Department of Health and Human Services
National Institutes of Health (NIH)
Office of the Director (OD)
Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)

Council of Councils Meeting
June 29, 2011

Meeting Minutes

I. WELCOME

James M. Anderson, M.D., Ph.D., Chair, welcomed participants, NIH staff members, and members of the public to the meeting of the Council of Councils (the Council). The meeting opened at 8:31 a.m. on Wednesday, June 29, 2011, in Building 31c, 6th Floor, Room 6, on the NIH Campus, Bethesda, Maryland.

A. Attendance

1) Council Members Present

Chair: JAMES M. ANDERSON, M.D., PH.D., Director, DPCPSI, OD, NIH
Executive Secretary: ROBIN KAWAZOE, Deputy Director, DPCPSI, OD, NIH
STEPHEN L. BARNES, PH.D., University of Alabama at Birmingham
ELIZABETH B. CONCORDIA, M.A.S., University of Pittsburgh Medical Center, Pittsburgh, PA
RICHARD L. EHMAN, M.D., Mayo Clinic College of Medicine, Rochester, MN
JACK A. ELIAS, M.D., Yale University School of Medicine, New Haven, CT
CECILE A. FELDMAN, D.M.D., M.B.A., University of Medicine and Dentistry of New Jersey, Newark, NJ
EDWIN FLORES, PH.D., J.D., Chalker Flores, LLP, Dallas, TX
MAE O. GORDON, PH.D., Washington University School of Medicine, St. Louis, MO
PETER J. HOTEZ, M.D., PH.D., The George Washington University, Washington, DC
MARK O. LIVELY, PH.D., Wake Forest University School of Medicine, Winston-Salem, NC
HERBERT KIM LYERLY, M.D., Duke University Medical Center, Durham, NC
JEAN MCSWEENEY, PH.D., R.N., F.A.H.A., F.A.A.N., University of Arkansas Medical Sciences, Little Rock, AR
REGIS O'KEEFE, M.D., PH.D., University of Rochester School of Medicine and Dentistry, Rochester, NY
REGINA RABINOVICH, M.D., Bill & Melinda Gates Foundation, Seattle, WA
JOHN W. WALSH, Alpha-1 Foundation, Miami, FL
GARY L. WESTBROOK, M.D., Oregon Health and Science University, Portland, OR
TERRIE FOX WETLE, PH.D., Brown University Medical School, Providence, RI
LUTHER WILLIAMS, PH.D., Tuskegee University, Tuskegee, AL

MARINA E. WOLF, PH.D., Rosalind Franklin University of Medicine and Science, North Chicago, IL

2) Council Members Absent

ENRIQUETA C. BOND, PH.D., Burroughs-Wellcome Fund, Research Triangle Park, NC
DONNA BATES BOUCHER, Bates Group, Inc. Denver, CO
JORDAN COHEN, M.D., The George Washington University, Washington, DC
DAVID W. CRABB, M.D., Indiana University School of Medicine, Indianapolis, IN
GARRET A. FITZGERALD, M.D., University of Pennsylvania, Philadelphia, PA
DANIEL H. GERSCHWIND, M.D., PH.D., David Geffen School of Medicine, University of California, Los Angeles, CA
JOSEPH H. GRAZIANO, PH.D., Columbia University, New York, NY
JUANITA L. MERCHANT, M.D., PH.D., University of Michigan, Ann Arbor, MI
DAVID VALLE, M.D., Johns Hopkins University School of Medicine, Baltimore, MD

3) Ad Hoc Representatives

PAUL M. COATES, PH.D., Acting Director, Office of Disease Prevention, DPCPSI, OD
ROBERT M. KAPLAN, PH.D., Director, Office of Behavioral and Social Sciences Research, DPCPSI, OD
STACY CARRINGTON-LAWRENCE, PH.D., Chair of Etiology and Pathogenesis, Office of AIDS Research, DPCPSI, OD
VIVIAN W. PINN, M.D., Director, Office of Research on Women's Health, DPCPSI, OD
RASHMINA GOPAL SRIVASTAVA, PH.D., Program Officer, Office of Disease Prevention, Rare Diseases Research, DPCPSI, OD
JACK WHITESCARVER, PH.D., Director, Office of AIDS Research, DPCPSI, OD
ELIZABETH L. WILDER, PH.D., Director, Office of Strategic Coordination, DPCPSI, OD

4) Presenters in Attendance

Francis S. Collins, M.D., PH.D., Director, NIH
PHILIP SMITH, PH.D., Deputy Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases and Co-Chair, Common Fund Metabolomics Working Group
RICHARD CONROY, PH.D, Program Director, Division of Applied Science and Technology, National Institute of Biomedical Imaging and Co-Chair, Common Fund Single Cell Analysis Working Group
MARK GUYER, PH.D., Director, Division of Extramural Research, National Human Genome Research Institute and Co-Chair, Common Fund H3Africa Working Group

5) NIH Staff and Guests

In addition to Council members, presenters, and Directors, others in attendance included NIH staff and interested members of the public.

B. Meeting Procedures

Ms. Robin Kawazoe reviewed the following:

- Each member of the Council has submitted updates to their Conflict of Interest statements in accordance with the Federal Advisory Committee Act.
- Members were reminded not to speak individually on the Council's behalf or on activities not cleared by the Council.
- Although the members serve on advisory councils from various Institutes and Centers (ICs), their Council of Councils role is much broader since they are charged with advising the NIH Director on trans-NIH initiatives.
- Time has been allotted for each member to speak. Time for questions from the council members has been allocated at the end of the speaker's allotted time, however limited time is available for members of the public to ask questions. Comments can be submitted by the public after the meeting through the DPCPSI web site.
- Meeting minutes will be posted on the DPCPSI web site.

C. Future Meeting Dates

Future meetings and information will be posted on the DPCPSI web site.

II. DPCPSI UPDATE: EVOLUTION OF THE DIVISION OF PROGRAM COORDINATION, PLANNING, AND STRATEGIC INITIATIVES

Dr. James Anderson, Director of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), provided an update on the current and future directions of DPCPSI. With the proposed establishment of the National Center for the Advancement of Translational Sciences (NCATS), there will be marked changes to the structure and functions of DPCPSI and the Council of Councils. To address these proposed changes, Dr. Anderson provided an overview of the evolution of the Division and the transformation that will occur if NCATS is established.

While DPCPSI does not award grants, it is central to the planning, coordination, and management of the Common Fund, which was created to support trans-NIH projects that fundamentally transform the way science is conducted. Initiatives funded through the Common Fund are reviewed and recommended for approval by the Council of Councils.

In 2010, Dr. Francis Collins, NIH Director, sought advice from the NIH Scientific Management Review Board (SMRB) regarding how the NIH could support and administer translational and therapeutic sciences. In their report, submitted in December 2010, the SMRB recommended that the NIH establish a new center focused on translational and therapeutic medicine. The mission of this new center, the National Center for Advancement of Translational Sciences, will be "to advance the discipline of translational science and catalyze the development and testing of novel diagnostics and therapeutics across a wide range of human diseases and conditions." Three planning committees were convened to establish the mission and organization of NCATS, to

advise the NIH director on how best to leverage and organize NIH resources and synergize with the private sector on activities related to NCATS' mission, and to propose a reorganization plan for NIH to incorporate these changes.

Reorganization recommendations that are specific to DPCPSI are:

The role of the Council of Councils would be expanded to include a second level review of all grants moving to DPCPSI, concept clearance for all new programs, and creation of targeted subcommittees to increase the expertise and oversight by the Council.

DPCPSI would be reorganized, and a new Office of Research Infrastructure Programs (ORIP) would be established which would be composed of: the Division of Comparative Medicine; Division of Instruments, Infrastructure Resources, and Construction; and the Office of Science Education (which would be transferred from its current home in the OD Office of Science Policy).

The proposed programs to be included within NCATS are: Components of Molecular Libraries Program; Therapeutics for Rare and Neglected Diseases; Office of Rare Diseases Research; Rapid Access to Interventional Development; Clinical and Translational Science Awards; FDA-NIH Regulatory Science Program, and the proposed Cures Acceleration Network.

All other programs administered by NCRR will be transferred to specific institutes based on the "goodness of fit" model that would place programs adjacent to other programs with a similar mission and objective.

Discussion Highlights

- The grouping of Construction and Shared/High-End Instrumentation together under the ORIP may not be appropriate since major construction grants are multi-year and require long-term monitoring of usage, whereas Shared and High-End instrumentation grants are awarded on a year-by-year basis and require a different level of staff involvement. A suggestion was offered to pair Shared/High-End Instrumentation with Biomedical Technology Research resources.

- It was suggested that the Office of Science Education could be combined with the Office of Medical Applications of Research or moved to NIGMS.

- Many programs currently funded through the Common Fund may be incorporated into NCATS after the Common Fund granting period is completed. The idea of the Common Fund is to fund broad initiatives that cross many ICs and to facilitate the creation of new infrastructure.

Dr. Anderson requested that the members who had offered suggestions re the NCATS structure and programs email their suggestions to him.

III. REMARKS FROM THE DIRECTOR, NIH:

Francis Collins, M.D., Ph.D., Director of the NIH, provided an update on federal funding and insights into the future direction of the NIH. He emphasized the mission of the NIH as a steward of medical and behavioral research for the US. Dr. Collins also noted that NIH is looking for careful, thoughtful guidance related to the Common Fund, noting that how CF research is funded is particularly interesting because of the intent for such studies to be high-risk and high-reward, and covering many different diseases and organ systems. He mentioned the decline in NIH's budget, from $31.238 billion in FY 2010 to $30.924 billion in FY 2011 and noted that we are facing a very uncertain budget climate with FY 2012 deliberations caught up with negotiations about extending the debt ceiling.

Dr. Collins highlighted the successes of the NIH in three main areas, in terms of investments in innovation: accelerating discovery through the development of technology, advancing translational science, and supporting novel funding mechanisms to encourage both new investigators and new ideas. New sequencing technology has rapidly decreased the cost of genomic sequencing. This has not only advanced research, but has been translated into clinical success. Using sequencing technology, it is now possible to detect genetic or molecular aberrations in patients. This has allowed for new diagnoses in cancer and rare diseases that have previously remained undetected. Because of this technology, a new field has emerged that has provided new avenues of research in the creation of novel therapeutics aimed at molecular targets.

Currently, over 4000 diseases are known to have some molecular alteration that contributes to the development of disease. However, only 200 of such diseases currently have a molecular based therapy. This highlights a huge potential for conducting new research and developing new molecular therapeutics that exists. The NIH has and will continue to aid in this arena by leveraging the knowledge it has previously gained in this field and by applying its resources to aid in clinical trial implementation. In addition, NIH has the resources to study and improve the process of drug development by evaluating the pipeline of drug development and by working with industry partners, academic researchers, and the FDA to streamline the process. Collaborations have already begun with the FDA to improve FDA science and to inform NIH researchers about the FDA requirements.

To catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions Dr. Collins has proposed the creation of the National Center for Advancing Translational Sciences (NCATS). A supplemental request for approval and appropriations for NCATS was included in the President's FY 2012 budget request and is under consideration. NCATS will study the steps in diagnostics and therapeutics development, testing, and implementation into patient care; identify bottlenecks amenable to re-engineering; and experiment with innovative methods to streamline the process.

NCATS will complement—not compete with— translational research being carried out by the private sector. By focusing on the development of innovative new ways of doing

therapeutic and diagnostic discovery as opposed to developing therapeutics themselves, NCATS can enable others to bring safer and more effective medicines to patients. This Center will not reduce NIH's commitment to basic science. Establishing this Center will require a reorganization of parts of the NIH. NCATS will subsume several existing programs, including the Clinical and Translational Sciences Awards that are managed by NCRR as well as the proposed Cures Acceleration Network.

Dr. Collins went on to note that NIH continues to be committed to encouraging diversity within the scientific community. Several programs have been established to enhance diversity among new researchers and novel ideas. These include the Transformative R01 (TR01) awards that seek to transform or create a new research area, the Pioneer Awards that promote and support exceptionally creative scientists, the New Innovator Award that supports creative new investigators, and the Early Independence Awards that support the transition of superior graduate students or clinical trainees directly into faculty positions without requiring further postdoctoral training.

While challenges to the research community are many, there is power in numbers. Scientists need to advocate for their work to inform the public of the benefits of research and raise the profile of institutions like the NIH.

Discussion Highlights

- In light of reduced funding for NIH and the creation of NCATS, it is particularly critical to continue the support of areas of research such as behavioral research. New ideas regarding the establishment or incorporation of new technologies into behavioral research are necessary.

- Global health initiatives, as part of NCATS and the Common Fund, will encourage biotechnology companies to occupy a global space and will aid in research and drug development in rare diseases.

- Efforts should be taken to work with other foundations like the Gates Foundation and the Wellcome Trust to increase global health initiatives.

- Intrusion by political forces on the grant process and on funding decisions will limit the ability and flexibility of NIH and other organizations to support the most meritorious science, including clinical trials.

- New therapeutics or new applications of developed therapies will benefit science in the long term.

- The inclusion of minorities, and lack thereof, has been studied in the past. No one has been held accountable for making changes or improvements, including the evaluation of whether scientific training is appropriate and adequate for our workforce. A new taskforce has been established, to be led by Dr. Shirley Tilghman, that will evaluate Ph.D. training programs to understand how training should be altered to better prepare the workforce for any scientific career. A cultural change in training approaches may be necessary so that "alternative careers" in science are not deemed failures or taboo.

- Studying the process of drug development throughout all the stages, from initial target identification to application in humans, can aid in streamlining the process. For example, initial identification of toxicity through a primary screen may save time and money by avoiding use of toxic drugs in studies that determine mechanism.

IV. REVIEW OF THE NIH COMMON FUND INITIATIVE CONCEPTS: PROCESS AND CRITERIA

Dr. Elizabeth Wilder, Director, Office of Strategic Coordination, DPCPSI, explained that as part of Phase 2 of the strategic planning process, one goal of this meeting is to determine if the Common Fund Initiatives proposed meet the overall objectives of the Common Fund. Common Fund programs should transform an area(s) of research and be able to do so in a reasonable timeframe. Ideally, these programs should be sustainable or have other mechanisms for funding after 5-10 years. Programs should also have a broad impact across the objectives of multiple ICs, not just limited to the scope of an individual Institute.

V. PRESENTATION: COMMON FUND INITIATIVE CONCEPT #1: METABOLOMICS

Dr. Phillip Smith, co-chair of the Metabolomics Working Group, presented the Common Fund Initiative Concept in Metabolomics. Metabolomics is the study of the unique chemical footprint left behind by specific cellular processes. This involves the systemic interrogation of these metabolic processes analyzed using mass spectrometry (MS) and nuclear magnetic resonance (NMR) approaches. These approaches are very powerful and can provide valuable insight into metabolism. However, few core facilities exist and few researchers are properly trained in biochemistry, physiology, and spectrometry to conduct and properly evaluate these data.

NIH has funded several successful metabolomics projects. These projects have propelled their respective fields in many ways and provided insight into disease processes. Studies include the identification of new branched-chain amino acid alterations that identify those most at risk for developing diabetes, the identification of specific plasma lipids that aid in diagnosis of heart disease, and insights into the interaction of the microbiome in normal and obese individuals. Evaluation of the NIH portfolio of funded metabolomics grants revealed that most of the NIH investment is in investigator-initiated awards. While these projects represent a substantial investment, metabolomic projects are funded to a much lesser extent than other 'omics projects including genomics and proteomics. It is thought that limited access to facilities and properly trained personnel have contributed to the lack of development of this field.

Metabolomics projects were previously funded through a Roadmap Initiative in 2004. This program was dedicated to improving MS and NMR technology and to develop standards in collaboration with the National Institute of Standards and Technology (NIST). As a result, metabolomics has expanded in the U.S. and 38 core facilities offering metabolomics analysis have been established. The pace of this expansion, however, has greatly lagged behind that of the genomics or proteomics fields, as has the

production of standards. Current core facilities are working at capacity and have little resources available to collaborate with new investigators on new projects. Therefore, the field has not been able to move forward effectively.

The Working Group has identified a need for investment in metabolomics infrastructure, training, research, data sharing, and the development of standards. Comprehensive core facilities would expand on existing resources and be aligned with the Clinical and Translational Science Award resources that are already established. This would be accomplished by increasing the equipment and infrastructure within core facilities, by providing seed funding to hire appropriate, well-trained staff, and to provide funding for pilot programs aimed at new areas of research.

Lack of sufficient training is seen as a major limiting step to the expansion of the metabolomics field. Therefore, to facilitate hands-on training of young investigators, this Common Fund Initiative would fund training programs including short courses at Cold Spring Harbor or Jackson Labs and K18 career development or supplement awards. This strategy will provide short-term and long-term training to increase the expertise in the field.

The Initiative will seek to improve technology to scale down the applicability of the approach to a single cell level. Technological improvements will also facilitate quantitation. Reference standards will be created and shared in order to improve the identification of novel pathways and metabolites. Metabolomic data generated will be shared through newly developed storage and analysis tools and cloud-based IT approaches. Data sets will be standardized to provide useful data for meta-analysis.

Discussion Highlights

- Currently, many of these core facilities are focused on proteomics instead of metabolomics. Both of these fields use MS and NMR, however few researchers are currently trained in how to conduct metabolomics research. Training is essential to drive the field forward.
- Investing in metabolomics will have broad impact across the ICs.
- Currently, few groups exist that can integrate the data further than just producing a profile that is associated with a specific disease state.
- Infrastructure for core facilities can come from Common Fund Initiatives but can be sustained in the future through fee-for-service models. These models already exist within core facilities for processing and analysis of other 'omics data.
- Creating computer infrastructure to share standardized data sets will aid in international collaboration.

Recommendation

The Council voted unanimously to approve this Initiative without modification.

VI. DISCUSSION OF THE TRANSFORMATIVE R01 GRANT MECHANISM

Dr. Wilder updated the Council on the strategic planning process of the Common Fund Initiatives. To gain insight from a varying group of scientists, DPCPSI gathered a group of new investigators, Associate Professor or more junior, and convened the Innovation Brainstorm: Transforming Discovery into Impact meeting. Participants were selected by IC directors and were asked to identify a recent publication they deemed to be of very high impact. These papers were shared among participants and a consensus of 8 high impact areas was reached. These areas included:

Moving beyond genome-wide association studies: synthesis and validation of data

Beyond the Microbiome project: understanding how the microbiome influences health

Comprehensive analysis: how to study multiple aspects that affect health at one time. For example, nutrition and infectious agents.

Artificial organs as tools for translation

Proteomics and therapeutics

NIH Award strategies: multidisciplinary approaches

Computational analysis

Molecular classification of disease

These topics are under review by IC directors in an effort to establish new program directions for FY 2013. Input will be sought from the Council and public about these initiatives. Topics selected for Phase 2 planning will be submitted to Drs. Anderson and Collins in October.

The Transformative R01 program is designed to fund transformative work without limiting the scope or budget for the project. This program has met with a few concerns. Unexpectedly, the number of applications and the size of the budgets requested are significantly lower than anticipated. There are concerns that applications for this program are not addressing the objectives of this program and are not truly transformative. This could be due to dwindling reviewer enthusiasm for this program, or applicants and reviewers are unable to avoid treating this mechanism like the traditional R01 grant.

Dr. Wilder added that the NIH Director's Early Independence Awards will undergo second tier review by the Council in August. This program is aimed at graduate students, or those who recently graduated with a doctorate who have the maturity, solid projects, and the ability to run a research laboratory without the need to complete a postdoctoral fellowship.

Discussion Highlights

- Self-identifying if one has high impact or transformative ideas may be preventing people from applying for TR01s. It may be more effective if ICs selected the top five applications they deemed transformative for further review or for additional funds.

- The title of high risk/high reward may be inappropriate for clinical studies. Having a high-risk clinical trial does not exude confidence in the outcomes.

- Many scientists may not be aware of the TR01 funding mechanism. A reeducation workshop may increase the awareness of this program.

- These grants are currently nonrenewable, which may be a limiting factor to submission of projects. A potential continuation of funds may be considered.

- Low success rates of receiving these grants may be discouraging many from applying. Submission of pre-proposals that are then selected for a full proposal submission, if the first tier review expresses interest in the project, could increase the potential success rate for the applicant and increase the application pool. These pre-proposals would have to provide enough content for a thorough review.

- Funding of behavioral science programs may be difficult under the TR01 program as these studies tend to be transformative but not high impact.

- Established researchers with more access to infrastructure may be more likely to obtain these grants.

- Increasing numbers of publications in top-tier journals are published from foreign labs. It would be interesting to investigate how these labs are supported and if foreign governments fund these labs differently than the US.

VII. CLOSED SESSION—DR. ELIZABETH WILDER, Ph.D.

This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c)(4), 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 Council conducted the second-level review of applications submitted in response to RFA RM-10-010, "Roadmap Transformative R01 Program." Members were instructed to exit the room if they deemed that their participation in the deliberation of any matter before the Council would be a real conflict or that it would represent the appearance of a conflict.

VIII. PRESENTATION: COMMON FUND INITIATIVE CONCEPT #2: SINGLE CELL ANALYSIS

Dr. Richard Conroy, co-chair of the Single Cell Analysis Working Group, presented the Common Fund Initiative concept in Single Cell Analysis. Increasing data suggest that

cell populations, including those believed to be of a single subtype, are heterogenous. These observations have reinforced the need to study cells on a single cell basis and have led to the development of this Common Fund Initiative. This Initiative has three overall goals; to develop and validate new technologies that will allow for single cell analysis both *in vitro* and *in vivo*, to increase the understanding of the importance of cell heterogeneity, and to assemble multidisciplinary teams that can address challenges to developing single cell approaches.

By studying cell populations instead of single cells, an average of responses is detected. Averaging data from a diverse population obscures critical parameters that are relevant to health and disease including identification and study of rare cells and understanding the dynamic states of differentiation. To be able to study single cells, many challenges will have to be overcome. These are not trivial elements, but rather they address the fundamental understanding of cells, organs, and organisms. To gain insight into health and disease, it will be important to understand a cell state, to understand how environmental or spatial-temporal parameters influence cell dynamics, how to differentiate signal from noise and improve signal detection, and to coordinate cell responses with cell phenotypes and outcomes. This can only be achieved through single cell analysis.

Single cell analysis projects are currently funded by 22 Institutes and Centers at NIH. This clearly demonstrates the broad interest in single cell analysis, however to date there has not been a coordinated effort within NIH to advance the field. Additionally, these awards have been for projects that are using conventional techniques, which further highlights the importance of developing new technology aimed at single cell analysis. The funding level and interest in scaling down to the individual single cell level has been steadily increasing both within NIH and worldwide. Clinical interest in studying and diagnosing diseases at the single cell level has also been increasing. Together this demonstrates a significant level of support and rationale to develop new technologies and methodologies that are able visualize parameters at the single cell level.

Mass cytometry is among the new technologies under development. This technique, developed by Dr. Gary Nolan, labels internal components of cells using isotopes of transitional metals. Since these metals do not exist in the cells naturally and there is no spectral overlap of fluorescent signals, the number of markers that can be interrogated at one time is much greater than current fluorescent labeling methods used in flow cytometry. Once labeled with transitional metals, cells can be analyzed by mass spectrometry and flow cytometry analysis tools. This will be a powerful technique that can be applied in many fields.

The goal of this Initiative is to improve detection at the single cell level, to produce a first-in-class clinical diagnostic tool, and to create methods to identify single cells based on defined criteria and characteristics. This proposal is transformative and has the potential for a high impact over many fields.

Discussion Highlights

- There is a need to study a single cell within the context of a heterogenous cell population in a parallel format that interrogates many parameters simultaneously.
- Studying cells in the context of external environmental influences is critical, and it may be feasible as a result of this Common Fund Initiative in 5 to 10 years.
- Heterogeneity is a term that can be used to describe a mixed population of cells, but can also be used to describe different stages of differentiation or activation of one cell type.

Recommendation

The Council voted unanimously to approve this Initiative without modification.

IX. PRESENTATION: COMMON FUND INITIATIVE CONCEPT #3: HUMAN HEREDITY AND HEALTH IN AFRICA (H3AFRICA)

Dr. Mark Guyer, co-chair of the Human Heredity and Health in Africa (H3Africa) Working Group, presented the Common Fund Initiative concept for improving health and research in Africa. Global health is a national priority. As the recent increase in non-communicable diseases continues to spread across Africa, a concomitant increase in the opportunity for biomedical researchers to harness new information and to access new ideas from new investigators also exists. However, in order to successfully research these disease states and to promote new African investigators, new infrastructure and research capacity are needed. To that end, two NIH-funded global health initiatives have been proposed. The Medical Education Partnership Initiative (MEPI) is a currently supported NIH Common Fund Initiative, aimed at increasing clinical education and research capacity within African medical institutions. The Human Heredity and Health in Africa (H3Africa) Initiative is still under consideration.

Although the NIH currently funds genetic research in Africa, few of these research grants are awarded to African investigators that are established in African institutions. In collaboration with the Wellcome Trust and the African Society for Human Genetics (AfSHG), NIH established working groups to generate ideas on how to address the feasibility and potential of an African Genome Project. From these working groups, H3Africa emerged. A formal collaboration was established and a white paper proposing an African genome project was published, publicly reviewed, and ratified. This proposal had three main goals: to bring new technology and research approaches in genomics to Africa, to increase the training and competitiveness of African researchers within Africa, and to build bioinformatics and biorepository infrastructure that expand collaborations among researchers in Africa. The H3Africa initiative encompasses these three goals.

The H3Africa programs will be established throughout the African continent. Nodes housing administrative, research, bioinformatics, and biorepository functions will be distributed throughout the continent, but will be interconnected to facilitate research

capabilities. When possible, these programs will align with the MEPI program that is already established and operational.

Enhancing bioinformatics in Africa will require enhancing the communication and computing infrastructure throughout the Continent. This will also require increased training for scientists in this field. A request for applications (RFA) for bioinformatics networks has been released.

Building biorepositories at one or more locations on the African continent will allow for the receipt, storage, and distribution of samples (DNA, cell lines, and serum) among researchers both in Africa and internationally. To establish such a resource, issues regarding transportation, shipping, and intellectual property will have to be addressed. It is envisioned that 2 year planning grants will be necessary to assess the needs of building a repository prior to awarding full-scale grants. Sustainability of these biorepositories will have to be addressed in each grant proposal to ensure funding availability after the Common Fund program ends.

Investigator-initiated research projects will focus on genetics and genomics in Africa. New technology to conduct genetic-based research is now readily available. Such technology establishes the ability to link genetic variability to disease predisposition and increases the understanding of the biology of disease. This will aid in the development of novel diagnostic measures and procedures. The African population is currently underrepresented in such genetic studies. Therefore, a tremendous opportunity for increased understanding of many diseases exists. Potential projects will encompass genetic and environmental influences on diseases including non-communicable diseases, communicable diseases, Mendelian diseases, pharmacogenomics, and the microbiome. These projects will also contain a training component to help establish new investigators in genomics. Data generated through research efforts will be linked to the bioinformatics network and samples will be deposited in the biorepository. By integrating these, the research will help develop the biorepository, bioinformatics, and communication networks.

In collaboration with the Fogarty International Center, projects will be supported to investigate the societal implications of genetic and genomic research. It is envisioned that these will be small grants, but will evaluate large topics including research ethics, legal considerations of, and societal outcomes from genetics research.

Success of the H3Africa program will be measured as the ability of African scientists to develop their own independent research program, to be able to publish their findings, and to become competitive for grants. Overall, the goal of H3Africa is to improve African health and to increase collaborations among African researchers.

Discussion Highlights

- Other organizations akin to the Wellcome Trust may be able to help sustain this venture when Common Funds are no longer available.

- As proposed, this program is longer than a 5-year project. Discussions within NIH Institutes are required to address sustainability after 5 years. If plans for future funding are not agreed upon and established, this money will be wasted.

- Research projects on ethics may require more than $50,000 grants. Other funding organizations have supported ethics projects that cost $10 million. Their experience has been that this level of support is justified and necessary, especially for collaborative efforts.

- Global health issues need to be funded. Although acquiring significant co-funding from the Wellcome Trust is an enormous advantage, projects will be funded in parallel, not co-funded. There will be a joint website established and project announcements will be coordinated, but projects will be funded and administered separately.

- Currently, $59 million is spent by the NIH for grants in Africa. It is surprising that with this level of support that no African investigators are self-supporting. This raises significant questions about how to measure success.

- There is concern that purchasing expensive, specialized equipment in a region with limited infrastructure and training will result in the equipment being abandoned or stolen at the end of the funding period.

- Tight controls on spending will be required to avoid abuse when money is provided to these institutions. Working in less advanced countries has unique issues that need to be addressed and controlled. Lessons from other organizations that have provided funding to third world nations should be heeded before moving forward with taxpayer dollars.

- It is unclear why genetics and genome research is the basis for this proposal when research into vaccine or low-cost diagnostic development may be a better use of the money and resources.

- Provisions are under consideration for access to and use of bioinformatics data. Additional provisions regarding publication and embargo of materials are necessary to protect researchers and allow them use of their data first.

- Diseases that afflict the U.S. population are also increasing in Sub-Saharan Africa. Research in these populations will directly benefit patients in the U.S.

- Neglected diseases that afflict poor populations are present in both U.S. and African populations.

- The experience from the Gates Foundation has been that increasing training in Africa has brought African investigators back to Africa. This occurs as long as there is continued funding to support the work after they return and the initial source of funding has expired. There is concern that these trained researchers will leave for other countries when the funding no longer exists.

- Having matching funds from other organizations is the approach that is required to funding this type of initiative. Future support can be phased in as the Common Fund support ends. This could be from ICs or other organizations, although it is hard to determine where the source of funding will be 5 years in the future.

- It appears that the assumption is that some part of the NIH will be the source of continued funding after the Common Fund support expires.

- The overall goal of studying genetics in Africa should be clearly stated. Understanding gained through the study of African populations can improve global health and benefit the research community.

- African governments do not appear to be committed to this process. No evidence of their support is included. They do appear to support biotechnology as having a viable economic benefit to them.

- The level of research currently being conducted across Africa is unclear. Providing details about the current research activities and funding support will aid in deciding if this is appropriate for approval. If researchers are on the cusp of sustainability and have institutional and governmental support, then enthusiasm for this program is elevated.

- Other countries including Spain and Japan have provided research funding to African investigators. This proposal is building on existing infrastructure. It is not building an entire research program from the ground floor.

- Current infrastructure within African institutions can be leveraged to support expanded research programs.

- Initiatives under the African Union currently exist to enhance the science infrastructure in African countries.

Recommendation

A motion to approve the Initiative as proposed received a vote of five in favor of the motion and eight against. Although the Council members generally supported the Initiative, two main areas of concern were expressed: 1) sustainability of the project long term and; 2) it was unclear whether this was ultimately a project to improve science in Africa or to improve health in Africa. The Council felt that if the goal is to improve health in Africa, additional rationale supporting the use of resources for a global health initiative should be addressed.