National Arthritis and
Musculoskeletal and
Skin Diseases Advisory Council

MINUTES OF MEETING

September 23, 2008

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES ADVISORY COUNCIL

MINUTES OF THE 66th MEETING

September 23, 2008
8:30 a.m. to 2:30 p.m.

I. CALL TO ORDER

The 66th meeting of the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council was held on September 23, 2008, at the National Institutes of Health (NIH) Campus, Building 31, Conference Room 6. The meeting was chaired by Dr. Stephen Katz, Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

Attendance

Council members present:

Mr. George Beach
Dr. S. Wright Caughman
Dr. Gena Carter
Ms. Carmen Cheveres
Dr. Betty Diamond
Dr. Kathleen Green
Dr. Joshua Jacobs
Ms. Ann Kunkel
Dr. Martin J. Kushmerick
Ms. Patricia McCabe Estrada
Dr. Lawrence G. Raisz
Dr. Clifford J. Rosen (by teleconference)
Dr. H. Lee Sweeney
Dr. James Weinstein

Council members not present:

Dr. Kevin Campbell
Dr. B. Lee Green
Dr. Bevra H. Hahn
Dr. John H. Klippel
Dr. Robert J. Oglesby (*Ex Officio*)

Staff and Guests:

The following NIAMS staff and guests attended:

Staff

Dr. Janet Austin
Dr. Carl Baker
Ms. Susan Bettendorf
Dr. Amanda Boyce
Mr. Gahan Breithaupt
Dr. Eric Brown
Dr. Branden Brough
Ms. Justine Buschman
Dr. Faye Chen
Mr. Richard Clark
Ms. Robin Diliello
Ms. Teresa Do
Dr. Jonelle Drugan
Mr. Erik Edgerton
Ms. Sharon Fair
Ms. Barbara Footer
Ms. Gail Hamilton
Ms. Katie Jaffee
Mr. Andrew Jones
Dr. Daniel Kastner
Dr. Stephen Katz
Ms. Shahnaz Khan
Mr. Mark Langer
Dr. Gayle Lester
Dr. Helen Lin
Ms. Anita Linde
Ms. Leslie Littlejohn
Dr. Kan Ma
Dr. Marie Mancini
Ms. Melanie Martinez
Dr. Joan McGowan
Ms. Leslie McIntire
Ms. Melinda Nelson
Ms. Anna Nicholson
Dr. Glen Nuckolls
Dr. John O'Shea
Dr. James Panagis
Ms. Wilma Peterman-Cross
Dr. Paul Plotz
Ms. Natalie Reyes

Ms. Trish Reynolds
Dr. Louise Rosenbaum
Ms. Karin Rudolph
Dr. William Sharrock
Ms. Sheila Simmons
Ms. Theresa Smith
Dr. Susana Serrate-Sztein
Ms. Yen Thach
Dr. Phil Tonkins
Dr. Bernadette Tyree
Ms. Marcia Vital
Dr. Fei Wang
Dr. Ping Wang
Dr. Yan Wang
Dr. Chuck Washabaugh
Mr. Elijah Weisberg
Ms. Sara Wilson

Guests

Dr. Rebecca Aronson, Practicing Physician
Dr. Bruce Bebo, Jr., National Psoriasis Foundation
Mr. Randy Beranek, National Psoriasis Foundation
Mr. Michael Bykowski, Consolidated Solutions and Innovations
Dr. Robert Carter, University of Alabama at Birmingham
Ms. Jodie Curtis, National Psoriasis Foundation
Ms. Ann Elderkin, American Society for Bone and Mineral Research
Ms. Christy Gilmour, American Academy of Orthopaedic Surgeons
Ms. Patricia Brandt Hansberger, Office of Legislative Policy and Analysis, NIH
Ms. Kim Holmes, IQ Solutions
Ms. Jennifer Isenberg, IQ Solutions
Dr. Alan Krensky, Office of Portfolio and Strategic Initiatives, NIH
Ms. Sheila Rittenburg, National Psoriasis Foundation
Ms. Audrey Spolarich, Spectrum Science Communications

II. CONSIDERATION OF MINUTES

A motion was made, seconded, and passed to accept with no changes the minutes of the 65th NIAMS Advisory Council meeting, held on June 6, 2008.

III. FUTURE COUNCIL MEETING DATES

Future Council meetings are currently planned for the following dates:

February 3, 2009
June 2, 2009
September 16, 2009
February 2, 2010
June 15, 2010
September 8, 2010

Dr. Katz noted that the September 8, 2010, date conflicts with a holiday and may be changed.

IV. DIRECTOR'S REPORT AND DISCUSSION

Dr. Katz welcomed Council members, NIAMS staff, and guests. He began his report by announcing that Dr. Madeline Turkeltaub, Director of NIAMS Division of Extramural Research Activities and Advisory Council Executive Secretary, passed away on June 21, 2008. Dr. Katz noted that Dr. Turkeltaub was a critical part of the Institute's executive group who had a tremendous impact on many dimensions of the Institute and its activities. Dr. Turkeltaub leaves behind a considerable scientific and personal legacy and will be greatly missed.

Dr. Katz invited attendees to review the NIAMS Shorttakes online, which include more details on many of the topics covered in his report. He noted that the September 2008 Shorttakes focuses on changes to the Web site clinicaltrials.gov, which is maintained on NIH's behalf by the National Library of Medicine. The site has become increasingly popular, among the research community and the public.

Dr. Katz also noted that four Council members were unable to attend the meeting: Drs. Kevin Campbell (Investigator at the Howard Hughes Medical Institute and Department Head, Roy J. and Lucille A. Carver Biomedical Research Chair at the University of Iowa), Bevra Hahn (Professor in the Department of Medicine, University of California, Los Angeles School of Medicine); John Klippel (President and Chief Executive Officer of the Arthritis Foundation); and B. Lee Green (Professor of Health Outcomes and Behavior at the H. Lee Moffitt Cancer Research Institute). Council member Dr. Clifford Rosen, Director of Translational Research at the Maine Medical Center, participated via teleconference.

Four outgoing Council members were recognized by Dr. Kats and thanked for their service and contributions to the council and NIAMS: Dr. Gena Carter (a radiologist and patient advocate), Dr. Bevra Hahn; Dr. Martin Kushmerick (Professor in the Department of Radiology at the University of Washington), and Dr. Lawrence Raisz (Director of the University of Connecticut Center for Osteoporosis, University of Connecticut Health Center).

Personnel Changes at the NIH and NIAMS

Dr. Katz announced that Dr. Robert H. Carter, former Director of the Division of Clinical Immunology and Rheumatology at the University of Alabama at Birmingham (UAB), has been selected as NIAMS Deputy Director following an extensive nationwide search. Dr. Carter is a Professor of Medicine at UAB, board certified in rheumatology and internal medicine, and has an established record of exemplary career achievements in the fields of rheumatology and immunology. Dr. Carter also is a NIAMS grantee who has been a leader in contributing to the understanding of molecular regulation of B lymphocyte activation to identify targets for therapeutic control of autoantibody production. When he assumes his official responsibilities on October 1, 2008, Dr. Carter will work with Dr. Katz in coordinating all activities related to the mission and functions of the Institute, developing and implementing NIAMS plans and policies, and allocating resources. He also will provide advice and counsel to the NIAMS and to NIH leadership on the development of opportunities for national research and research capacity building, on the Institute's national and international research and training initiatives, and on the development and dissemination of research information.

Dr. Joan McGowan has been appointed as Director of the Division of Musculoskeletal Diseases, NIAMS, and Dr. Susana Serrate-Sztein has been named Director of the Division of Skin and Rheumatic Diseases, NIAMS. Dr. Glen Nuckolls has agreed to serve as the Acting Director of the NIAMS Division of Extramural Research Activities, overseeing the Scientific Review Branch, the Grants Management Branch, and the clinical coordinators. Before announcing additional personnel changes at the NIAMS, Dr. Katz thanked and recognized Dr. Paul Plotz, who served as Acting Deputy Director of the Institute.

Within the NIAMS Extramural Program, Dr. William Tonkins has joined as a Program Director in the Division of Skin and Rheumatic Diseases. Dr. Faye Chen is currently on detail with the Extramural Program's Division of Musculoskeletal Diseases. Dr. Cheryl Lapham, former Director of the NIAMS Division of Skin and Rheumatic Diseases' Skin Immunobiology and Immune Diseases Program, has left the Institute for a position within the National Institute of Allergy and Infectious Diseases (NIAID). Within the NIAMS Intramural Program, Dr. Robert Colbert has joined the Institute as Chief of the Pediatric Translational Research Branch within the Office of the Clinical Director.

At the NIH level, Dr. Alan Guttmacher has been named Acting Director of the National Human Genome Research Institute (NHGRI). Dr. Guttmacher replaces Dr. Francis Collins, who stepped down as NHGRI Director after 15 years.

Update on Budget and Congressional Activities

On June 30, 2008, the President signed into law the Supplemental Appropriations Act, which provided the NIH with $150 million in supplemental funds, including $2.7 million for the NIAMS. The Institute used these funds to support four new competing research project grants and to increase its investment in intramural research and management support programs.

With regard to fiscal year (FY) 2009 appropriations, the Senate Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies held an NIH Overview Hearing on July 16, 2008. The House Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies held its hearing on March 5, 2008. Testimony from NIH Director Dr. Elias Zerhouni at both hearings is available on the NIH Web page; Dr. Katz's statement to the House and Senate Subcommittees is available on the NIAMS Web page.

The House and Senate Appropriations Subcommittees have marked up their respective FY 2009 appropriations bills. The House bill includes $30.4 billion for the NIH, which is $1.2 billion more than the President's request and $1.2 billion over the FY 2008 comparable amount. The Senate mark provides $30.3 billion for the NIH, an increase of about $1 billion above the President's request and $1 billion above the comparable FY 2008 level. The allocation for the NIAMS proposed by the House is $527 million, an increase of $18 million and 3.5 percent over FY 2008. The amount proposed by the Senate for the Institute is $523 million, representing an increase of $15 million and 2.9 percent over FY 2008. House and Senate conferees must now reconcile the differences in the two bills before the final appropriations bill can be passed. It is anticipated that the NIH will begin FY 2009 with a continuing resolution.

Dr. Katz discussed pending legislation of interest to the NIH and NIAMS. The House Committee on Energy and Commerce has been assigned the newly introduced Access to America's Orthopedic Services Act of 2008. The bill would require the Secretary of the Department of Health and Human Services (DHHS), in consultation with the NIH and other DHHS agencies to: (1) establish criteria for accounting and reporting of musculoskeletal research funded by the NIH and Agency for Healthcare Research and Quality and of the percent effort expended by investigators on musculoskeletal research; (2) report on new investigators awarded grants for musculoskeletal research, the race and ethnicity of new investigators, and a description of NIH efforts to encourage minority groups to apply for grants; (3) perform a cost effectiveness study on bone mass measurements; and (4) conduct a third longitudinal study on aging in the United States.

Another new bill of interest is the Comparative Effectiveness Research Act of 2008, which would establish a nonprofit corporation—the Health Care Comparative Effectiveness Research Institute—to contract with appropriate federal agencies or the private sector to conduct comparative effectiveness research. This bill was referred to the Senate Committee on Finance.

Congress also has been considering reauthorization of the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. Dr. Katz reminded the Council that by law, 2.5 percent of the NIH extramural budget is set aside for the SBIR program, which funds research and development projects that have potential for commercialization. In a similar fashion, 0.3 percent of the extramural budget is set aside for the STTR program, which facilitates cooperative research and development projects that move ideas from research institutions into the commercial market. Although the reauthorization bills being considered by the House and Senate differ considerably, both would increase the set aside for SBIR for all participating agencies except for the NIH. It would double the set-aside for STTR for all agencies, including the NIH, by 2014.

The Arthritis Prevention, Control, and Cure Act of 2007 is being discussed in the House. The bill would establish an Arthritis and Rheumatic Diseases Interagency Coordinating Committee and expand programs on juvenile arthritis control. Also, on July 31, 2008, the National Pain Care Policy Act of 2008 was introduced in the Senate. Among other provisions, the bill would require the NIH Director to establish a new office, which would be known as the Pain Consortium.

Highlights of Selected Recent Scientific Advances

Extramural Research

- Council member Dr. James Weinstein, Professor and Chair of the Department of Orthopaedics at Dartmouth-Hitchcock Medical Center, and colleagues built on early findings of the Spine Patient Outcomes Research Trial (SPORT), which showed that many people who have pain due to a herniated disc are likely to feel better over time, even without surgery. Although surgical repair of a herniated lumbar disc is more expensive than non-operative treatment, this demonstrated that surgery, when indicated, represents a reasonably cost-effective health care intervention compared with other options. (*Spine.* 2008 Sep 1;33(19):2108-15). It was noted that an article in the *Journal of Bone and Joint Surgery* on lumbar discectomy reported that patients with upper lumbar herniations (e.g., L2, L3, L4) showed a significantly greater treatment effect from surgery than patients with lower herniations (e.g., L5, S1). The higher up the herniation, the greater the difference in terms of outcomes between surgery and non-surgery.

- A study of almost 1,000 participants of the Framingham Study showed that meniscal damage is common among middle-aged and elderly persons, irrespective of knee symptoms. Although other studies have demonstrated that between 67 and 91 percent of patients who have symptomatic knee osteoarthritis also have meniscal damage, this work by Dr. D.T. Felson and colleagues revealed that 61 percent of people who had meniscal damage were asymptomatic. The investigators noted that clinicians who order knee MRIs should take into account the high prevalence of incidental tears when interpreting the results and planning therapy (*N Engl J Med.* 2008 Sep 11;359(11):1108-15).

- Dr. Jane Cauley and colleagues from the Women's Health Initiative have confirmed the association between very low Vitamin D blood levels and hip fractures, independent of falls and measures of fragility. Although studies have largely failed to reduce the risk of hip or other fractures with Vitamin D supplements alone, this finding provides another clue to help physicians identify patients who are at risk for fractures and encourage them to take steps to protect their bones (*Ann Intern Med.* 2008 Aug 19;149(4):242-50).

- Dr. R.M. Evans and colleagues have identified two drugs that appear to confer many of the healthful benefits of long-term exercise in mice—giving them more fat-burning muscle and better endurance. The investigators report that PPAR-delta and AMPK work synergistically to activate genes responsible for muscle endurance. The publication received considerable coverage from the press because it appeals to anyone who would like to improve their level of fitness. The findings also might lead to better treatments for certain muscle disorders,

frailty, obesity, and other conditions in which exercise is known to be helpful but not always practical (*Cell.* 2008 Aug 8;134(3):405-15).

- A study by Dr. Paul Khavari and associates supports a model of an orchestrated equilibrium between repression and activation of gene expression. The proper balance between growth of skin cells and differentiation to form an effective barrier layer is important for the health of the skin. Uncontrolled growth is a hallmark of skin cancer, whereas defects in the skin barrier layer are associated with diseases such as atopic dermatitis (eczema) and asthma. Therefore, understanding the role of epigenetics in the regulation of growth and differentiation may lead to new targets for drug development for these diseases (*Genes Dev.* 2008 Jul 15;22(14):1865-70).

- Dr. Joyce Bischoff and colleagues published results of a study identifying a stem cell as the cellular origin of infantile hemangioma and describing for the first time an animal model for this common tumor of infancy. The researchers isolated multipotential stem cells from hemangioma tissue. The stem cells gave rise to hemangioma-like lesions after transplantation into immunodeficient mice. The hemangioma-derived cells recapitulated the unique evolution of infantile hemangioma — the formation of blood vessels followed by atrophy to fatty tissue (*J Clin Invest.* 2008 Jul 118:2592-2599).

- Drs. Damien Chaussabel and Jacques Banchereau published a paper on translational research, proposing a new strategy for microarray analysis based on the identification of transcriptional modules that are formed by genes expressed in multiple disease data sets. The researchers showed that mapping changes in gene expression, at the module level, can generate disease-specific transcriptional fingerprints. The latter provides a framework stable enough for visualizing and interpreting microarray data. The researchers then used transcriptional modules to select biomarkers and develop multivariate transcriptional indicators of disease progression in patients with systemic lupus erythematosus (*Immunity*. 2008 Jul;29(1):150-64).

- Dr. Mark J. Shlomchik and colleagues have shown that T cells are not required for initiation of rheumatoid factor responses as part of AM14 B cell activation, but toll-like receptors (TLR) signals are essential. The authors also identified overlapping yet important roles for TLR7 and TLR9, along with qualitative alterations that occur in the absence of either receptor. Finally, they showed a B cell-intrinsic requirement for MyD88 signaling, and showed that these signals are needed to initiate proliferation (*Immunity.* 2008 Aug;29(2): 249-60).

- It is important for clinicians to maintain diagnostic vigilance for Klinefelter's syndrome when seeing male patients with SLE. Dr. R. Hal Scofield and colleagues have shown that the prevalence of Klinefelter's syndrome (47,XXY) is increased in men with (SLE) by up to 14-fold, compared with its prevalence in men without SLE. On the other hand, the risk of developing SLE in men with Klinefelter's syndrome is up to 14-fold higher than in men with 46,XY, consistent with the notion that SLE susceptibility is partly explained by an X chromosome gene-dose effect (*Arthritis Rheum*. 2008 Jul 30;58 (8):2511-2517).

- Dr. Rhonda R. Voskuhl and colleagues used two disease models to examine if there was a contribution of sex chromosomes to sex differences in susceptibility to experimental autoimmune encephalomyelitis (EAE) and pristane-induced lupus. The authors reported that mice with the XX sex chromosome complement, as compared with those with XY, demonstrated greater susceptibility to both EAE and lupus, proving for the first time that the XX sex chromosome complement increases susceptibility to autoimmune disease (*J Exp Med*. 2008 May 12;205(5):1099-108).

Intramural Research

- Researchers in Dr. John O'Shea's laboratory of the Molecular Immunology and Inflammation Branch have found that the conditional deletion of the protein furin in T cells resulted in systemic autoimmune disease in mice, making it a promising target for therapy. The study also implies that inhibiting furin—which has been thought to reduce malignant cells, block infection, and play a part in a variety of human diseases—may have the side effect of increasing autoimmune disease (*Nature.* 2008 Aug 13 [Epub ahead of print]).

- Investigators in Dr. Richard Siegel's laboratory of the Autoimmunity Branch, have found that blocking DR3 (a TNF receptor related to white blood cell activity) could slow or stop the damaging inflammation characteristic of autoimmune diseases such as asthma and multiple sclerosis. These findings open up new avenues for inflammation therapy for other autoimmune diseases in which white blood cells play a role in causing or perpetuating the disease. It was determined that removing DR3 did not appear to suppress the immune response or the ability to fight infection, which is a problem with many other treatments for autoimmune disease (*Immunity.* 2008 Jul 29;1-11).

NIH/NIAMS Activities and Plans for the Future

Dr. Katz explained that as part of its continuing educational efforts to improve and enhance compliance with financial conflict of interest requirements, the NIH has developed a Web-based tutorial that reviews the requirements of and the responsibilities for compliance with federal financial conflict of interest regulations. The tutorial is designed for use by Institutional officials responsible for managing NIH-funded grants, cooperative agreements, and/or contracts and for individuals who are responsible for the design, conduct or reporting of NIH-supported research.

Earlier this month, NIH leadership held its Annual Forum to discuss priority issues that transcend the interests of single Institutes. Preliminary recommendations for improving the peer-review process at the NIH were discussed. Plans for adopting these recommendations continue to be discussed at all levels of the NIH. Dr. Zerhouni has announced plans to implement key recommendations in three broad priority areas: (1) engage the best reviewers, (2) improve the quality and transparency of reviews, and (3) ensure balanced and fair reviews across scientific fields and career stages, and reduce administrative burden.

Dr. Katz noted that there are plans to eliminate the A2 applications. He presented a slide showing that across the NIH and NIAMS, in 1998, of the applications that were funded, 60 percent were A0 applications, 30 percent were A1s, and 10 percent were A2s. In 2007, most

of the applications being funded were A1 applications, followed by A2s and then A0s. Dr. Katz commented that the science in the A0 applications has not changed—rather, the system has changed. There is a sense that eliminating the A2 application will allow for earlier on A0 and A1 applications. A0 applications will be percentiled against A0 applications; A1s will be percentiled against A1s. It is expected that this policy will be in place for new and competing applications received by the NIH as of February 2009. In addition, starting in 2010 the page length requirement of submissions will be decreased, and the grading system will be modified to a 1-7 scale rather than a 1-5 scale.

Dr. Katz discussed a recent meeting that the National Coalition for Osteoporosis and Related Bone Diseases (which comprises the American Society for Bone and Mineral Research, the National Osteoporosis Foundation, the Osteogenesis Imperfecta Foundation, and the Paget Foundation for Paget's Disease of Bone and Related Disorders) convened to develop a coordinated national action plan to promote bone health. The meeting featured comments from Acting Surgeon General Dr. Steven Galson, Representative Patrick Kennedy of Rhode Island, and Dr. Katz. Drs. Raisz and McGowan led a session on Building the Science Base and Changing the Paradigm of Preventing and Treating Fractures.

In terms of the Institute's information dissemination efforts, Dr. Katz drew Council members' attention to several items provided to them in their meeting materials:

- A new, easy-to-read booklet called "Bone Health for Life," which emphasizes the importance of taking care of one's bones for general health and for the prevention of osteoporosis.

- Papers published by Drs. O'Shea and Siegel (in *Nature* and *Immunology*, respectively), which were described earlier by Dr. Katz in his discussion of recent scientific advances.

- An article from *Wired* Magazine featuring the work of Dr. Rocky Tuan's laboratory. Dr. Tuan, Chief of NIAMS' Cartilage Biology and Orthopaedics Branch, has been using adult stem cells to grow cartilage, muscle, and intervertebral disks *in vitro*.

Dr. Katz also noted that at NIAMS' offices on the fourth floor of Building 31 on the NIH Campus, there is a new display featuring information of interest to the Institute and its communities.

Discussion

Council member Dr. H. Lee Sweeney, the William Maul Measey Professor and Chair of the Department of Physiology at the University of Pennsylvania School of Medicine, noted that without knowing the percentage A0s represented out of the total pool of applications in 1998, the slide presented by Dr. Katz could be somewhat misleading. His sense is that the number of A0 applications as a percentage of total grants is decreasing. He also suggested that changes to the peer review process should focus on changes related to the reviewers, not to the format of the applications. Dr. Sweeney commented that the NIH must decide whether to simply fund a certain number of scientists or to fund the best science; the peer review process then should be structured accordingly. Dr. Katz agreed, noting that NIH Institute and Center (IC) Directors

always favor supporting the best science. The NIH is working in many areas to identify the best types of reviewers and what incentives can be used to attract and retain them. Dr. Katz explained that the Institute has made a commitment to try to maintain a steady payline (which has been at about the 15th percentile, with a success rate of approximately 27 percent) from year to year, even in difficult fiscal times. Even so, there are many good applications that go unfunded.

Dr. Betty Diamond, a member of the Council and Chief of the Laboratory of Autoimmune Diseases at The Feinstein Institute of Medical Research, voiced her support for any activity that decreases the amount of time between application submission and funding decision. She suggested that the NIH monitor the current system for a few more cycles before eliminating the A2 applications to determine where those applications would end up.

Dr. Raisz asked for clarification on the changes that will be made to the scoring system. Dr. Katz explained that the revised 1-7 scale scoring system will include integers and will only go out to one decimal place, not two. Dr. Diamond noted that moving to a 1-7 scale scoring system with one decimal place would increase the number of potential scores from 50 to 70. Reviewers will now have more degrees of discrimination, not fewer, which will not increase consistency across reviews and reviewers. Dr. Katz clarified that the reviewers will give their scores as single integers; the decimal place will be used once the scores are averaged.

V. FUNDING INNOVATIVE RESEARCH: PIONEER, EUREKA, AND TR01S

Dr. Alan Krensky, Director of the Office of Portfolio and Strategic Initiatives (OPASI) and NIH Deputy Director, began his presentation by discussing some of the key provisions of the NIH Reform Act of 2006, which was the first omnibus reauthorization of the NIH in 14 years. The NIH Reform Act of 2006:

- Established the Division of Program Coordination, Planning, and Strategic Initiatives.
- Established the use of a Common Fund to support trans-NIH research.
- Created a Council of Councils to guide trans-NIH priorities.
- Established a Scientific Management Review Board to oversee evaluation or organizational structures and authorities that may be used for improvements.
- Initiated a public process to review potential organizational changes.
- Established Demonstration Oversight Groups for high-risk, high-reward and bridging the sciences initiatives (Dr. Katz serves on the High-Risk, High-Reward Demonstration Oversight Group).

Dr. Krensky briefly reviewed OPASI's structure and function, noting that the Office has three cores: (1) strategic initiatives, (2) evaluation, and (3) portfolio analysis. A new NIH grant

program, Transformative R01 awards (TR01s), was recently established. The concept for TR01s was initially introduced during the first Roadmap discussions, but it was not advanced at that time in lieu of the Pioneer Awards. In December 2007, OPASI sponsored a workshop on the topic of fostering innovations—outside investigators highlighted the difficulties associated with fostering innovative science at the NIH, and the topic of TR01s was again raised. TR01s also have been promoted through efforts related to enhancing NIH's peer review system and by members of the High-Risk, High-Reward Demonstration Oversight Group.

The TR01 Program includes open competition to all potentially transformative ideas from all relevant fields. There is no cost limit per project. Dr. Krensky explained that an announcement will be issued once per year for 5 years; each issuance will award $25 million per year for 5 years (for a total of $675 million over 9 years). The TR01 Program is intended to address conservative review hurdles that are specific to the extramural community. Therefore, intramural research program investigators are not eligible.

Dr. Krensky explained that TR01 applications will be short, in an essay format of 5-8 pages. The primary required element will be a statement of paradigm disruption/creation, addressing the following questions:

- If a paradigm exists, why is it wrong and how will it be disrupted?

- If no paradigm exists, how will the project create one?

TR01 application review criteria focus on transformative potential (i.e., the ability of the application to be paradigm disrupting, not just paradigm shifting). A new type of multi-tiered review that implements an editorial board will be utilized. The editorial board will be made up of 12 members who are high-level, experienced experts who will receive and triage the applications. If any editorial board member deems the application worthy of going out for review, the application will be reviewed through NIH's Center for Scientific Review. Three content experts then will review the application electronically. Following this review, applications will return to the editorial board, which will meet face-to-face to review the applications for transformative potential and rank order them. The editorial board will make advisory recommendations that will be submitted to IC Directors, Dr. Krensky, and ultimately, the NIH Director for final approval.

Dr. Krensky presented a slide that compares NIH high-risk, high-reward and transformative grant programs to put the TR01 Program in context with the Pioneer, New Innovator, EUREKA, Quantum, and CEBRA awards. Dr. Krensky noted that TR01 awards will be funded through the Common Fund as well as through the ICs. The TR01s, which will be made available for the first time in 2009, are unique in terms of their review approach, flexibility, and potential award size. Dr. Krensky commented that the TR01 Program represents a test case to see if this approach can be used in other ways across the NIH.

Discussion

Dr. Katz opened the discussion session by noting that there were an enormous number of Pioneer award applications in that program's first year (2004), and the New Innovator awards, which started in 2007, still have a large number of applications each cycle. Dr. Krensky explained that there were 8 or 9 awards (from 2,000 applicants) in the first year of the Pioneer Award Program; this year there are 16 such awards (from 450 applicants). The numbers of applications and awards for the New Innovator Awards have followed a similar pattern, with fewer applications but more awards. One concern being examined at the NIH level is keeping these investigators in the research pool once their 5-year "outside the box" grant expires. In terms of the mechanics of the TR01s, Dr. Krensky noted that a 12-member editorial board will triage the applications (the two Chairs of the editorial board are both members of the Advisory Council to the Director). The final details of when ICs become involved in the process have yet to be worked out.

Dr. Diamond asked about the evaluation mechanisms established for the TR01 and other similar programs. Dr. Krensky noted that every major grant program is being evaluated. In terms of the Pioneer Awards, Office of Behavioral and Social Sciences Research staff oversee two contractors, one to analyze the award process, and one to evaluate outcomes. Publications, patents, start-up companies, citation indices, etc., all are included in these evaluations. Dr. Diamond asked for clarification regarding the criteria for the New Innovator Awards, particularly in terms of years of clinical/research training for the Principal Investigators. Dr. Krensky commented that these criteria have been controversial, and that there has been some leniency in applying the criteria to applicants. Dr. Katz added that the criteria have been refined to take into consideration residencies, fellowships, etc. Dr. Krensky also clarified that new investigators are not necessarily young investigators—they are new investigators to the NIH.

Dr. Raisz commented that paradigm shifts typically tend to involve many individuals outside of biomedicine (e.g., physics, psychology, etc.), and asked whether the TR01 Program takes this into account. Dr. Krensky agreed, noting that some grants include as many as 20 disciplines. The review process does take this into consideration, as does the composition of the editorial review board. Bringing these various areas of expertise together is an important part of the process. Council member Dr. Joshua Jacobs, an orthopaedic surgeon at Rush University Medical Center, asked to what extent efforts are being made to maintain a balanced portfolio across disciplines and diseases. Dr. Krensky explained that portfolio analysis is a very complex undertaking. OPASI does not dictate to IC Directors, but can provide information and identify redundancies.

VI. BIOMEDICAL RESEARCH ON THE INTERNATIONAL SPACE STATION

Dr. Katz, who sits on the National Aeronautics and Space Administration (NASA) Advisory Committee and serves as the NIH liaison to NASA, briefly discussed the Meeting on Space-Related Health Research, which was held December 6, 2008, with the goals of: (1) sharing information across key federal agencies about space-related health research interests and activities, and (2) identifying opportunities for collaborations to facilitate space-related health

research. Meeting participants included representatives from NIH ICs, NASA, U.S. Food and Drug Administration, National Institute of Standards and Technology, National Science Foundation, U.S. Department of Agriculture, and National Space Biomedical Research Institute.

There is great potential to apply the microgravity environment of the International Space Station (ISS) to health-related research in a number of areas, including bone and muscle loss, cardiovascular and endocrine systems, cell biology (including cellular and molecular repair processes), embryogenesis and central nervous system development, immune response, and stem cell activity and tissue regeneration. The ISS is expected to be fully operational in 2011, with the availability of resources such as laboratory equipment, data processing capabilities, and crew time. NASA is not expecting the NIH to cover the costs associated with transportation expenses, but does need considerable lead time to include experiments on the ISS.

After showing a brief video clip highlighting the structure of the ISS, Dr. Katz noted that on September 12, 2007, the NIH and NASA entered into a Memorandum of Understanding (MOU). As part of the MOU, the NIH will use reasonable efforts to: (1) publicize, to the intramural and extramural communities, the availability of the ISS as a research environment; and (2) give careful consideration through the standard review process to well-developed, investigator-initiated extramural applications and potential intramural activities linked to space-related health research. Dr. Katz described examples of unique ISS research equipment, such as the BioServe Culture Apparatus (which accommodates tissue engineering and other studies and allows for passive gas exchange in a sterile environment); Advanced Space Experiment Processor (which accommodates rotating cell cultures and provides cells with fresh medium); T-Cell Growth System (which propagates live thymus tissue in a closed Petri dish system); and Microgravity Experiment Research Locker/Incubator (which can be used as a freezer, refrigerator, or incubator).

Next steps involve developing a funding opportunity announcement. As part of this effort, it will be important to:

- Articulate NIH interests (i.e., the studies must be directly related to the NIH mission and make use of the unique microgravity environment of the ISS).

- Address outstanding issues (which include evaluating feasibility and selecting/payment of implementation partners who will prepare experiments for flight).

- Decide which solicitation and funding mechanisms are most appropriate (e.g., Program Announcement with Review, phased cooperative agreements or supplements, etc.).

- Define costs to the NIH—Phase I basic research is expected to cost approximately $150,000 per year; Phase II basic research is expected to cost about $300,000 per year.

Discussion

Dr. Kushmerick commented that the concept of conducting experiments in zero gravity with tissue culture might be difficult to justify given the expense. His impression is that any effects

would be limited. However, the adaptation of humans in space is a very interesting topic—humans have managed to adapt quite well to the zero gravity environment. He asked whether the health-related experiments to be conducted on the ISS will focus mostly on *in vitro* studies. Dr. Katz agreed that there are tremendous opportunities in terms of behavioral research, and that the health-related experiments represent only a microcosm of all research possibilities. Some experts believe that the virulence of an organism differs in zero gravity, and there may be opportunities to gain a better understanding of mechanical stimuli in organ systems in zero gravity. In response to a question from Dr. Raisz, Dr. Katz clarified that the NIH is not proposing to conduct a series of studies on the astronauts themselves.

Dr. Weinstein commented that issues related to wound healing, particularly in terms of musculoskeletal and skin diseases, appear to be a good focus of study on the ISS. Dr. Katz agreed that this topic represents a good opportunity.

Additional A0/A1/A2 Discussion

Following the discussion on biomedical research on the ISS, the Council revisited the discussion of removal of the A2 applications, with the added context of the presentation given by Dr. Krensky. Dr. Caughman expressed some concern about the composition of study sections and whether or not there is going to be a hierarchy of where top-notch scientists and reviewers want to be. He asked if that has been considered as an unintentional impact on the competition of study sections and what they see as their role, particularly in terms of traditional versus innovative science. Dr. Katz indicated that the study sections described by Dr. Krensky are only a very small portion of the approximately 16,000 reviewers used annually, and that this likely will not be an issue.

Dr. Katz clarified that A0 and A1 applications will be reviewed using the same criteria when the A2 applications are dropped. He reiterated that the purpose of removing the A2s is to speed up the overall process and, especially given the current fiscal environment, provide investigators with more timely information on funding decisions.

Dr. Diamond emphasized the need to pay attention to the psychology of the investigators as well as the reviewers. As a result of the decision to remove the A2 application, it is likely that researchers will begin writing their A0 applications and start the A0 process earlier. It will be important to monitor the quality of the A0 applications to ensure that it does not suffer. This unintended consequence also may increase workloads for reviewers. Dr. Katz commented that these issues have been discussed extensively, and that the NIH will be monitoring this. He added that the NIH currently has good numbers in terms of the number of applications coming in per applicant.

Following this discussion, Dr. Jacobs briefly discussed House Resolution 6478, which Dr. Katz referred during his Director's Report. Dr. Jacobs, who is President-elect of the U.S. Bone and Joint Decade, explained that the resolution addresses the disparities between the burden of musculoskeletal disease and the allocation of federal research funding. The resolution also includes provisions for public education and the establishment of national joint registries. He encouraged Council members to review the resolution.

VII. ROUNDTABLE DISCUSSION ON RESEARCH CAREER PATHS IN RHEUMATIC DISEASES

Dr. Serrate-Sztein informed Council members that this Roundtable Meeting was held on March 25, 2008, on the NIH Campus, with the overall goal of determining how to attract, train, and sustain a strong rheumatology research workforce. Another meeting is planned approximately 1 year from then to measure progress. She reviewed the NIH participants as well as extramural participants (which included representatives from the American College of Rheumatology [ACR], ACR-Research and Education Foundation [ACR-REF], Arthritis Foundation [AF], and rheumatology fellows as well as other participants).

Dr. Serrate-Sztein discussed a number of obstacles in rheumatic diseases research career paths. The number of physician-scientists in the rheumatology field has been in decline over the past few decades. At the roundtable meeting, it was recognized that career paths are influenced to some extent by the early training mechanism that is chosen. Both the T32 (fellow)-to-K award and the K award-to-R (independent) transitions represent major challenges to trainees. Therefore, there is an increasing importance associated with mentoring in the successful transition of trainees to independent investigators. Another challenge is the relatively low salaries throughout the training period, which may be prohibitive for many trainees.

There also is increased anxiety over the ability to obtain NIH research grant funding. Dr. Serrate-Sztein commented that at the meeting, fellows reflected that as young investigators, they are constantly reminded about how difficult it is to obtain funding. Fellows are very aware of the funding environment and this is a significant consideration in their decisions to pursue a research career.

In discussing potential solutions to some of these obstacles and challenges, Dr. Serrate-Sztein noted the following:

- The ACR-REF will soon offer 1-2 year bridge awards to promising rheumatology researchers who were initially unsuccessful in obtaining K08 or K23 awards.

- To ease challenges during the K-to-R01 transition, the AF is currently designing a program to supplement K awards.

- Some highly qualified trainees should be encouraged to move more quickly from K funding to R01 funding.

- Better mentoring on career issues is needed to reduce attrition during the T32-to-K phase.

- It is important to raise awareness about the NIH Loan Repayment Program to alleviate low salary burden during the T32-to-K period (and expand scope to basic researchers).

- Additional training surveys and evaluations may inform future training needs (the ACR is producing a new action plan to address looming shortages in the academic rheumatology workforce; the NIAMS will implement a system for prospective data collection from training award recipients).

- Dr. Serrate-Sztein closed her presentation by again noting that the NIAMS plans to meet with community representatives in 2009 to continue the dialogue.

Discussion

Advisory Council member Dr. Kathleen Green, Joseph L. Mayberry Professor in the Department of Pathology/Cancer Center at Northwest University Medical School, noted that the issues raised by Dr. Serrate-Sztein are of broad importance to many different groups. She asked if there are any data on other careers such as cutaneous biology and how they might compare with young rheumatologists. She also noted that the roundtable discussion meeting format can be a valuable way of bringing together other groups. Dr. Katz noted that the Institute could facilitate a roundtable meeting or meetings in other areas.

Dr. Diamond explained that NIH money is more important at the independent moment for a researcher rather than at the training moment because of overhead. As institutions become more and more concerned about finances, they are not allowing researchers to obtain grants that do not come with NIH-style overhead. She also noted that the ACR has been concerned about the number of investigators. The ACR with the AF will hold a meeting every other year focused on fellows and young faculty members. Meeting sessions include two senior faculty and two junior researchers as speakers. One of the goals of these meetings is to ensure that trainees have a cadre of resources that can be referred to if they encounter scientific or career issues.

VIII. NIAMS SMALL BUSINESS INNOVATION RESEARCH/SMALL BUSINESS TECHNOLOGY TRANSFER WORKING GROUP REPORT

Dr. McGowan reminded Council members that the SBIR program, a set-aside program for small businesses to engage in federal research and development with the potential for commercialization, represents 2.5 percent of the NIH extramural research budget. Similarly, the STTR program represents 0.3 percent of the NIH extramural research budget and is a set-aside program to facilitate cooperative research and development between small businesses and U.S. research institutions with potential for commercialization.

The NIAMS SBIR/STTR Working Group has been charged with exploring the scientific areas that may be targeted to request applications from the small business community. Questions guiding the Working Group's activities include the following:

- Which NIAMS scientific areas are ripe for small business research?

- How can these opportunities be targeted to the businesses?

- Can NIAMS' SBIR/STTR plans be tied to other initiatives driven from the NIAMS long-range plan, or recent NIAMS Retreat and Planning Panel topics?

- Should small business audiences be targeted at national scientific meetings to advertise the Institute's interest?

Dr. McGowan reviewed NIAMS SBIR/STTR Working Group activities in 2008. Two focus group meetings were held based on a previous Working Group topic suggestion related to tissue engineering and regenerative medicine. The first of these meetings was held in March at the 54th Orthopaedic Research Society Annual Meeting; the second was held in April at the Would Healing Society Meeting. At the 10th Annual NIH SBIR/STTR Meeting in July of this year, the NIAMS SBIR/STTR Coordinator (Mr. Elijah Weisberg) presented current NIAMS mission areas related to the SBIR/STTR program to more than 100 small business attendees. The NIAMS also is participating in two new NIH SBIR/STTR announcements ("Lab to Marketplace: Tools for Biomedical and Behavioral Research" and "Technological Innovations for Interdisciplinary Research Incorporating the Behavioral and Social Sciences").

Of note regarding the SBIR/STTR program, the House reauthorization bill updates venture capital investment standards, creates an SBIR Advisory Board for all agencies awarding more than $50 million in SBIR funds, and increases the award size guidelines for the SBIR and STTR programs. The Senate Reauthorization bill reauthorizes the SBIR and STTR programs for 14 years, includes a compromise on the participation of companies majority owned and controlled by multiple venture capital companies, doubles the STTR allocation, and increases the award size guidelines for both programs.

Dr. McGowan explained that future NIAMS SBIR/STTR activities include: (1) continuing the current small business outreach activities, (2) identifying unmet needs in the small business community relevant to the NIAMS mission areas, (3) working on small business initiatives in NIAMS priority areas, and (4) including small business in NIAMS-wide solicitations if appropriate. She presented a slide showing the impact of a $1 million or $2 million set-aside in the NIAMS SBIR program relative to past paylines—from 2003 to 2007, the impact of these set-asides would not have been significant.

Discussion

Dr. Diamond commented that one of the areas in which there has been a stated need and some SBIR interest is evaluative tools for assessing and measuring different clinical variables. She noted that it may be useful to advertise the hyperaccelerated program to small businesses within the context of the SBIR program, because they may be able to validate some associated tool. Dr. Diamond also suggested trying to work with the Immune Tolerance Network (ITN) and the Autoimmunity Center of Excellence (ACIS) to use very well defined clinical patients and well defined measures to leverage SBIR funds. Dr. McGowan suggested this may an action item that the Working Group could move on. She added that there are tools coming out of PROMIS that also may qualify; furthermore, the Institute has an outcomes-related RFA, and some of the content may be amenable to commercialization.

Dr. Jacobs noted that there are specific corporate advisory councils or groups of individuals that represent the corporate sector that should be involved in these discussions. Dr. Jacobs also explained that as the Association of American Medical Colleges is tightening up its conflict of interest regulations for academic medical centers, some of the corporate-related research is becoming more and more challenging, particularly if the clinical investigator has some type of financial interest in the product involved.

IX. BUILDING INTERDISCIPLINARY RESEARCH TEAM (BIRT) REVISION AWARDS

Dr. Fei Wang, Health Science Administrator in the NIAMS Division of Musculoskeletal Diseases, opened her presentation by explaining that the purpose of the NIAMS BIRT Program is to promote collaborations among groups of investigators in disciplines that have not interacted traditionally to pursue a clear scientific opportunity in an area of shared interest of relevance to the NIAMS. The BIRT Program was approved as a concept by the NIAMS Advisory Council in 2007. An RFA was released in November of that year; 36 applications were received for an R01 pilot program. Most (14) were in the area of soft tissue biology – imaging technologies.

The applications underwent a "pre-scientific" review, during which the responsiveness of each application was: (1) checked by scientific program staff, (2) discussed at a scientific staff meeting and followed by individual discussions, and (3) presented to senior staff. Nine of the 36 applications were deemed not responsive and returned to the applicant with review. 27 went on to scientific review in June 2008. The scientific review focused on collaboration and impact, risk versus benefit, and novel technology versus the investigator team.

Following scientific review, 3 applications were rated as "Good," 15 applications scored as "Excellent," and 9 were graded as "Outstanding." A total of 11 awards were made in the following areas: developmental biology – systems biology (two awards), soft issue biology – imaging technologies (five awards), tissue engineering – immunology (one award), tissue engineering – developmental biology (two awards), and other (one award). Dr. Wang provided the titles and investigator names for each of the 2008 BIRT awards according to the areas noted above.

Dr. Wang noted that the NIAMS Advisory Council approved the concept for BIRT for 2009. An RFA was released on August 22, 2008, and included the following areas:

- Autoimmunity – gender and sex factors
- Autoimmunity – systems biology
- Developmental biology – systems biology
- Regenerative medicine – immunology
- Soft tissue biology – imaging technologies

- Tissue engineering – developmental biology.

Applications are due February 19, 2009. Dr. Wang concluded her presentation by noting that in the future, BIRT will be open to all NIAMS scientific areas to: (1) build interdisciplinary teams, (2) add new dimensions to grants, and (3) yield insights that could not have been achieved by an isolated laboratory or individuals.

Discussion

Dr. Kathleen Green asked for clarification on whether any members of teams given BIRT awards can be from outside of the NIAMS. Dr. Wang indicated that this is the case, although the award was designed as a supplement to NIAMS grantees. She explained that investigators also supported by other organizations are welcome to apply, but the funding goes to the NIAMS grant.

X. NIAMS LONG-RANGE PLAN: FISCAL YEARS 2010 THROUGH 2014

Ms. Anita Linde, Director of NIAMS' Office of Science Policy and Planning, explained that the Institute's new long-range plan's purpose is guided by the following overarching questions: (1) Why is the NIAMS developing this plan? (2) How will it be used to guide future efforts? (3) How have past plans been used? (4) How will this plan align with NIH activities?

She noted that development of this plan was a collaborative effort relying heavily on the vision and expertise of NIAMS' extramural program scientific staff. Every NIH IC has a long-range plan, sometimes referred to as a "strategic plan." NIAMS' current long-range plan runs from FY 2006 through FY 2009. The new plan will cover FY 2010 through FY 2014. The plan was developed as part of the Institute's larger process to identify scientific needs, opportunities, and gaps that the portfolios in NIAMS' extramural program can cover across the spectrum of basic, translational, and clinical research. The plan itself, because of its 5-year window, complements NIAMS' annual scientific planning process, and is meant to articulate a broad scientific outline in terms of areas of interest and priorities of the Institute. The process of developing the long-range plan took into account existing plans at the NIH level overall.

The long-range plan for FY 2010 through 2014 takes into account research progress that has been made during the period encompassed by the current plan. It also was developed within the context of NIAMS' role in research progress, scientific opportunities and needs, and future NIAMS planning activities.

Ms. Linde explained that NIAMS' long-range plan for FY 2010 through 2014 has been conceptualized to include the following programmatic topic areas:

- Arthritis and rheumatic diseases

- Skin biology and diseases

- Muscle biology and diseases
- Musculoskeletal biology and diseases
- Bone biology and diseases.

The plan also includes the following broader, cross-cutting topic areas:

- Behavioral and biopsychosocial research
- Biomarker (biochemical, genetic, and imaging) identification, measurement, and validation
- Clinical research
- Complex genetic influences
- Immunology
- Regenerative medicine
- Research infrastructure.

In terms of next steps, Ms. Linde explained that a request for comments from the Institute's constituent communities will be posted online in September/October 2008, followed by roundtable discussions in November/December 2008. An update to the Advisory Council will be provided in January 2009. In January/February 2009, NIAMS Coalition representatives will meet to discuss the plan. A draft of the plan will be presented to the Council for review in June/July 2009, and the plan will be posted online for public comment in July/August 2009. In September 2009, it is planned to present the final plan to the Council and post it online.

XI. PROPOSED 2010 INITIATIVES

Dr. Katz explained that one proposed 2010 initiative requires concept clearance. Dr. Glenn Nuckolls introduced the concept and clarified the concept clearance procedure. Contract initiatives must be presented to the open Council. If the concept is approved, the Institute can request proposals, which will be peer reviewed, followed by NIAMS staff negotiating contract award(s).

Dr. Gayle Lester, Health Science Administrator in the NIAMS Division of Musculoskeletal Diseases, reminded Council members that they were sent background materials on this concept prior to the meeting. The concept's title is "Ancillary and Complementary Research to the Osteoarthritis Initiative." The Osteoarthritis Initiative (OAI) is a large effort by the NIAMS and six other NIH ICs as well as private partners from the pharmaceutical industry to create a research resource. The resource has been created and continues to be used by the community.

However, there is a great need for the NIAMS to provide direction and incentive for encouraging investigators to work towards specific discoveries using the database.

Dr. Lester explained that the purpose of this contract initiative is to: (1) accelerate the discoveries that could be made using the OAI dataset, (2) facilitate identification of modifiable and non-modifiable risk factors for the development and progression of knee osteoarthritis, and (3) expedite the development of sensitive and specific indices that can be used in diagnosis and characterization of knee osteoarthritis. Much more work will be put into the development of the RFP with more specifics on what the Institute would like to obtain with these contract initiatives. Contract solicitations are important for this particular purpose to promote the wider use of the OAI resource by the broader research community in a directed way. The data created can then be used to enrich the OAI dataset.

The complete text of the background information provided to Council members is included at the end of this report as Attachment 1.

Discussion

Dr. Gena Carter asked whether the final product will put more emphasis on having an ideal body weight as a modifiable risk factor. Dr. Lester indicated that the information on this concept did not reach that level of specificity, and agreed that body weight is an important risk factor. Dr. Jacobs, who was a member of the advisory panel evaluating the OAI, noted that the panel is very enthusiastic about the database and what it has been used to accomplish to date. There has been a significant investment in the OAI already, but it would benefit from additional investment. Dr. Jacobs added that the areas identified for additional focus by the advisory panel are well addressed by the initiative Dr. Lester described.

Council member Dr. S. Wright Caughman, Professor in the Department of Dermatology at Emory University, asked about the reliability, quality, and timeliness of the data within the context of recent technology advances (particularly imaging). Dr. Jacobs emphasized that in the OAI, all of the MRI images are acquired with state-of-the-art machines (i.e., three tesla).

Council members voted unanimously to approve the "Ancillary and Complementary Research to the Osteoarthritis Initiative" concept.

Additional new potential NIAMS Funding Opportunity Announcements (FOAs) were discussed briefly. These included:

- "Ancillary Studies to Large Clinical Projects." Dr. Katz noted that this project arose from discussions at a NIAMS retreat held earlier in the year. Dr. Weinstein asked whether it is possible to take advantage of existing infrastructure to prevent duplication of efforts on the part of researchers. Dr. Katz indicated that this FOA explicitly addresses this issue.

- "Replication, Fine Mapping and Sequencing: Following up on Genome-Wide Association Studies for Arthritis and Musculoskeletal and Skin Diseases." Dr. Katz reminded Council

members that this topic was discussed at a previous meeting, and added that this FOA includes fine mapping.

- "NIAMS SBIR Initiative To Promote Translation, Scale-Up, and Commercialization in Musculoskeletal and Skin Tissue Engineering and Regenerative Medicine."

- "Biomedical Research on the International Space Station."

In closing this session, Dr. Katz drew Council members' attention to the list of NIAMS FOAs that had been previously presented to the Council and noted that not all of these initiatives will be coming out in 2009, based on fiscal considerations.

XII. NIH CENTER FOR HUMAN IMMUNOLOGY, AUTOIMMUNITY AND INFLAMMATION (CHI)

Dr. Dan Kastner, Clinical Director at the NIAMS opened his presentation with a brief description of the NIH Clinical Center, which currently is underutilized and represents a somewhat untapped research opportunity on the NIH Campus. He commented that the current approach to clinical immunology research is fractured among NIH ICs. The NIH Intramural Roadmap, first proposed as a concept by NIH Director Dr. Elias Zerhouni in early 2006, includes a mandate to rethink the organization and operation of the NIH Intramural Program in a transformative manner. An NIH retreat in July 2006 included a focus on initiatives related to translational immunology, systems biology, and imaging. Three trans-NIH planning committees were formed in late 2006/early 2008. As a result of these activities, a new paradigm for pathophysiology-oriented research was developed for NIH ICs. This new paradigm includes: (1) a focus on common pathophysiologies; (2) goal-oriented, team-based research; (3) shared advanced technologies; (4) immune-based therapies in clinical protocols; and (5) integrated cell-animal-clinical-population studies.

Dr. Kastner discussed the rationale forming the new Center for Human Immunology, Autoimmunity, and Inflammation (CHI), which was based on the following points:

- Important and common diseases share immunological/inflammatory pathophysiologies, but basic immunology and immunology as applied to medicine are highly fragmented. The goal is to tie basic immunological science to multiple subspecialties in order to achieve real benefits in patient outcomes and to learn from human biology.

- Biological science is increasingly driven by large, multidisciplinary projects based on novel (expensive) technologies, but the traditional NIH incentive is to independent laboratory contributions. The CHI would be a large-scale intramural effort for trans-NIH integrated teams—increasing interaction, innovation, and the impact of the NIH.

- The NIH has world-class immunology expertise and a unique clinical research facility. The CHI would take advantage of the unique resources of the NIH Clinical Research Center.

Specific expectations for the CHI include: (1) true trans-NIH integration, beyond Institute barriers and with focused goals; (2) expanded human immunology training to excite and train young researchers; (3) novel technologies to advance both basic science and clinical research to develop the technical capacity to interrogate the human immune system in depth; (4) efficient, specialized efforts to reduce existing administrative barriers to true clinical research. (5) Daily interactions and coordination of efforts involving both basic and clinical scientists.

A well-attended and successful CHI Inaugural Conference was held on June 23, 2008, to obtain input from outside experts on scientific themes and organizational paradigms for the CHI, present the existing vision of the CHI to the larger NIH intramural community, and assess the level of enthusiasm on the part of NIH basic and clinical immunologists for participation in the CHI. The consensus theme that arose from the meeting was that the common denominator that could be developed as a strategic initiative for the CHI was creating a multidimensional atlas of human immunology. This effort would include:

- Multicolor flow cytometry, intracellular cytokines and signal transduction pathways, gene expression profiling of cell subsets, single nucleotide polymorphism analysis, mRNA, and epigenetic data.

- Studies of healthy volunteers, patients with well-characterized immune-mediated diseases and inflammatory processes, immunologically challenged individuals and patients before and during therapeutic intervention.

- A major emphasis on systems biology integration.

Dr. Kastner presented an organizational chart for the CHI and described its governance. Dr. Neal Young is the CHI Director; there are three CHI Associate Directors. Three cores are being developed within the CHI that focus on: (1) immunophenotying, (2) genomics and systems biology, and (3) clinical protocol development. Several NIH Institutes have contributed funds to the development of the CHI. These include the NIAMS, National Institute of Diabetes and Digestive and Kidney Diseases, National Cancer Institute, National Heart, Lung and Blood Institute, National Institute of Allergy and Infectious Diseases, and National Institute of Neurological Disorders and Stroke. It is hoped that as the CHI develops resources, there will be eventual buy-in from investigators interested in using these resources, resulting in a “standing” operation.

CHI clinical activities will include establishing a protocol-development service to streamline protocol writing and implementation, developing protocols for sampling the immunesome in normal individuals and patient populations, a Clinical Scholars in Immunology and Inflammation program, and new protocols based on available technologies. The CHI will be located on the seventh floor of Building 10 on the NIH Campus. Current CHI-related activities are occurring at the participating NIH Institutes. Dr. Kastner briefly outlined CHI benchmarks for FY 2009 and FY 2010, including those related to personnel, space, clinical activities, core platforms, and laboratory activities.

Discussion

Dr. Raisz asked how the NIH plans to hire and retain staff at the CHI given the issues academia wrestles with related to promotions and tenure. Dr. Kastner responded that it is currently planned that those at the CHI will have an affiliation at an NIH Institute (and therefore, promotion and tenure will be through those respective Institutes). Dr. John O'Shea, Scientific Director of the NIAMS, noted that the NIH Rules for Tenure have been changed and now encompass team science, so that participation in efforts such as the CHI can now be recognized. Dr. Katz closed the open session of the meeting, encouraging Council members to view the new exhibit located outside of the NIAMS offices in Building 31. The open session was adjourned at 12:30 p.m.

XIII. CONSIDERATION OF APPLICATIONS

The Council reviewed a total of 1,204 applications in closed session requesting $360,000,000 and recommended 1,204 for $360,000,000.

XIV. BONE BIOLOGY PROGRAM

This presentation was given to the Council during closed session.

XV. ADJOURNMENT

The 66th National Arthritis and Musculoskeletal and Skin Diseases Advisory Council Meeting was adjourned at 2:30 p.m. Proceedings of the public portion of this meeting are recorded in this summary.

I hereby certify that, to the best of my knowledge, the foregoing summary and attachments are accurate and complete.

Susana Serrate-Sztein, MD
Executive Secretary, National Arthritis and Musculoskeletal and Skin Diseases Advisory Council

Director, Division of Skin and Rheumatic Diseases, National Institute of Arthritis and Musculoskeletal and Skin Diseases

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Chairman, National Arthritis and Musculoskeletal and Skin Diseases Advisory Council

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