DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

NATIONAL ADVISORY COUNCIL FOR BIOMEDICAL IMAGING AND BIOENGINEERING

Summary of Meeting[1]
January 21, 2016

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was convened for its 40th meeting on January 21, 2016, at the Bolger Center in Potomac, Maryland. Dr. Roderic I. Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), presided as Council chairperson. In accordance with Public Law 92-463, the meeting was open to the public from 9:00 a.m. to 12:45 p.m. for review and discussion of program development, needs, and policy. The meeting was closed to the public from 1:45 p.m. to 3:20 p.m. for the consideration of grant applications.

Council members present:

Dr. Kristi Anseth, University of Colorado, Boulder, Boulder, CO
Dr. Carol Espy-Wilson, University of Maryland, College Park, MD
Dr. Karen Hirschi, Yale University, New Haven, CT
Dr. Raphael Lee, University of Chicago, Chicago, IL
Dr. John H. Linehan, Northwestern University, Evanston, IL
Dr. Carolyn Meltzer, Emory University Hospital, Atlanta, GA
Dr. Charles Mistretta, University of Wisconsin, Madison, Madison, WI
Dr. A. Gregory Sorensen, Imris Deerfield Imaging USA, Minnetonka, MN
Dr. Daniel Sullivan, Duke University Medical Center, Durham, NC
Dr. James Thrall, Massachusetts General Hospital, Harvard Medical School, Boston, MA
Dr. Bruce Tromberg, University of California, Irvine, CA
Dr. Sheldon Weinbaum, The City College of New York, New York, NY

Ex officio members present:
Dr. P. Hunter Peckham, U.S. Department of Veterans Affairs, Cleveland, OH
Dr. Anne Plant, National Institute of Standards and Technology, Gaithersburg, MD

Ex officio members attending by telephone:
Dr. Sohi Rastegar, National Science Foundation, Arlington, VA

Ex officio members absent:
Ms. Sylvia Burwell, U.S. Department of Health and Human Services, Washington, DC
Dr. Francis Collins, National Institutes of Health, Bethesda, MD

Chairperson:
Dr. Roderic I. Pettigrew

[1] For the record, it is noted that members absent themselves from the meeting when the Council is discussing applications (a) from their respective institutions or (b) in which a conflict of interest may occur. This procedure only applies to applications that are discussed individually, not to "en bloc" actions.

Executive Secretary:
Dr. David T. George

Also present:
NIBIB staff present for portions of the meeting:
Mr. Carlos Arana
Ms. Holly Atherton
Mr. Angelos Bacas
Dr. Richard Baird
Ms. Barbara Cantilena
Mr. Christian Cartagena
Dr. Michael Cheetham
Dr. Richard Conroy
Ms. Christine Cooper
Ms. Zoe Ann Copeland
Mr. Anuraj Dandgaval
Ms. Monique Day
Dr. Michael Delarco
Ms. Angela Eldridge
Dr. Zeynep Erim
Ms. Shirley Finney
Mr. Anthony Fransella
Ms. Pam Glikman
Dr. John Hayes
Ms. Eunica Haynes
Dr. Jill Heemskerk
Dr. Dennis Hlasta
Ms. Alisha Hopkins
Dr. Rosemarie Hunziker
Mr. Tom Izzard
Ms. Heather Kalish
Dr. Krishnan Kandarpa
Dr. Chris Kelley
Ms. Margot Kern
Dr. Peter Kirschner
Dr. Steven Krosnick
Ms. Kai Lakeman
Dr. Tiffani Bailey Lash
Dr. Richard Leapman
Dr. Guoying Liu
Mr. Raymond MacDougall
Dr. Shadi Mamaghani
Mr. Rishi Mathura
Ms. Jessica Meade
Mr. Todd Merchak
Mr. Joe Mosimann
Dr. Vinai Pai
Dr. Grace Peng
Ms. Ruthann Rand
Dr. Edward Ramos
Dr. Mary Rodgers
Dr. Antonio Sastre
Dr. Seila Selimovic
Dr. Behrouz Shabestari
Mr. Shaun Sims
Dr. Manana Sukhareva
Ms. Florence Turska
Mr. Kwesi Wright
Dr. Ruixia Zhou
Dr. Steven Zullo

Non-NIBIB National Institutes of Health (NIH) employees:
Dr. Sara Ahlgren, CSR, NIH
Dr. Lawrence Boerboom, CSR, NIH
Dr. Douglas Lowy, NCI, NIH

Members of the public present for portions of the meeting:
Mr. Milton Berrios, Bolger Center, Potomac, MD
Ms. Renee Cruea, Academy of Radiology Research, Washington, DC
Ms. Erin Cadwalader, Lewis-Burke Associates, Washington, DC
Dr. Ralph Weissleder, Massachusetts General Hospital, Boston, MA

I. Call to Order: Dr. David T. George

Dr. David T. George called to order the 40th meeting of the National Advisory Council for Biomedical Imaging and Bioengineering. Dr. George reminded Council members of the importance of confidentiality and avoidance of conflict of interest during Closed Session deliberations, and of restrictions regarding lobbying. Council voted unanimously to approve the NACBIB Operating Procedures and prior Council minutes.

II. Director's Remarks: Dr. Roderic I. Pettigrew

A. Council Member Transitions

Dr. Pettigrew expressed his appreciation and acknowledged the departure from the Council of Dr. James G. Smirniotopoulos, who has retired from Uniformed Services University of the Health Sciences, Bethesda, Maryland.

He introduced three new council members: Drs. John H. Linehan, Carolyn Melzer, and Charles Mistretta.

John H. Linehan, Ph.D., is a professor at Northwestern University and a consulting professor at Stanford University's Biodesign and Entrepreneurship Program. He is an educator, administrator and thought leader with expertise in pulmonary mechanics and physiology. He is a past president of the American Institute for Medical and Biological Engineering and a member of the National Academy of Engineering. He was former Vice President at the Whittaker Foundation, which was critical to the establishment and growth of the biomedical engineering field.

Carolyn Meltzer, M.D., is an endowed Chair of Radiology at Emory University School of Medicine and serves as Associate Dean of Research. She is board certified in diagnostic radiology and nuclear medicine. She is active in the imaging community, serving on a number of boards of major organizations, including the Radiological Society of North America, and as president of the Academy of Radiology Research.

Charles Mistretta, Ph.D., is an endowed professor of medical physics at the University of Wisconsin. He developed digital subtraction angiography (DSA), which has improved the lives of millions around the world. In addition to his well-recognized scientific accomplishments, for which he has received major awards, Dr. Mistretta is also known for preparing the next generation of students and investigators—many dozens of his trainees are now prominent members of the field. He is a member of the National Academy of Engineering.

B. NIBIB Transitions

Dr. Pettigrew announced recent staff departures, including Dr. William Heetderks, who transitioned to the FDA as the Clinical Deputy Director in the Division of Neurological and Physical Medicine Devices. Mr. Jeff Domanski, Executive Officer, transitioned to an expanded role at the FDA.

Four new staff members have joined NIBIB: **Krishna Kandarpa, M.D., Ph.D.,** Director of Research Sciences and Strategic Directions, Office of the Director, **Michael Cheetham**, Senior Advisor, Office of the Director, **Michael Dellarco, Dr.P.H.,** Program Director, Division of Discovery Science & Technology, and **Seila Selimovic, Ph.D.,** Health Science Policy Analyst, Division of Health Informatics Technologies.

C. NIH Budget and Legislation

Members of Congress have visited NIH in recent months. Most recently, members of the GOP Doctor's Caucus came to campus, at which time Dr. Pettigrew delivered a presentation on federally funded research supported by NIBIB. The FY16 budget includes a $2 billion increase to NIH, with a 5% increase for NIBIB.

D. NIH Initiatives

Precision Medicine Initiative (PMI): Upcoming receipt dates were noted for a Biobank, a Coordinating Center, a Healthcare Provider Organization Enrollment Center, and a Participant Technologies Center.

The Interagency Working Group on Medical Imaging met at NIH in November to discuss emerging themes including quantitative imaging and measurement goals. The group included the Academy of Radiology Research, the Radiological Society of North America, the International Society for Strategic Studies in Radiology, and the American College of Radiology.

The NIH Strategic Plan was published in December 2015. The plan includes a list of 'bold predictions', some of which speak to the biomedical engineering community: application of mobile health technologies, a wearable sensor to monitor blood alcohol levels, technologies to reverse paralysis and restore some normal function, and a closed-loop approach to addressing diabetes with development of an artificial pancreas.

E. NIBIB Key Activities

DEBUT Challenge: NIBIB will partner with Venture Well in awarding prizes in NIBIB's ongoing Design by Biomedical Undergraduate Teams (DEBUT) Challenge to bioengineering students.

Quantum Grants: Three new grants were awarded following NACBIB concurrence at its previous session: 1) Point-of-care Microfluidics for Early Detection of Cancer, Dr. Mehmet Toner, Harvard University. 2) Building an Implantable Artificial Kidney, Dr. Shuvo Roy, University of California, San Francisco. 3) One-Stop Shop Imaging for Acute Ischemic Stroke Treatment, Dr. Guang-Hong Chen, University of Wisconsin.

Meyerhoff Scholars Program. The program at the University of Maryland, Baltimore County trains members of underrepresented groups in STEM fields. Meyerhoff scholars are five times more likely to pursue a PhD or MD/PhD than similar students attending other universities. NIBIB has provided support for students and recently hosted their visit to NIBIB intramural labs.

100 Year Starship Project. Former NIBIB Council Member Dr. Mae Jemison leads this joint DARPA-NASA project to plan interstellar travel in 100 years. Dr. Pettigrew participated in a two-day 100 Year Starship Crucible meeting at the Institute for Space Research, Graz, Austria. The focus of the meeting was virtual modeling for wellbeing of the human body during long-term space travel.

F. Science Highlights

Functional connectome. NIBIB-funded researchers at Yale have accomplished functional connectome fingerprinting to identify individuals using patterns of brain connectivity as published in the October 12, 2015 issue of Nature Neuroscience.

Future of micro-robotics. NIBIB-funded researchers at UC-San Diego developed a novel way to potentially deliver therapeutics precisely-- micro-robotic fish manufactured from hydrogels with three types of functionality: chemical reactions in the tail propel the fish, iron particles in the nose permit the fish to be magnetically directed, and nanoparticles could carry therapeutics to the target.

III. Task Force Implementation

A. Trailblazer FOA Proposal: Dr. Antonio Sastre

Dr. Antonio Sastre spoke about staff efforts to implement recommendations of the NACBIB Task Force charged with maximizing the effectiveness of NIBIB funding. As background for a newly proposed R21 initiative, he described analysis showing that an NIBIB R21 award to new and early stage investigators nearly doubles their probability of earning a subsequent R01. Additionally, R21s are used by investigators in STEM fields as a way to break into NIH funding. NACBIB discussions at the previous meeting supported the R21 mechanism as a way to: 1) nurture early stage investigators, 2) attract researchers from STEM fields to NIH, and 3) encourage high-risk/high-reward research. He proposed a new NIBIB R21 initiative, entitled the Trailblazer R21. This would be a new funding opportunity announcement (FOA) specifically targeted to new and early stage investigators and strongly encouraging underrepresented groups to apply. Unlike regular R21 grants, which are limited to 2 years and $275,000 in funding, it would allow three years of funding and $400,000 direct costs over those three years. Preliminary data would not be required, which would attract new investigators with early stage, developmental ideas for projects, different from those typically awarded under R01s. At this time, the NIBIB would continue to participate on the NIH "parent" R21 and Exploratory/Developmental Bioengineering Research Grants (EBRG) R21 FOAs.

A second aspect of the plan is that overall funding for R21 grants would be held constant at a level consistent with recent R21 funding levels. Distributing available funds among the Trailblazer, the parent R21 and the EBRG applications would preserve and potentially enrich the number of new investigators in the funded R21 pool. Establishing an upper limit on the overall R21 budget would protect the R01 payline from the rapidly increasing number of R21 applications that has been observed in recent years.

Finally, as recommended by the Task Force, funding decisions on NIBIB R21s received through the NIH parent R21 and EBRG announcements will emphasize high risk/high reward projects, rather than those that have sufficient preliminary data to be competitive as aims in R01 applications.

Discussion

Council members expressed strong support for the plan. Questions arose on whether the Trailblazer FOA would be available to only new investigators or to an investigator working on a new concept. Dr. Sastre said that, although the Trailblazer would be reserved for those PIs who are NIH-defined as being new or early stage, established investigators working on a new concept would continue to be welcome to apply to the parent R21 or EBRG FOAs.

Another question was asked concerning how focusing on high risk/high reward science might impact the success rates for R21s and whether it would be possible to increase success rates. Dr. Sastre supposed that results would depend on the response of scientific community. He said that, thus far, there has been a

decrease in the success rate of early stage investigators. A goal of the new Trailblazer award program is to stabilize and maintain their success rate. Council members suggested that the Trailblazer award would focus attention on NIBIB goals and sharpen what NIBIB supports. There was a question on the impact of this plan on the total number of grants. Dr. Sastre said NIBIB modeled a number of scenarios and sustainable models, the details of which would be discussed at an upcoming NACBIB meeting. However, the goal is to maintain the number of grants at a level that is similar to current levels.

It was asked whether Trailblazers and regular R21s would be evaluated by the same panel. Dr. Sastre indicated that the NIBIB would work with the Center for Scientific Review to identify the best review method to accomplish the goals of the Trailblazer award.

Finally, the council suggested that the NIBIB should seek continuous feedback and plan a quantitative evaluation of the new program.

B. NIBIB Partnerships: Dr. Kris Kandarapa

Dr. Kris Kandarpa reported on the NIBIB objective of increasing the number of NIBIB partnerships and building on the many that already exist. His team will evaluate NIBIB programs in terms of their needs and capacity to absorb partnerships. In evaluating partners, they will consider the NIBIB mission, funding, reciprocal technical expertise and access they can provide to targeted communities.

Public-private partnership mechanisms include partnerships with industry and research consortia. The NIBIB has several existing trans-national partnerships, including intergovernmental and public-private partnerships. The office plans to improve outreach to potential partners, the NIBIB research community, advocacy groups, and to the general public in the United States.

Dr. Kandarpa presented a snapshot of existing and potential partnerships. There are active partnerships with NIH Institutes, for example through the BRAIN Initiative, and other US Government Agencies, such as the Interagency Working Group on Medical Imaging. In terms of public-private partnerships, NIBIB is working with the Gates Foundation and the IEEE on Point of Care, with RSNA on Image Share, and with Venture Well on the DEBUT Challenge. The NIBIB works with foreign governments, including with India on remote hypertension sensor research and with Mexico on glucose measurement.

He indicated that an immediate goal is to develop a small number of new partnerships to leverage NIBIB resources and improve NIBIB visibility.

Discussion:

Council expressed satisfaction with the NIBIB's rapid pursuit of partnerships, which was a high priority recommendation of the NACBIB Task Force.

IV. The President's Precision Medicine Initiative in Oncology (PMI-O): Dr. Douglas Lowy

Dr. Douglas Lowy described the current state of cancer research and the rationale for the President's Precision Medicine Initiative in Oncology (PMI-O). While overall mortality rates for cancer have declined in recent decades (attributed to prevention, screening and treatment), this is not the case for all cancers and too

many are still dying of cancer (about 600,000 Americans per year). PMI-O has an investment of $70 million for cancer research. PMI-O is focused on cancer treatments based on molecular mechanisms with the goals of targeting patients who stand to benefit and sparing side effects for those who would not.

Components of PMI-O include: 1) clinical therapy trial expansion, 2) improvements in predictive oncology targeting and immunotherapy, 3) laboratory models to understand cancer biology, and 4) a national cancer knowledge system/database. This knowledge system will include an NCI Genomic Data Commons to facilitate the identification of subtypes of cancers and targets. It will include interoperable interfaces and large-scale clinical data and allow for multiple data types.

Discussion

Discussion focused on the challenges of developing new treatments, including addressing tumor heterogeneity, the high morbidity and mortality of pancreatic cancer, overcoming tumor adaptability to drug therapy, and overcoming the need for multiple biopsies. Discussions of possible diagnostics and treatments included NIBIB-funded projects to analyze circulating tumor cells, the use of computational modeling, the changing of the mindset of cancer treatment from organ-based to genotype-based, collaborations with NIST on the development of standards and assays, and strong support for the value of combining imaging with cancer diagnostics and treatments, including surgery.

V. Developing Next Generation Molecular Diagnostics: Dr. Ralph Weissleder

Dr. Ralph Weissleder discussed the next generation of molecular diagnostics. Most current pathology analyses are based on tissues, but multiple core biopsies lead to complications. It would be advantageous to move from tissue to less invasive quantitative cell analysis where rapid, repeatable measurements may be made to assess treatment progress. For example, serial measurements could be done to compare protein and mRNA profiles for a more complete picture of what is happening in cells. In the future, patients could have their cancers diagnosed based on molecular characteristics rather than organ type, leading to more precise and effective treatment. Dr. Weissleder's laboratory has adapted a technology called surface plasmon resonance that, with high sensitivity, electronically profiles the molecular contents of cells. This technology has the potential to be used for less invasive and more precise diagnosis of cancer. He has also developed technology for bacterial detection/profiling using micro nuclear magnetic resonance spectroscopy. This technology has matured in the field of pathogen detection and analysis and is used commercially for detection of fungal infection. Dr. Weissleder suggested that there is a unique opportunity for NIBIB to address the big biomedical engineering challenges, including 1) next generation molecular diagnostics that inform costly treatments, 2) microbial profiling and rapid testing, 3) immunoengineering, 4) more precise drug delivery systems from precision medicine to precision wellness, and 5) convergence of expertise as an essential part of precision medicine.

Discussion

Council questions and discussion clarified the advantages of using whole blood samples and that only a limited amount of blood (only a finger prick) is required. It was pointed out that Dr. Weissleder's presentation showed a convergence where genomic and chemical parameters are a unifying theme. Commercialization strategies were mentioned and there were some discussion about improving the speed of the process and that methods remain in need of improvement for detecting mutations for pancreatic cancer.

Finally, Dr. Weissleder pointed out that, from the big picture view, there is an extraordinary opportunity in immunoengineering. Immunotherapies have shown remarkable response rates in some cancers, but are only effective in some patients. More work is required to build on these initial very promising results.

VI. Adjournment

The open session of the NACBIB meeting was adjourned at 12:45 p.m.

VII. Closed Session

Review of Council Procedures and Regulations: Dr. David T. George

The grant application review portion of the meeting was closed to the public in accordance with provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code, and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2). The closed session was adjourned at 3:20 p.m.

Certification:

We certify that to the best of our knowledge, the foregoing minutes are accurate and complete. [2]

David T. George, Ph.D.
Executive Secretary
National Advisory Council for Biomedical Imaging and Bioengineering
Acting Associate Director for Research Administration
National Institute for Biomedical Imaging and Bioengineering

Roderic I. Pettigrew, Ph.D., M.D.
Chairperson,
National Advisory Council for Biomedical Imaging and Bioengineering
Director
National Institute of Biomedical Imaging and Bioengineering

[2] These minutes will be approved formally by the Council at the next meeting on May 19, 2016,and corrections or notations will be stated in the minutes of that meeting.