The National Advisory Environmental Health Sciences Council convened its one hundred thirty-eighth regular meeting on February 20-21, 2013 in the Rall Building, Rodbell Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, NC. Dr. Linda Birnbaum presided as Chair.

The meeting was open to the public on February 20, 2013 from 8:30 a.m. to 5:00 p.m. In accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), the meeting was closed to the public on February 21, 2013 from 8:30 a.m. to 12:00 p.m. for consideration of grant applications. Notice of the meeting was published in the Federal Register.

Council Members Present

Kim Boekelheide, MD, PhD
Julia Brody, PhD
Marie-Francoise Chesselet, MD, PhD
Vivian Cheung, MD
Lisa Conti, DVM, MPH
Thomas Gasiewicz, PhD
Andrea Hricko, MPH
Howard Hu, MD, MPH, ScD (by telephone)
Randall Kramer, PhD
Mary M. Lee, MD
R. Stephen Lloyd, PhD
Yvonne Maddox, PhD (ex-officio) (by telephone)
Thomas McKone, PhD
Jennifer Orme-Zavaleta, PhD (ex-officio)
Sem Phan, MD, PhD
Edward Postlethwait, PhD
Palmer Taylor, PhD
Viola Waghiji
Deborah Winn, PhD (ex-officio)
Elizabeth Yeampierre, JD
NIEHS Staff

Kathy Ahlmark
Janice Allen, PhD
Beth Anderson
Robin Arnette, PhD
Joellen Austin
John Balbus, MD
David Balshaw, PhD
Martha Barnes
Linda Bass, PhD
Sharon Beard
Linda Birnbaum, PhD
Abee Boyles, PhD
Rebecca Boyles
Danielle Carlin, PhD
Trisha Castranio
Lisa Chadwick, PhD
Pamela Clark
Jennifer Collins
Gwen Collman, PhD
Caroline Dilworth, PhD
Christina Drew, PhD
Serena Dudek, PhD
Lisa Edwards
Benny Encarnacion
Suzanne Fenton, PhD
Symma Finn, PhD
Christine Flowers
Stavros Garantziotis, MD
Barbara Gittleman
Kimberly Gray, PhD
Astrid Haugen
Michelle Heacock, PhD
Jerry Heindel, PhD
Heather Henry, PhD
Michael Humble, PhD
Laurie Johnson
Ed Kang
Helena Kennedy
Annette Kirshner, PhD
Cindy Lawler, PhD
Leping Li, PhD
Chris Long
Robin Mackar
J. Patrick Mastin, PhD
Kim McAllister, PhD
Steven McCaw
Liz McNair
Sri Nadadur, PhD
Liam O’Fallon
Ted Outwater
Jerry Phelps
Kristi Pettibone
Nicole Popovich
Molly Puente
Leslie Reinlib, PhD
Andrew Rooney, PhD
Elizabeth Ruben
Angie Sanders
John Schelp
William Schrader, PhD
Thad Schug, PhD
Daniel Shaughnessy, PhD
Carol Shreffler, PhD
William A. Suk, PhD, MPH
Kimberly Thigpen Tart, JD
Claudia Thompson, PhD
Sally Tilotta, PhD
Frederick Tyson, PhD
Mary Wolfe, PhD
Leroy Worth, PhD
Rick Woychik, PhD
Darryl Zeldin, MD

Members of the Public Present

Maureen Avakian, MDB, Inc.
Dan Baden, PhD, University of North Carolina Wilmington
Rich Cohn, SRA International
Sally Darney, PhD, USEPA
Andrew Feinberg, MD, Johns Hopkins University
Michele Forman, PhD, University of Texas Austin
Nevin Fouts, ICF
Michael Gould, PhD, University of Wisconsin-Madison
Ernie Hood, Bridport Services
Nancy Lamontagne, MDB, Inc.
Pia MacDonald, PhD, SSS
Laura McGuinn, UNC
Michael Phillips, RTI International
Jeanne Rizzo, RN, Breast Cancer Fund
William Wade, SAIC
Robert Yates, SSS
I. Call To Order and Opening Remarks

NIEHS/NTP Director and Council Chairman Dr. Linda Birnbaum welcomed attendees and called the meeting to order. She mentioned that Council members Dr. Yvonne Maddox and Dr. Howard Hu would be attending by telephone. She then asked all present in the room to introduce themselves, which they did.

II. Review of Confidentiality and Conflict of Interest

NIEHS Director of the Division of Extramural Training and Research and Designated Federal Official Dr. Gwen Collman reviewed the Conflict of Interest and Confidentiality procedures, which had been provided earlier to Council members in written form, and went over various other administrative matters.

III. Consideration of September 2012 Meeting Minutes

Approval of the September 2012 minutes was moved and seconded, and Council voted unanimously to approve the minutes. Dr. Collman noted the dates of the upcoming Council meetings for members to put on their calendars.

IV. Report of the Director, NIEHS

Dr. Birnbaum updated Council on institute developments in the five months since the September 2012 Council meeting.

Recent activities have included the identification of eight trans-divisional priorities under the new NIEHS Strategic Plan, receipt of grant applications for time-sensitive research in environmental health related to Superstorm Sandy, celebration of the 20th anniversary of the NIEHS-FDA cooperative agreement, the holding of a "Virtual Forum on Obesity using webinar technology, and participation by NIEHS grantees and staff scientists in the Global Burden of Disease 2010 report published in the January edition of The Lancet. Dr. Fred Miller has stepped down from the position of Acting Director of the NIEHS Clinical Research Unit, with Dr. Stavros Garantziotis assuming the role of Acting Director, with the search for a permanent Director underway.

Regarding budgetary considerations, Dr. Birnbaum reported that the Federal government is currently operating under a Continuing Resolution (CR) due to expire March 27, when a shutdown could be triggered if Congress does not pass either another CR or a budget. Sequestration is also looming, with the prospect of substantial, automatic budget cuts if Congress does not act to avert them. She noted that NIEHS leadership is paying close attention to developments and planning as much as possible, but that the situation is changed on a daily basis. She also summarized recent legislative activities, including three Congressional briefings.
She provided brief synopses of several recent scientific advances involving publications by NIEHS/NTP personnel or grantees, and reported on recent institute news and highlights, including a planned reinvention of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), where Rear Admiral William Stokes, DVM had served as director, along with the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). Stokes retired from NIEHS and the Public Health Service in January, and Dr. Warren Casey is now serving as Acting Director of the agencies. She also related several developments regarding research on breast cancer and the environment, including the February 13 release of the report prepared for the Secretary of HHS by the Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC).

She described several recent NIEHS-related meetings at the National Academy of Sciences, and reported on a variety of both recent and upcoming meetings and events. She also provided a rundown of awards and recognitions given to NIEHS employees in recent months, as well as an update on developments from Building One and HHS, and a bit of background information on the new NIH and NIEHS logos.

Regarding sequestration, Dr. Lloyd asked Dr. Birnbaum what the guiding principles for implementation would be at NIEHS, if it should come to pass. Dr. Birnbaum replied that if the deep, automatic cuts did come, everyone would feel some pain. Regarding the grants program, she said that different ICs would be expected to handle their cuts differently, depending on their own wants and needs. Dr. Boekelheide asked that Council be included in priority deliberations regarding budget cuts. Dr. Birnbaum replied that although much of that process would take place among leadership, Council would certainly have opportunity for discussion and involvement in some parts of the process. Dr. Taylor recommended expanded efforts at collaboration, particularly in areas such as global health. Dr. Birnbaum noted that that was one of the overarching themes in the new NIEHS Strategic Plan, and that collaboration in that area is necessary.

V. Report of the Director, DERT

DERT Director Dr. Gwen Collman updated Council on DERT developments, beginning with staff activities.

She described the Worker Training Program response to Hurricane Sandy, which included response activities by current grantees and partnerships with various agencies in the affected areas. As of February 13, over 400 workers had been trained on site-specific health and safety awareness, and more than 45,000 informational booklets had been distributed to clean-up workers.

Turning to the budget, Dr. Collman said that research project grants (RPGs) represented 76.6% ($248 million) of the NIEHS budget in FY 2012. RO1 grants
comprised 70.6% ($174.6 million) of that total. She related several other pieces of budgetary information designed to provide an overview of the FY 2012 budget expenditures, as well as data on RFAs and PARs planned for FY 2013.

Dr. Collman informed Council on changes to FY 2012 language in Council Delegated Authorities, and requested a motion to accept the Authorities. It was so moved, and Council voted unanimously in favor. She then described the Biennial Report to Council on Gender and Minority Inclusion, which Council voted unanimously to accept.

Dr. Gasiewicz noted that other institutes had cut "R" grants, and asked whether NIEHS was considering reducing the number of R grants, particularly R21s, in its portfolio. Dr. Collman said there were no plans to do away with involvement in the R21 mechanism.

Grantee Dr. Andrew Feinberg from Johns Hopkins University praised the DERT staff for its extraordinary level of engagement with and service to grantees. Dr. Collman said she appreciated the recognition, and that customer service is very important at NIEHS.

VI. Report of the Interagency Breast Cancer and Environmental Research Coordinating Committee

Dr. Birnbaum introduced the speakers: Dr. Michele Forman, who was the committee's chair and also chaired one of the three subcommittees (State-of-the-Science), Dr. Michael Gould, who chaired the Research Process subcommittee, and Ms. Jeanne Rizzo, RN, who chaired the Research Translation, Dissemination and Policy Implications (RTDPI) subcommittee. She directed Council members to a four-page summary of the committee's recommendations (http://www.niehs.nih.gov/about/assets/docs/summary_of_recs.pdf) and to the full 270-page report, Breast Cancer and the Environment: Prioritizing Prevention (http://www.niehs.nih.gov/about/assets/docs/ibcercc_full.pdf), which was released February 12, 2013.

Dr. Forman provided an overview of the IBCERCC which was established as a result of the Breast Cancer and Environmental Research Act of 2008. The committee, to be composed of federal and non-federal members, was mandated to review research on breast cancer and the environment and make recommendations for eliminating knowledge gaps. Its first meeting was held September 30, 2010. The committee’s charge was to:

- Review federal research on environmental and genomic factors related to breast cancer, and outline key research questions, methodologies, and knowledge gaps
- Identify scientific advances in breast cancer research
• Develop a comprehensive strategy for accelerating transdisciplinary, innovative and collaborative research on breast cancer and the environment across federal agencies and in partnership with nonfederal organizations
• Determine how to increase public participation in decisions about breast cancer research and dissemination of information on research progress

The committee, which included three working subcommittees, met in person 4 times and via conference calls and webinars 33 times over the course of the process. The IBCERCC was a chartered federal advisory committee reporting to the NIEHS Director. The process was overseen by the Co-Executive Secretaries, Dr. Collman from NIEHS and Dr. Debbie Winn from the National Cancer Institute.

Dr. Forman provided statistics regarding the disease burden of breast cancer, and its incidence. She described the major recommendations contained in the report:

• Make prevention a priority.
• Transform how research is conducted.
• Intensify the study of chemical and physical factors.
• Plan strategically across Federal agencies.
• Engage public stakeholders at every phase of the research process.
• Train transdisciplinary researchers.
• Translate and communicate science to society by building the platform from the start into every funded program.

As its chair, Dr. Forman also reported on the deliberations of the State-of-the-Science (SOS) subcommittee, which was based on the core premises that timing matters, and animal and human research matters. Timing matters because there are windows of susceptibility during the life course when environmental exposures could influence development and cancer. The animal to human research paradigm provides an optimal approach to discovery of windows of susceptibility, mechanisms underlying and pathways related to derangement of normal breast development and cancer risk. The subcommittee felt that it was important to consider the entire body of evidence in elucidating the complex relationships between breast cancer and the environment, emphasizing transdisciplinary research and the life-course approach.

The SOS identified several areas where additional research is needed, including: environmental exposures and breast cancer risk overall and by subtype, by race and ethnicity, and in low-income communities; responses to mixtures; monitoring of environmental exposures with quick feedback to the public; and methodological issues such as risk assessment. The subcommittee also sought to answer the question, "Why don't we know more?"
• We have not been looking at environmental exposures at the correct life stage.
• We have not examined the correct environmental agents.
• We have not asked the right questions about complex mixtures, genetic susceptibility, and breast cancer subtypes.

Dr. Gould presented a synopsis of the work of the Research Process subcommittee, which he chaired. The subcommittee’s charge was to analyze the Federal investments in breast cancer and environment research. Its purpose was to understand the investment in terms of its goals, gaps and overlaps. It used currently available classification coding systems (particularly the Common Scientific Outline), and contacted agencies directly. In FY 2008-2010, NIH spent $2.4 billion on breast cancer research—approximately 83% was administered by NCI, 5% by NIEHS and 2% or less by the other ICs. For FY 2006-2010, the Department of Defense (DoD) Breast Cancer Research Program spent approximately $610 million, roughly 75% of which was for basic biology and treatment research. Additionally, the subcommittee received information on smaller breast cancer research investments from the CDC, USEPA, and the FDA. It also compiled data on significant breast cancer research funding by major NGOs such as the American Cancer Society and the Susan G. Komen for the Cure organization. The six major NGOs invested a total of $1.66 billion for the fiscal years 2005-2009. The subcommittee’s analysis revealed that environmental and prevention studies made up just 10-11% of all breast cancer projects funded by NIH and DoD during the fiscal years examined. Prevention research by the NGOs comprised less than 7% of the total breast cancer research investment. The subcommittee posits that the low funding levels in these areas may be due to research funding strategies focused more on developing cures than on prevention. Thus, the group states that the number of applications for funding directed to breast cancer and the environment needs to be increased, and funding for projects focusing on environmental etiology and prevention should be prioritized. The group formulated a substantial list of recommendations for improving the research process.

Ms. Rizzo reported on the findings of the RTDPI subcommittee, which she chaired. The group defined the concepts of research translation, research dissemination, and research communication. They found that to be effective, translation should be planned and advocates should be engaged early in the research process. They identified strategic elements common to successful programs:

• They had formal structures for translation, dissemination and communication built in from the inception of the research.
• They included participatory approaches for involving stakeholders.
• They funded advocates and community involvement.
• They considered environmental justice.
• They evaluated partnerships, dissemination and communication, and research impact.

Ms. Rizzo delineated the subcommittee’s specific recommendations to achieve effective research translation, dissemination and communication:

• Require research projects on breast cancer and the environment to integrate research translation, dissemination and communication plans early and throughout the research process in ways that facilitate partnerships with stakeholders from scientific, breast cancer advocacy, environmental justice and provider communities.
• Translate, disseminate and communicate research findings to stakeholders in a timely manner while targeting a wide range of disciplines, professions and communities.
• Use interagency and inter-organizational collaborations to coordinate and amplify message regarding what is known about the environmental causes of breast cancer.
• Identify strategies for determining when and how (i.e., at what point of evidence) to take action when breast cancer risk or survival is suspected to be associated with environmental exposures or risk factors.

Ms. Rizzo described several reasons why the subcommittee also addressed the policy implications of the report, and summarized the many implications the group had identified.

Dr. Conti praised the report’s focus on collaborative issues, and noted that breast cancer and the environment is truly a “One Health” issue in terms of the overlap of human, veterinary and environmental health. She urged inclusion of study of breast cancer in companion animals, as they often have the same environmental exposure risks as humans.

Ms. Waghiyi, noting that she is from a small Alaskan village, asked about how breast cancer rates in small populations might be studied and inquired about the relationship between early puberty, exposure to endocrine disruptors and heightened risk of breast cancer. Dr. Forman said that the SEER registries across the US were an excellent resource for collecting incidence and mortality data. She added that when the committee looked at trends over time, they were based on accumulated SEER data. She noted that there are many projects currently researching a connection between puberty and environmental exposures, including several funded by NIEHS, such as the Breast Cancer and the Environment Research Program (BCERP), which includes a puberty study encompassing more than 1200 young girls. Ms. Rizzo noted that the reported breast cancer rates do not reflect the incidence among indigenous tribal
peoples such as Alaska Natives. Ms. Waghiyi agreed, stating that the rates of cancer among her people are alarming.

Ms. Yeampierre said she was pleased to see that environmental justice was included in the report, and asked whether the committee would be able to track the legacy of generational exposure to environmental hazards and health care over time. Ms. Rizzo explained that the committee's responsibility was to issue the report, and that implementation of its ideas would be in the purview of the HHS Secretary. Dr. Forman noted that the report had included several recommendations about the potential transgenerational effects of environmental exposures, including recommendations along the lines of what Ms. Yeampierre was suggesting.

Dr. Kramer asked what the committee representatives saw as the most important barriers to implementation of the report's recommendations. Dr. Forman said that the major barrier would be insufficient funding for prevention-related research.

Dr. Brody noted that this was the third recent major report on breast cancer, and asked how many of the major recommendations could be implemented by the institutes at present, including the recommended interagency committee. Dr. Forman said that the group had recommended that the HHS Secretary meet soon with her peers to develop an interagency strategic plan that would include benchmarks to highlight progress, or lack of progress, and a knowledge integration tool to map the universe of breast cancer and the environment research. She emphasized that IBCERCC “wants to keep the ball rolling,” and asked for help and suggestions to do so.

Dr. Taylor said that the committee had done a great job of setting up the priorities in the area. He asked if there was an estimate of how much the efforts would cost over the next 20-25 years. Dr. Forman said there was no magic number to be able to predict the long-term costs. She said that continuing to prioritize while being parsimonious would be necessary. Dr. Gould added that the report clearly showed that the goal of establishing primary prevention of breast cancer is not being fulfilled, but it was not the committee's charge to suggest specifics in terms of funding or shifting funding.

Dr. Lloyd asked whether the 20-year window described in the report may be too short to discern trends that may actually be improving in terms of breast cancer incidence and survivorship. With that in mind, he wondered whether the window to be able to quantitate real changes in the incidence rates going forward as a result of prevention efforts should be much longer. Dr. Forman noted that most of the currently available research focused on exposures around the time of diagnosis, which is not satisfactory given knowledge about in utero exposures and other exposure windows during the life course. She said it would be important to use the animal studies to help screen which windows might be critical, along with monitoring in humans and maintaining surveillance.
of high-risk groups. She agreed it would be a long window, but said that prevention would only occur when it is understood when and how it can be applied effectively through the life course.

VII. DNTP Report

Dr. Andrew Rooney from the Office of Health Assessment and Translation (OHAT) in DNTP reported to Council on the draft OHAT approach for systematic review and evidence integration for literature-based health assessments.

He provided background information about the process of systematic review, and described the 7 steps in the draft OHAT approach. The draft OHAT approach builds on and extends existing systematic review methods, which are currently mostly used for assessment of healthcare interventions. Step 4 comprises the OHAT method of assessing risk of bias in studies. That data is used in the subsequent steps, which rate confidence in the body of evidence, translate confidence ratings into evidence of health effects, and finally (Step 7), integrate the evidence to develop hazard identification conclusions.

The draft OHAT approach will be released for public comment on February 26, with a 60-day comment period. Ultimately, two case studies will be added to assess and refine the methods, and eventually the updated guidance will be released, which will be updated periodically to incorporate new best practices.

VIII. Investigating Epigenetic Plasticity in Development and in Response to the Environment

Dr. Andrew Feinberg from Johns Hopkins University, a long-time NIEHS grantee, briefed Council on his work on epigenetics. By developing an integration of new conceptual, technological, epidemiological and statistical approaches, Feinberg’s group is working to advance the epigenetics field from cancer to common disease.

He said that epigenetics is where genes meet the environment in a complex interplay, in that the epigenome can integrate information that comes from one’s environment and from one’s genotypes, and the genotypes themselves can have an effect on the epigenome. By adapting some of the statistical tools employed by astronomers, his group at the Johns Hopkins Center for Epigenetics has developed new tools to help understand the epigenetic contribution to diseases such as cancer and neuropsychiatric disorders. One of them, Comprehensive High-Throughput Relative Methylation (CHARM) analysis, allows an unbiased look at the “whole sky” of epigenetic marks within the entire genome. Using CHARM to measure up to four million DNA methylation sites throughout the genome, the team discovered that contrary to prior assumptions, most variable DNA methylation is not in “islands” but in nearby sequences they termed
"shores." They discovered that aberrant methylation in cancer involves roughly equal gains and losses of DNA methylation at these shores, and involves much the same sequences involved in normal differentiation of widely disparate tissues.

Feinberg also shared his ideas regarding a non-Lamarckian model for a role for epigenetics in evolution, involving stochastic epigenetic variation as a driving force of development and evolutionary adaptation. He said the inherited stochastic variation model would provide a mechanism to explain an epigenetic role of developmental biology in selectable phenotypic variation, as well as the largely unexplained heritable genetic variation underlying common, complex disease.

IX. Common Fund: Technology Development to Enable Large Scale Metabolomics Analyses

Dr. David Balshaw provided Council with an overview of the NIH Common Fund Metabolomics Program. He briefly described the Common Fund itself, and the trans-NIH Metabolomics Working Group that oversees the program, in which he leads the Technology Development Project Team.

The working group held a workshop in Spring of 2011, from which four major ideas about needs in the metabolomics area emerged: to increase the national metabolomics capacity, to train a new generation of scientists in metabolomics, the need for more standard compound preparations, and the development of new technologies and adoption of existing technologies and methods. Those identified needs spawned the Common Fund Program, with 5 central thrusts, including those based on the 4 needs and an initiative establishing an open access data repository for metabolomics. The largest component is a network of Regional Comprehensive Metabolomics Research Cores. Three regional core centers were funded in 2012, and 2-3 more are planned for 2013. He described the suite of metabolomics services available at the core centers, and how to access them. The intent is for the centers to eventually be self-sustaining.

Data sharing and international collaboration is another aspect of the program, with cloud-based data repository at UCSD offering a public access database for all data from the regional cores and technology development projects. An international coordinating committee will provide interface between metabolomics efforts in North America, Europe and Asia.

Dr. Balshaw leads the group’s Technology Development program, which is working to increase the number of unique chemical entities that can be detected in a sample while also reducing sample volume and cost. The initiative is supporting technological development to improve sample extraction techniques, to invent “more-better-faster-cheaper” systems for detection and analysis, and to enhance automated analysis and analyte identification.
He described the program’s training activities, which include a K01 mentored development program, R25 programs to support development of courses and workshops, and a Supplement program to support collaborative activities. To provide consistent reference standards, a contract will be awarded to support GLP/GMP synthesis and characterization of metabolomic standard reference materials, with the award expected in July 2013.

X. SBIR Program Concept

Dr. Dan Shaughnessy presented the SBIR Program Concept to Council. He provided background information about the SBIR/STTR process, which is a 3-phase program. He noted that re-authorization legislation passed in 2011 mandates increasing set-aside requirements for agencies, culminating in an SBIR set-aside of 3.2% in 2017, with a 0.45% set-aside for STTR. For NIEHS, this would mean $15.5 million and $1.7 million respectively at that time. He went over several other key re-authorization provisions, and described new programs being proposed:

- An RFA on biomonitoring technology
- An RFA on assays for toxicant effects on cell differentiation

Proposed new SBIR topics include:

- Improved sensors for integrated measurement of the personal environment
- Novel methods for obtaining molecular information from archived tissue samples
- Validation of specific technologies through the Phase IIB grant mechanism

He described each of the proposed topics in detail, and presented a proposed timeline, which would effectively stagger the funding phases for the various projects through 2018.

Council reviewers Dr. McKone and Dr. Brody supported the concept, with Dr. Brody noting that there is an enormous need for new technologies in the proposed categories. There was a motion and second to approve the concept; Council voted unanimously in favor, with one abstention.

XI. Bioinformatics in Environmental Health Sciences Research

NIEHS intramural researcher Dr. Leping Li of the Biostatistics Branch updated Council on the innovative work his group has been doing in bioinformatics, developing new bioinformatic tools and methods designed specifically to address questions related to environmental factors. For example, he and his Biostatistics Branch group have developed novel tools for detection and analysis of transcription factor binding sites in the DNA sequences. The “motif analysis tools” apply to large-scale, high-throughput
DNA sequencing technologies such as ChIP-Seq: GADEM performs motif discovery and identification, while coMOTIF identifies primary motifs and potential co-regulatory motifs in ChIP-Seq data. Such computational analysis methods facilitate new discovery and hypothesis generation.

Li described how the tools have been used to yield important new insights regarding the functions of ERα receptors in the uterus, which are critical for establishment and maintenance of pregnancy and are subject to environmentally influenced perturbations.

The motif analysis tools have been made freely available to the public.

Li and his colleagues are also developing statistical and computational methods to identify differentially expressed isoforms from mRNA-seq data. As he explained, tools for detecting differential splicing could have a major impact in toxicogenomics, as examples exist where changes or imbalances in isoforms have been implicated in tumor development.

XII. Neurodegeneration Concept

NIEHS Program Administrator Dr. Annette Kirshner presented the Neurodegeneration Research Concept to Council.

She briefly described neurodegeneration, which is the progressive loss of structure or function of neurons eventually leading to their death, and is seen in various neurodegenerative diseases such as Alzheimer’s (AD) and other dementias, Parkinson’s (PD) and other movement disorders, and more. There is considerable evidence for involvement of environmental exposures in neurodegeneration; thus NIEHS has long had an active research portfolio in the area, which has yielded several significant scientific advances.

Dr. Kirshner outlined several events over the past two years designed to aid program planning for the future. Major priorities addressing identified data gaps going forward will be:

- The role of exposure across the life span
- Consideration of neuronal and non-neuronal cell function
- The role of inflammation
- The role of genetic and especially epigenetic variability in response to exposure and disease risk

Two RFAs are proposed initially: an R01 initiative that will focus on Alzheimer’s disease, and another RFA using the R21 mechanism to develop new feasibility data for new concepts in neurodegeneration or to adapt new technologies, tools and methods in
neurodegeneration. Those RFAs could be followed in a phased manner by other initiatives in ALS and PD as well as AD in a 5-year plan.

Council reviewers Dr. Chesselet and Dr. Hu supported the concept. There was a motion and second to approve the concept and Council voted unanimously in favor.

XIII. Consideration of Grant Applications

This portion of the meeting was closed to the public in accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

XIV. Adjournment

The meeting was officially adjourned at 12:00 pm on February 21, 2013.

CERTIFICATION:

/s/
Linda S. Birnbaum, PhD, DABT, ATS
Chairperson
National Advisory Environmental Health Sciences Council

/s/
Gwen W. Collman, PhD
Executive Secretary
National Advisory Environmental Health Sciences Council

Attachment:
Council Roster