

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

**NATIONAL ADVISORY COUNCIL FOR
BIOMEDICAL IMAGING AND BIOENGINEERING**

**Summary of Meeting¹
September 18, 2015**

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was convened for its 39th meeting on September 18, 2015, 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 8:30 a.m. to 2:20 p.m. for review and discussion of program development, needs, and policy. The meeting was closed to the public from 2:20 p.m. to 3:20 p.m. for the consideration of grant applications.

Council members present:

Dr. Karen Hirschi, Yale University, New Haven, CT
Dr. Cato T. Laurencin, University of Connecticut, Farmington, CT
Dr. Raphael Lee, University of Chicago, Chicago, IL
Dr. Mark Musen, Stanford University, Stanford, CA
Dr. A. Gregory Sorensen, Siemens Healthcare North America, Malvern, PA
Dr. Daniel Sullivan, Duke University Medical Center, Durham, NC
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. Sohi Rastegar, National Science Foundation, Arlington, VA

Council members attending by telephone:

Dr. Kristi Anseth, University of Colorado, Boulder, Boulder, CO
Dr. Carol Espy-Wilson, University of Maryland, College Park, MD
Dr. James Thrall, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Council members absent:

Dr. John C. Gore, Vanderbilt University Medical Center, Nashville, TN

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
Dr. P. Hunter Peckham, U.S. Department of Veterans Affairs, Cleveland, OH
Dr. Anne Plant, National Institute of Standards and Technology, Gaithersburg, MD
Dr. James G. Smirniotopoulos, Uniformed Services University of the Health Sciences, Bethesda, MD

Chairperson:

Dr. Roderic I. Pettigrew

Executive Secretary:

Dr. Jill Heemskerk

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 and (b) in which a conflict of interest may occur. This procedure only applies to applications that are discussed individually, not to "en bloc" actions.

Also present:

NIBIB staff present for portions of the meeting:

Ms. Holly Atherton	Dr. Richard Leapman
Dr. Richard Baird	Dr. Guoying Liu
Ms. Shirley Coney-Johnson	Dr. Raymond MacDougall
Dr. Richard Conroy	Dr. Shadi Mamaghani
Ms. Christine Cooper	Dr. Mark Martin
Ms. Zoe Ann Copeland	Ms. Jessica Meade
Mr. Jeff Domanski	Mr. Todd Merchak
Mr. Anthony Fransella	Mr. Joe Mosimann
Dr. David George	Dr. Vinay Pai
Ms. Pam Glikman	Dr. Grace Peng
Dr. John Hayes	Dr. Karen Peterson
Dr. William Heetderks	Dr. Edward Ramos
Dr. Dennis Hlasta	Ms. Ruthann Rand
Ms. Alisha Hopkins	Ms. Mew Rattanawatkul
Dr. Rosemarie Hunziker	Dr. Mary Rodgers
Dr. Thomas Johnson	Dr. Antonio Sastre
Ms. Shelley Jones-Johnson	Dr. Behrouz Shabestari
Dr. Chris Kelley	Mr. Shaun Sims
Ms. Margot Kern	Mr. Russell Songco
Dr. Steven Krosnick	Dr. Manana Sukhareva
Ms. Kai Lakeman	Ms. Li-Yin Xi
Dr. Tiffani Bailey Lash	Dr. Ruixia Zhou
Ms. Truc Le	Dr. Steven Zullo

Non-NIBIB National Institutes of Health (NIH) employees:

Dr. Peter Kozel, Center for Scientific Review, NIH
Dr. Tara Schwetz, Office of the Director, NIH
Dr. Lawrence Tabak, Principal Deputy Director, NIH

Members of the public present for portions of the meeting:

Mr. Milton Berrios, Bolger Center
Ms. Erin Cadwalader, Lewis-Burke Associates, Washington, DC
Ms. Anna Fernandez, Booz Allen Hamilton, Rockville, MD
Ms. Madelione Halpern, ICF, Fairfax, VA
Mr. Michael Kalutkiewicz, Academy of Radiology Research, Washington, DC
Dr. Krishna Kandarpa, Delcath Systems, Inc., New York, NY
Dr. Shayna Knazik, American Association of Physicists in Medicine, College Park, MD
Dr. John H. Linehan, Northwestern University, Evanston, IL
Dr. Richard Martin, American Association of Physicists in Medicine, College Park, MD
Dr. David Mooney, Harvard University, Cambridge, MA
Mr. Michael Peters, American College of Radiology, Washington, DC
Dr. Bruce Rosen, Massachusetts General Hospital, Charlestown, MA
Ms. Kathy Sedgwick, NOVA Research Company, Silver Spring, MD

I. Call to Order: Dr. Jill Heemskerk

Dr. Jill Heemskerk called to order the 39th meeting of the National Advisory Council for Biomedical Imaging and Bioengineering. She welcomed attendees, including Dr. John Linehan, whose official term on the Council will begin at the January 2016 Council meeting.

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

A. Welcome

Dr. Pettigrew welcomed guests to the meeting, including Dr. Krishna Kandarpa, past chair of Radiology at the University of Massachusetts Medical School and now Chief Scientific Officer and Executive Vice President for Delcath Systems, a medical devices company. He will soon join NIBIB as the Director of Research Sciences and Strategic Directions in the Office of the Director.

B. NIBIB Awards and Honors

Dr. Pettigrew congratulated Council member Dr. James Thrall who received the Gold Medal from the International Society for Strategic Studies in Radiology and the inaugural Visionary Leadership Award from the Society for Chairs of Academic Radiology.

NIBIB intramural investigator Dr. Hari Shroff has been invited by the National Academy of Sciences (NAS) to present the sixth annual Seymour Benzer Lecture in April 2016. The Lecture is part of the NAS Distinctive Voices public lecture series.

The Department of Health and Human Services (DHHS) Innovates Awards include the Annual DHHS IDEA Lab competition for innovative approaches to solving major problems. This year, the Neuroimaging Informatics Tools & Resources Clearinghouse (NITRC), part of the NIH Blueprint for Neuroscience program, received the "Biggest Bang for the Buck" award. NIBIB's Dr. Vinay Pai is project management leader for the NITRC, which produced estimated savings of \$35M in data collection and analysis. At the DHHS Demo Day, 11 teams presented innovative programs. Dr. Pai presented the Tool for Enhancing Agency Knowledge, a project aimed at quickly identifying and connecting subject matter experts and areas of common interest across the federal government.

C. New NIBIB Staff

Dr. Pettigrew introduced new NIBIB staff: Scientific Review Officer Dr. Mark Martin and Senior Grants Management Specialist Ruthann (Rudy) Rand.

D. Legislative Update and NIBIB Budget

The House passed the 21st Century Cures Bill, which would create a five-year Cures Innovation Fund, including \$1.75B for NIH and \$110M for the U.S. Food and Drug Administration (FDA) annually. The Bill requires FDA to streamline approval of drugs and devices. The Senate is considering similar legislation.

NIBIB's payline for fiscal year (FY) 2015 increased from the 10th to the 12th percentile, and the Expanded Opportunity Zone (EOZ) increased from the 20th to the 24th percentile. Fifteen EOZ applications are among those proposed at today's meeting for funding.

E. NIH Activities

Precision Medicine Initiative

Dr. Pettigrew reported on the status of the Precision Medicine Initiative (PMI). NIBIB helped to organize a workshop in July that stimulated robust and vigorous discussion about the role of mobile technology in realizing the vision of precision medicine. The PMI report has been delivered to the Advisory Council to the NIH Director (ACD) and unanimously approved. Next steps include developing an implementation plan and drafting Funding Opportunity Announcements (FOAs) for FY2016.

Interagency Working Group on Medical Imaging

The 2015 Congressional Budget Report established a Medical Imaging Subcommittee, with NIH as lead agency, to coordinate federal investments in imaging research. A working group co-chaired by Dr. Pettigrew and Dr. Richard Cavanagh, Director of the National Institute of Standards and Technology, met at the White House on July 9. The working group is charged with leveraging trans-federal activities and resources to broadly advance imaging development, utilization, and commerce.

Proposed Revisions to the Common Rule for Protection of Human Subjects

A notice of proposed rulemaking was published earlier this month for revisions to the Common Rule for Protection of Human Subjects (1991), which promulgates federal policy related to protection of research participants. Proposed revisions will expand the rule's purview to all clinical trials at federally funded institutions. Key revisions will facilitate broad participation in research by instilling greater participant confidence through simplified, clarified informed consent as well as increased privacy and security safeguards. In addition, proposed changes will increase efficiency by requiring a single Institutional Review Board for multisite studies and by the use of exclusions and exemptions to calibrate oversight to level of study risk.

F. NIBIB Activities

Design by Biomedical Undergraduate Teams (DEBUT) Challenge Winners

Dr. Pettigrew announced the winners of the 2015 DEBUT Challenge. First prize (\$20,000) was awarded to a team from Lehigh University for a point-of-care device that uses gold and silver nanoparticles to measure viral load in HIV patients. The device costs \$2.38 to produce, is easier and faster to use than the standard device, and is potentially suitable for use in low-resource settings.

A University of Texas at Austin team took second place (\$15,000) for a low-cost device to monitor heart rate and function as well as percent saturated oxygen. The device costs \$72 to manufacture, is durable, reliable, and easy-to-use in low-resource settings, and provides visual alerts for health care professionals.

A Stanford University team won third place (\$10,000) for a portable, wearable vibrating device to assist breathing in cystic fibrosis patients. The customizable device would improve quality of life, reduce time spent on active treatment, and lower overall costs.

Reverse Paralysis Consortium

The NIBIB-led Spinal Stimulation Consortium has developed a framework for a research study to move epidural spinal stimulation toward FDA approval. Preliminary studies have shown promise for improving bladder, bowel, and sexual function in individuals with spinal cord injuries, dramatically improving quality of life.

New NIH-Bill and Melinda Gates Foundation Point-of-Care Working Group

Dr. Pettigrew reported that NIH and the Bill and Melinda Gates Foundation (BMGF) have established a working group to focus on planning and coordinating initiatives and partnerships to advance point-of-care diagnostic testing for low-resource settings. Dr. Pettigrew and Dr. Jim Gallarda (BMGF) are co-chairs.

NIH-Institute of Electrical and Electronics Engineers Strategic Conference

NIH, the Institute of Electrical and Electronics Engineers, BMGF, and others are co-sponsoring a conference in November: Healthcare Innovations and Point-of-Care Technologies for Precision Medicine. The conference will be co-chaired by NIBIB's Dr. Tiffani Bailey Lash and Dr. Atam Dhawan, New Jersey Institute of Technology.

In the News

NIBIB grantee Dr. V. Reggie Edgerton has reported success with a non-invasive spinal stimulation technique that allows paralyzed individuals to voluntarily move their legs. In previous studies, stimulation was provided via implanted devices.

Dr. Pettigrew described volunteer activities of Drs. Grace Peng and Tiffani Lash, two Program Directors in the NIBIB Division of Discovery Science & Technology. During the summer, Dr. Peng taught robotics to Native Americans at the Baltimore Dakota Learning Camp in Granite Falls, Minnesota. Dr. Lash is co-founder of the Brilliant and Beautiful Foundation, which held its Third Annual Science and Math Advanced Research Training (SMART) Scholars Workshop at North Carolina State University, Raleigh.

The second Global Grand Challenges Summit—co-sponsored by national academies of engineering of China, the United States, and Great Britain— was convened in Beijing, China. The event focused on sustainability, infrastructure, energy, health, joy of living, education, and security/resilience. Dr. Pettigrew chaired the health session, which included presentations on informatics, wearable and implantable devices, and the aging population.

Dr. Pettigrew was named Honorary Professor, South China University of Technology, Guangzhou. Dr. Xiaoming Du, Chairperson of University Affairs, bestowed the honor at a recent ceremony.

G. Science Highlights

NIBIB-funded researchers Drs. Hyungsoon Im and Cesar Castro at Massachusetts General Hospital have developed a digital diffraction diagnosis (D3) device that can be used as a low-cost molecular diagnostic tool. Attached to a standard smartphone, the D3 device uploads diffraction pattern images to a secure cloud for off-site analysis. Investigators have used the device successfully for molecular profiling of breast cancer cells and classifying cervical cancer risk.

III. Review of Council Procedures and Regulations: Dr. Jill Heemskerk

Dr. Heemskerk reported the absence of Council Member Dr. John Gore and noted for the record that a quorum had been achieved for the Council meeting. She acknowledged Ms. Pam Glikman and Ms. Alisha Hopkins for organizing meeting logistics.

The next meeting of the Council is scheduled for Thursday, January 21, 2016. Dr. Heemskerk asked Council members to review future council dates and report any conflicts.

Proceedings of the Council meeting are governed by the Federal Advisory Committee and Government in the Sunshine Acts. Dr. Heemskerk reminded attendees that the morning and early afternoon sessions would be open to the public, and the later afternoon session would be closed for discussion of individual applications.

A. Approval of the May 18, 2015 NACBIB Meeting Minutes

A motion to approve minutes of the May 18, 2015 NACBIB meeting was forwarded, seconded, and approved unanimously.

IV. Task Force Implementation and Common Fund Initiatives: Dr. William Heetderks

Several working groups have been formed to address issues raised by the NACBIB Task Force on Strategies for Efficient Use of Research Dollars: building partnerships and leveraging resources; small grant mechanisms and early investigators; the R35 mechanism; improving communication with the research community; and novel approaches. Approximately \$40 million worth of activities coming

before Council during the closed session represent the leveraging of other resources, including two programs from the NIH Common Fund and one from the National Children's Study. The Common Fund activities are the 4D Nucleome, for which NIBIB is leading the imaging component, and Stimulating Peripheral Activity to Relieve Conditions (SPARC), under which NIBIB is leading development of exploratory technologies to understand control of organ function by the peripheral nervous system. The third initiative, Pediatric Research Using Integrated Sensor Monitoring Systems (PRISMS), is aimed at monitoring the effects of environmental exposures on child health. NIBIB is leading the development of new sensors to monitor environmental, physiological, and behavioral factors in epidemiological studies of children with asthma.

V. Task Force Implementation: Small Grant Mechanisms: Dr. Richard Conroy

Dr. Conroy presented findings in response to a Task Force recommendation to examine the value of the R21 small grant program and consider alternatives. Factors contributing to concern about the status of R21 funding include dramatic growth in the number of R21 applications; the possibility that NIBIB could become a dumping ground for R21s that are a poor fit for the institute's mission; and concerns that R21s may not be fulfilling the mechanism's purpose to fund exploration of novel, high risk research ideas.

Referring to portfolio data analysis, Dr. Conroy addressed each of these factors. The number of R21 applications doubled from 400 in 2008 to 800 in 2014. However, NIBIB spending on R21s has not significantly changed since 2007, despite the dramatic rise in applications, and the R21 success rate has dropped. NIBIB funding for R21s is less than 20 percent of R01 funding. The rate of R21 application submission appears to have leveled off.

Major institutes such as the National Heart, Lung, and Blood Institute, National Institute of Diabetes and Digestive and Kidney Diseases, National Human Genome Research Institute, National Institute of General Medical Sciences (NIGMS), and National Institute on Minority Health and Health Disparities no longer participate in the parent R21 FOA, which could pressure NIBIB to accept applications that otherwise would more appropriately go elsewhere. However, statistics indicate that when need be, most applications are successfully and appropriately reassigned; over a three-year period, NIBIB retained assignment on only four R21 applications that were considered by program staff to be peripheral to the NIBIB mission.

The R21 mechanism is intended to support high-risk/high-reward research and generate preliminary evidence for R01 applications. Preliminary data indicate that NIBIB R21s outperform R01s on simple measures, such as the number of publications and patent applications generated. There is a strong correlation between having an R21 and obtaining an R01 three years later; and the R21-to-R01 conversion rate is between 30 and 40 percent.

The R21's lack of a preliminary data requirement is especially appealing to new investigators. However, experienced principal investigators (PIs) are out-competing them. The distribution of R21 scores for 2014 shows that experienced PIs were twice as likely as new investigators to score within the 10th percentile. This may be because some study sections do not adhere to the high-risk/high-reward purpose of R21s and are rewarding experienced PIs for preliminary data.

Dr. Conroy outlined the following strategies for consideration.

Strategy 1: Retain current R21 funding because the mechanism appears to fulfill a complementary purpose to that of R01s. R21s generally outperform R01s in terms of publications. There is no significant difference between R21 and R01 publication quality based on citations per year, journal impact, and relative citation ratio.

Strategy 2: Modify the R21 funding plan to equalize success rates for new and experienced investigators, target programmatic priorities, or target high-risk, high-impact research.

Strategy 3: Withdraw from R21 funding altogether and reallocate funds to support R01s. This would increase the R01 payline by 2.5 percentile points and enable NIBIB to fund an additional 19 R01s each year. However, this would eliminate 79 R21s per year—a net loss of 60 NIBIB-supported investigators, consequently reducing diversity and negatively affecting the engineering, physics, and biostatistics departments that submit many R21 applications.

Strategy 4: Withdraw from the parent R21 FOA (the source of about 60 percent of NIBIB's current R21 applications) and keep Exploratory/Developmental Bioengineering Research Grants (EBRGs). This would free up funds for additional NIBIB-mission-focused applications, but NIBIB could lose some important applications that come through the parent FOA.

Strategy 5: Replace R21s with a targeted, small R01. Models of small R01-type mechanisms include the EUREKA award developed by NIGMS; the R29 FIRST awards designed to equalize the payline for new versus established PIs; and the New Innovator Awards issued by the NIH Office of the Director in 2007 to support highly innovative research and early-career investigators. EUREKA was issued in 2008 to counter the perception that R21s were underpowered in both budget and duration. FIRST awards were touted as an opportunity to set up new investigators for future success with R01s; however, the R29-to-R01 transition rate for FIRST awards was lower than the rate of new investigator R01 renewals. An NIH Working Group on New Investigators called for replacing the R29 with the R01 application, but clearly identifying a new investigator on the face page. The New Innovator Awards are a hybrid of research project and person-not-project funding, and applications are evaluated based on individual creativity, innovativeness of research approaches, and project potential.

Discussion

Dr. Weinberg supported continued funding of R21s because they seem to be more productive than R01s and help support more investigators.

Dr. Hirschi asked whether there is a difference between the success rates for R21s coming in from the parent grant versus the EBRGs. Dr. Conroy responded that the parent grant and EBRG R21 applications are scored by the same study sections, and there is no real difference in their respective success rates. However, there is a significant difference in the way some study sections score R21s and R01s.

Dr. Espy-Wilson asked whether there is a difference between the new investigator success rates for R21s versus R01s. Dr. Conroy responded that the success rate for new investigators is higher for R01s (around 13 percent) than for R21s (6 to 7 percent).

Dr. Tromberg asked whether the loss of applications from the parent R21 FOA would be outweighed by gains in the payline resulting from the reduction in the number of R21 applications. Dr. Conroy responded that the NIBIB payline is the same for R21s and R01s. Dropping participation in the parent R21 would increase the institute's payline slightly but reduce the number of NIBIB-supported investigators significantly. It would help focus efforts on the EBRG announcement.

Dr. Hirschi stated that the most conservative approach would be to drop the parent R21 and keep the EBRG, making the opportunity more NIBIB-mission-specific.

Dr. Tromberg noted that dropping the parent R21 would narrow the overall pool yet build opportunities for the NIBIB community. A lot of R21s are going to physics and engineering departments, which seem better aligned with the NIBIB mission.

Dr. Rosen suggested that tweaking R21s rather than dropping them completely is a good idea. Part of the tension is expecting one mechanism to accomplish two goals: supporting innovative research and

supporting new investigators. Expanding opportunity for new investigators could be accomplished via administrative mechanisms. In some study sections, new investigators may not be perceived as viable R01 investigators, and R21s offer a ladder up.

Dr. Espy-Wilson agreed. She supports keeping R21s and making special considerations for new investigators.

Dr. Sorensen agreed that tweaking the R21 to fix the gaps makes sense and that R21s should be used for high-risk/high-impact research. Introducing a new mechanism carries a risk of causing confusion in the community.

There was some discussion about whether to extend the R21 funding period to three years. Dr. Laurencin favored increasing the period to three years, noting that by the time an R21 is awarded, investigators are already applying for another R21 or an R01. Dr. Weinbaum supported this recommendation; a three-year cycle contributes to continuity for new investigators. Dr. Tromberg and Dr. Rosen suggested offering supplemental funds for the third year. Dr. Rosen added that new investigators need the extra time and should be able to get no-cost extensions. Dr. Heetderks reported that about 86 percent of R21s receive no-cost extensions. Dr. Laurencin pointed out that the 86 percent of R21s that obtain no-cost extensions are essentially three-year grants.

Dr. Pettigrew remarked that some institutes perceive the funds and funding period for R21s as insufficient to develop a viable research program. Dr. Conroy's report refutes that stance for NIBIB R21s because of demonstrated effectiveness, including a high level of patent production. NIBIB can address concerns about the R21's short duration by modifying the award.

VI. BRAIN Multi-council Workgroup Report: Dr. Bruce Rosen

Dr. Rosen provided an update on the BRAIN Initiative—Brain Research through Advancing Innovative Neurotechnologies—which is focused on understanding how the brain generates thoughts and actions. The NIBIB community has a lot to contribute to this effort.

The initiative funded 58 awards in FY2014 and 67 awards in FY2015. The President's budget for FY2016 allocates \$70 million to BRAIN.

Following the NIH Ethical Issues in Neuroscience Research Workshop in November 2014, the BRAIN Neuroethics Workgroup was established to consult with BRAIN leadership and investigators about approaches for addressing ethics issues and to advise NIH on neuroethics questions. Recommendations include early and explicit integration of ethics throughout research; evaluation of existing and innovative approaches to ethics integration; integration of ethics and science through education at all levels; and explicit inclusion of ethical perspectives on advisory and review bodies.

Dr. Rosen noted that NIH is partnering with international institutions to expand support for BRAIN research. Canadian and Australian partnerships have been established through which researchers will be supported by their respective home countries.

Two new BRAIN Initiative activities have been announced. An FOA entitled "Theories, Models and Methods for Analysis of Complex Data from the Brain" is accepting applications due in October. Another FOA, "Foundations of Non-Invasive Functional Human Brain Imaging and Neuro-Recording Techniques," will be published in October.

BRAIN continues to receive media attention, including a recent National Public Radio report and an article in *The Journal of the American Medical Association* entitled, "How the New Neuroscience Will Advance Medicine." Also, "BRAIN Initiative in 2015: Updates and Outreach" will be featured at a town hall meeting and reception as part of the Society for Neuroscience conference in October.

Dr. Rosen highlighted several exciting emerging advances and new tools arising from BRAIN. Dr. Joshua R. Sanes and colleagues have developed a new cell classification tool to uniquely identify cell types contained in nanoliter droplets. The low-cost, high-throughput tool allows researchers to sequence and analyze mRNA transcripts toward creating a molecular atlas of gene expression. Dr. Lihong Wang is using photoacoustic tomography to measure activity of large groups of neurons. The non-invasive method targets defined subpopulations of neurons, and its deep penetration capability enables measurements of whole-brain activity.

VII. Biomaterials as Therapeutic Cancer Vaccines: Dr. David J. Mooney

Dr. Chris Kelly, Director of NIBIB's Division of Discovery Science & Technology, introduced Dr. David J. Mooney, the second annual Hector Lopez lecturer. Dr. Mooney is the Robert B. Pinkas Family Professor of Bioengineering at the Harvard School of Engineering and Applied Sciences. He expressed his appreciation to NIBIB and NIH for the opportunity to conduct high-risk research in his areas of interest, particularly cancer immunotherapy.

Although cancer cells are different enough from normal cells that our immune system should be able to recognize them and respond appropriately, the tumor environment is typically immunosuppressive. Immunotherapies attempt to retrain immune cells to perform their normal function. These approaches offer key advantages over standard treatment: immune cells traffic throughout the entire body, offering a systemic treatment; the immune system's memory component has potential for preventing cancer recurrence; and immune cell activity causes minimal damage to normal tissue.

Dr. Mooney's work focuses on therapeutic vaccines mediated by dendritic cells (DCs), which play a key role in immune response. When they encounter antigens that give off danger signals (e.g., bacteria, viruses), DCs carry pieces of the dangerous antigens to the lymph nodes, activating T cells that search for and destroy the dangerous cells.

In *ex vivo* DC manipulation, DCs are isolated in patient specimens, multiplied in a laboratory away from the immunosuppressive tumor environment, and then reinfused into the patient. The hope is that enough activated DCs will find their way to the lymph nodes and generate a potent T-cell response. This FDA-approved approach has been shown to extend life for prostate cancer patients by four months. However, the process is costly; has complex, highly regulated technology requirements; and lacks economy of scale because each patient requires a unique cell culture.

Dr. Mooney's team developed an implantable polymer vaccine that bypasses *ex vivo* cell manipulation. The biomaterial system recruits DCs into the device, where they are programmed and then released to travel to a specific site such as the lymph nodes. The device is made from the same polymer used for biodegradable sutures and is porous to allow cells to migrate in and out.

Dr. Mooney described several preclinical studies using the polymer vaccine approach. In a prophylactic study, vaccinated mice received an injection of a highly aggressive, poorly immunogenic melanoma. Controls typically die within 30 days, and 50–60 percent survive when treated via an *ex vivo* infusion. Using the three-dimensional polymer device method, 90 percent survived. In a therapeutic study, researchers introduced tumors into mice, allowed tumors to grow, and then vaccinated with the implanted device; about half of the mice demonstrated complete regression of the melanoma.

The team plugged different tumor antigens into the system to test the system's broad usefulness. In a glioblastoma study, animals were vaccinated seven days after tumor formation; 90 percent of the animals demonstrated complete regression of established tumors. Animals who exhibited complete tumor regression were re-challenged with more cancer cells 100 days later; about 70 percent were able to destroy cancer cells a second time without revaccination. This demonstrated the robustness of the immune system's memory component.

In 2013, the Wyss Institute and Dana Farber Cancer Institute initiated a phase I clinical trial of a therapeutic melanoma vaccine, WDVax. Thirteen participants have been treated with WDVax to date and the results are highly promising.

Dr. Mooney concluded by summarizing how biomaterial-based immunotherapeutics work and progress toward demonstrating their value as a platform for cancer vaccines. Future directions will focus on making these therapeutics broadly useful for different cancer types, moving away from personalized vaccine approaches, and developing therapeutic vaccines against infectious diseases and even reproductive vaccines.

Discussion

Dr. Hirschi asked about deleterious effects from the vaccine. Dr. Mooney responded that no deleterious effects have been noted to this point.

Dr. Hirschi asked about the types of cells the device recruits and the percentage of cells that are DCs. Dr. Mooney stated that an upcoming paper reports that 95 percent of cells are DCs.

Dr. Thrall commented on the synergy between the vaccination and checkpoint approaches. Overemphasizing the checkpoint upsets immune system checks and balances. Dr. Mooney responded that the checkpoint practice is a systemic treatment associated with severe toxicity. The combination of vaccine and checkpoint inhibition will be important in addressing these safety issues.

Dr. Tromberg asked about other compounds the patients in the trial are receiving. Dr. Mooney replied that trial participants are not receiving any other compounds.

Dr. Tromberg asked about the impact of immunotherapeutics on brain metastases. Dr. Mooney responded that some data in other models suggest that this approach could be effective in the brain.

Dr. Sorensen remarked that other cancer vaccines have sounded so promising but have not worked. Dr. Mooney's approach addresses a primary failure mode of vaccines: the lack of T-cell activity. He asked what other failure modes for vaccines Dr. Mooney is exploring. Dr. Mooney indicated that he would prefer to have a subset of defined antigens. If, for example, he combined 15–20 lines of melanoma, would that cover enough antigens so that a single vaccine could be used for a broad patient population?

Dr. Pettigrew pointed to the challenges of developing an HIV vaccine. He asked whether immunotherapeutic approaches might contribute to solving the HIV vaccine challenge. Dr. Mooney responded that there are some possibilities with regard to HIV.

At the conclusion of the discussion, Dr. Kelley presented the Hector Lopez Lecture award to Dr. Mooney.

VIII. NIH Strategic Plan: Dr. Lawrence A. Tabak

Dr. Tabak, NIH Principal Deputy Director, provided an overview of the congressionally mandated NIH-wide scientific strategic plan, which is due in December. The NIH strategic plan is a living document intended to guide NIH in fulfilling its mission over the next five years; articulate forward-looking approaches and opportunities; and identify major trans-NIH themes that will advance biomedical research. He noted that the plan does not describe everything NIH does or will do, nor does it address priorities of the individual institutes, Centers, and Offices (ICOs), which are addressed in individual strategic plans. The plan is not intended to make a case for Congress to increase funds for NIH.

The plan includes an overview, areas of opportunity across biomedicine, and unifying principles. The overview outlines the NIH mission, explains the unique moment of opportunity in biomedical research, summarizes the current NIH-supported research landscape, and describes constraints confronting the community in the face of lost purchasing power.

The plan presents three broad areas of opportunity across biomedicine: fundamental science; health promotion and disease prevention; and treatments and cures. For each area of opportunity, the plan presents a succinct description of emergent opportunities and what NIH must do to realize them, and highlights examples of recent breakthroughs, how these align with the HHS strategic plan, and the unique role of NIH within HHS. Dr. Tabak briefly described illustrative examples for each area of opportunity.

Two unifying principles—setting priorities and enhancing stewardship—are covered in the plan, including examples of recent breakthroughs for each principle.

Dr. Tabak noted that public feedback on the draft plan has been solicited via webinars, publication of a Request for Information (RFI), and presentations to national advisory committees of 21 ICOs. He briefly listed a number of suggestions received in response to the RFI.

Dr. Tabak asked the NIBIB Council for feedback on the plan framework and content as well as any trans-NIH themes and emerging research needs not captured by the draft.

Discussion

Dr. Musen described the plan framework as compelling. He noted that NIH is not well prepared to help investigators with stewardship of nontraditional products such as software and data sets. Dr. Tabak added that there are questions around reproducibility issues, granting of access to unpublished data, and identifying the most valuable data sets.

Dr. Laurencin remarked that the ACD had many comments on the first draft and commended Dr. Tabak and the development team for the way they incorporated that feedback. Dr. Tabak noted that ACD members have been very engaged and extremely helpful.

Dr. Sorensen commented on public mistrust of scientists and misperceptions about what researchers do. Communicating with the broader population and demonstrating the value of research are challenging. It is important for the audience to understand how the public and scientists are alike in order to build trust. If NIH does something to advance human health but people don't accept it, then human health has not been advanced. Dr. Tabak noted that the plan must articulate and illuminate how NIH does its business, how decisions are made, and the checks and balances that are in place to ensure good stewardship of public resources. This could make people more comfortable and more confident about what researchers do and how they do it.

Dr. Tromberg asked whether the plan includes language about convergent science and the unity of disciplines. Dr. Tabak responded that the strategic plan does lay out the principles of convergence.

Dr. Weinbaum stated that the public looks at what NIH does in terms of common experience. Rare diseases are not common experience. NIH will need a public strategy for making that case. Dr. Tabak noted that studying rare diseases informs treatments of more common diseases and conditions.

IX. Closing Remarks: Dr. Pettigrew

Dr. Pettigrew acknowledged the three Council members whose terms end after today's meeting: Drs. John Gore, Mark Musen, and Cato Laurencin. He presented them with honorary plaques and letters of appreciation from himself and DHHS Secretary Burwell.

He reported that Council meetings in 2016 will feature the following speakers: Dr. Ralph Weissleder, Massachusetts General Hospital/Harvard Medical School (January); Dr. Eric Betzig, Howard Hughes Medical Institute Janelia Research Campus (May); and Dr. Karl Deisseroth, Stanford University (September).

X. Adjournment

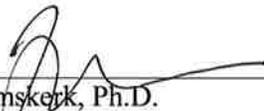
The open session of the NACBIB meeting was adjourned at 2:20 p.m.

XI. Closed Session

Dr. Heemskerk reminded Council members of the importance of confidentiality and avoidance of conflict of interest during Closed Session deliberations, and of restrictions regarding lobbying. 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 adjourned at 3:20 p.m.

Certification:

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



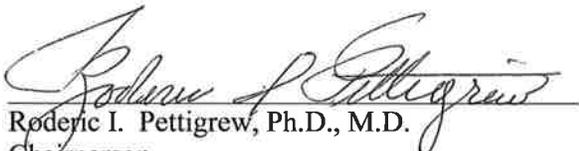
Jill Heemskerk, Ph.D.

Executive Secretary

National Advisory Council for Biomedical Imaging and Bioengineering

Associate Director for Research Administration

National Institute of 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 during the next meeting on January 21, 2016. Corrections or notations will be stated in the minutes of that meeting.