings to examine the research opportunities to be addressed as well as the potential barriers to implementation.



Looking Forward: Forum Activities in 2018

**Emerging neurotechnologies
promise increased
access to evidence
obtained from the
central nervous system.**

Neuroforensics: Exploring the Legal Implications of Emerging Neurotechnologies

Current developments in genome sequencing, neuroimaging, noninvasive neurophysiology, and other methods—together with rapid progress in computational and statistical methods and data storage—have facilitated the large-scale collection of human genomic, cognitive, behavioral, and brain-based data, with the potential to enable unprecedented insight into human cognition and behavior. The rapid development of neurotechnologies and associated databases has been mirrored by an increase in efforts to use neuroscience and behavioral genetic evidence in legal proceedings. Compared to earlier technologies such as the polygraph, emerging neurotechnologies promise increased access to evidence obtained from the CNS, and thus to brain function associated with complex behaviors and cognitive characteristics. To begin to explore the potential impact of emerging neurotechnologies on the legal system, the Forum, in collaboration with the National Academies' Committee on Science, Technology, and Law, will host a public workshop, bringing together leaders from academia, judicial and law enforcement systems, industry, government and regulatory agencies, nonprofit foundations and other stakeholders to advance efforts to identify and evaluate the potential positive and negative effects of emerging neurotechnologies on the legal system.

Harnessing Mobile Technology to Predict, Diagnose, Monitor, and Develop Treatments for Nervous System Disorders

Despite the prevalence of CNS disorders worldwide, there is limited understanding of the natural history of diseases, patients' own experiences of the illness, the manifestation of its symptoms, and responses to treatment. Assessment of function for many disorders—including Parkinson's disease, Alzheimer's disease, mood disorders, and schizophrenia—typically is based on subjective or self-report tests during clinical visits. These provide only snapshots in time and patients may use extra effort in a doctor's office, which obscures usual function. The miniaturization and proliferation of devices and mobile technologies have led to an explosion of interest in developing tools that provide reliable, high-quality, continuous data collection from large populations of patients in their natural settings and activities. The use of devices to advance research and treatment for CNS disorders holds tremendous promise; for example, enabling the identification of prodromal and subclinical states, but also raises important technological, methodological, ethical, privacy, security, and regulatory issues. The Forum will host a workshop to help advance the appropriate use of devices and mobile technology to predict, diagnose, monitor, assess adherence, and develop treatments for CNS disorders.

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

The translational disconnect from preclinical studies with predominantly rodent animal models to human clinical trials remains a key challenge associated with the 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. The Forum will host a public workshop bringing together experts and key stakeholders to explore the scientific opportunities afforded by new nonhuman primate models, as well as the important bioethical considerations involved in conducting neuroscience research in this domain.

Working Groups

The Forum has working groups to provide additional opportunities to address selected topics. Workshop topics may emerge from these efforts; any such workshops are then organized by an independently appointed workshop planning committee.

Clinical Research Data Sharing

The Forum is participating in a clinical research data sharing activity that is a collaboration across four National Academies forums that focus on neuroscience; drug discovery, development, and translation; genomics; and cancer. Building on the 2015 report published by the Institute of Medicine, *Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk*, the group's goals are to improve coordination and collaboration among stakeholders engaged in activities related to data sharing and to support implementation efforts by creating a mechanism for collaborative participants to identify priority issues and organize activities. A working group of this overall activity is currently convening nonprofit funders of clinical trials to develop data-sharing principles that could be brought to organizations' research boards and incorporated into funding policies.

Neuroscience Training and Workforce

Building on discussions from the 2014 Forum workshop Developing a 21st Century Neuroscience Workforce, the Forum established a working group to continue to examine the current challenges and gaps in neuroscience training and identify opportunities to strengthen training programs so that they are tailored to meet the current and future workforce needs. Following the workshop, members of the working group have continued to foster discussions in this area through their participation on scientific panels, webinars, and online discussions, and by authoring a perspective in *Neuron* titled "Neuroscience Training for the 21st Century."

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Mental, Neurological, and Substance Use Disorders in Sub-Saharan Africa

The Forum has a longstanding interest in identifying innovative solutions to enhance care for mental, neurological, and substance use disorders in sub-Saharan Africa. Since 2009, the Forum has hosted five workshops in Ethiopia, Ghana, Kenya, and Uganda to examine both general and country-specific barriers and potential innovative solutions, with particular focus on increasing human and financial resources to support current and future efforts. Using tools set forth by the World Health Organization, the Forum, in collaboration with global entities, is continuing to explore additional opportunities to contribute in this area, with a focus on maternal and child mental and neurological health.

2017 Publications

International Perspectives on Integrating Ethical, Legal, and Social Considerations into the Development of Non-Invasive Neuromodulation Devices: Proceedings of a Workshop—in Brief

Therapeutic Development in the Absence of Predictive Animal Models of Nervous System Disorders: Proceedings of a Workshop

Biomarkers of Neuroinflammation: Proceedings of a Workshop

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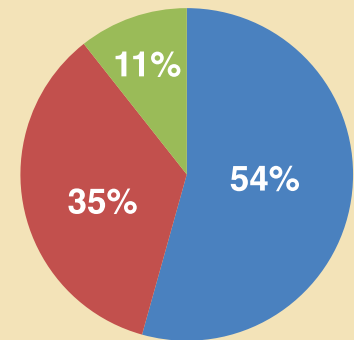
(as of December 2017)

SPONSORS

(as of December 2017)

Financial support for the Forum is derived from federal agencies, nonprofit disease-focused organizations, societies, and foundations.

Alzheimer's Association
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Cohen Veterans Bioscience
Department of Veterans Affairs
Eli Lilly and Company
Food and Drug Administration
Foundation for the National Institutes of Health
Gatsby Charitable Foundation
George & Anne Ryan Institute for Neuroscience
at the University of Rhode Island
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National Institute on Drug Abuse
National Institutes of Health Blueprint for Neuroscience Research
National Multiple Sclerosis Society
National Science Foundation
One Mind
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Society for Neuroscience
Takeda Pharmaceuticals International, Inc.



■ Industry
■ Federal
■ Nonprofit

TIMELINE

2006 | Establishment | 1st meeting

2007 | Biomarkers Workshop | 2nd meeting |
Autism and Environment Workshop | 3rd meeting | 4th meeting

2008 | 5th meeting | 6th meeting | Molecules to Mind:
Grand Challenges Workshop | Venture Philanthropy Strategies
Workshop | 7th meeting

2009 | 8th meeting | Suicidality Workshop | 9th meeting |
Uganda Workshop | SFN: Social Issues Roundtable |
10th meeting | Animal Law Workshop

2010 | Sex Differences Workshop | Glutamate Workshop |
11th meeting | ICAD 2010 Session | 12th meeting

2011 | 13th meeting | Neuroscience and the Law Workshop |
AAIC 2011 Session | Animal Regulations Workshop |
14th meeting | 15th meeting

2012 | 16th meeting | Animal Models Workshop |
Neurodegeneration Workshop | 17th meeting | SSA Human
Resources Workshop | Sharing Clinical Research Data
Workshop | 18th meeting

2013 | 19th meeting | Accelerating Therapeutic Development
Workshop | Meeting on Developing dMRI Standards |
20th meeting

2014 | SSA Essential Medicines Workshop | 21st meeting |
22nd meeting | 23rd meeting | Dry AMD Workshop |
SFN: Neuroscience of Gaming Session

2015 | Providing Sustainable Access to Mental Health Care:
Kenya Workshop | Financial Incentives Workshop | Cognitive
Dysfunction in Depression Workshop | Non-Invasive
Neuromodulation Workshop | Providing Sustainable Access to
Mental Health Care: Ghana Workshop | 24th meeting | Assessing
the Impact of Applications of Digital Health Records on
Alzheimer's Disease Research Session | 25th meeting

2016 | 26th meeting | Neuroscience Trials of the Future
Workshop | 27th meeting and Multimodal Therapies Workshop |
28th meeting and Development in Absence of Predictive
Animal Models Workshop | OECD Workshop

2017 | 29th meeting | Biomarkers of Neuroinflammation
Workshop | Blood–Brain Barrier Workshop | 30th meeting |
Advancing Therapeutic Development for Pain and Opioid
Use Disorder Workshop

2018 | 31st meeting | Neuroforensics Workshop | 32nd meeting |
Mobile Technology Workshop | 33rd meeting | Transgenic
Neuroscience Research Workshop

Making A Difference

The National Academies' Work in Health and Medicine

For millions of people across the United States and around the globe, improving health is a matter of daily survival and well-being.

Our consensus studies offer straightforward answers to critical questions in health and health care; our convening activities bring together stakeholders from across the health spectrum, creating a communal environment to explore complex health topics and work toward shared understanding. Below are some of the ways our work impacts the nation and world.

Influence Policies and Programs

Our work can inform policy and legislation; programmatic planning, direction, and budgets; educational initiatives, such as curricula and training programs; and other activities.

Foster Relationships and Collaboration

By bringing together a diverse group of participants around a particular topic, our activities foster new professional relationships, facilitate cross-sector collaborations, and enable professional development and networking, including the cultivation of new leaders.

Inspire New Ideas and Shape the Field

Our work can advance and shape the field by framing issues and shining a light on important topics, and by generating novel approaches to overcome existing challenges, spurring progress and inspiring action.



ABOUT THE NEUROSCIENCE FORUM

The Forum on Neuroscience and Nervous System Disorders at the National Academies of Sciences, Engineering, and Medicine was established in 2006 to bring together leaders from government, industry, academia, disease advocacy organizations, and other interested stakeholders. The Forum meets several times per year and provides its members with a neutral venue for exchanging information, ideas, and perspectives. At its meetings, the Forum examines significant—and sometimes contentious—issues concerning scientific needs and opportunities, priority setting, and policies related to neuroscience and nervous system disorders research; the development, regulation, and use of interventions for the nervous system; and related ethical, legal, and social implications. The Forum sponsors workshops (symposia), workshop proceedings, and commissioned papers as additional mechanisms for informing its membership, other stakeholders, and the public about emerging issues and matters deserving scrutiny. Information about past and upcoming meetings is available at the Forum's website, www.nas.edu/neuroforum.

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ABOUT THE NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE

The **National Academy of Sciences** was established in 1863 by an Act of Congress, signed by President Lincoln, as a private, nongovernmental institution to advise the nation on issues related to science and technology. Members are elected by their peers for outstanding contributions to research. Dr. Marcia McNutt is president.

The **National Academy of Engineering** was established in 1964 under the charter of the National Academy of Sciences to bring the practices of engineering to advising the nation. Members are elected by their peers for extraordinary contributions to engineering. Dr. C. D. Mote, Jr., is president.

The **National Academy of Medicine** (formerly the Institute of Medicine) was established in 1970 under the charter of the National Academy of Sciences to advise the nation on medical and health issues. Members are elected by their peers for distinguished contributions to medicine and health. Dr. Victor J. Dzau is president.

The three Academies work together as the **National Academies of Sciences, Engineering, and Medicine** to provide independent, objective analysis and advice to the nation and conduct other activities to solve complex problems and inform public policy decisions. The National Academies also encourage education and research, recognize outstanding contributions to knowledge, and increase public understanding in matters of science, engineering, and medicine.

Learn more about the National Academies of Sciences, Engineering, and Medicine at www.nationalacademies.org.

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The nation turns to the National Academies of Sciences, Engineering, and Medicine for independent, objective advice on issues that affect people's lives worldwide.

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