



Eunice Kennedy Shriver National Institute
of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH
AND HUMAN DEVELOPMENT
COUNCIL

MEETING MINUTES

September 14, 2017

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND
HUMAN DEVELOPMENT

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL
SUMMARY MINUTES

September 14, 2017¹

The National Advisory Child Health and Human Development (NACHHD) Council convened its 165th meeting at 8:00 a.m., Thursday, September 14, 2017, in Building 31, Conference Room 6, of the National Institutes of Health (NIH) in Bethesda, Maryland. The meeting was open to the public from 8:00 a.m. to 11:50 a.m. As provided in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of Public Law 92-463, for the Division of the Intramural Research's presentation on the confidential reviews of the Board of Scientific Counselors, the meeting was closed to the public from 1:00 p.m. to 1:30 p.m. and for the review, discussion, and evaluation of grant applications and related information, the meeting was closed to the public from 1:30 p.m. until 4:30 p.m.

Dr. Diana W. Bianchi, Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), presided.

Council members present:

Atul J. Butte, M.D., Ph.D.

Anne C. Case, Ph.D., M.P.A.

Barbara L. Collura

Patricia Flynn, M.D. (remote)

Melissa L. Gilliam, M.D., M.P.H.

Gregory S. Kopf, Ph.D.

Richard D. Krugman, M.D.

Stephen A. Petrill, Ph.D.

DeWayne M. Pursley, M.D., M.P.H.

Frederick P. Rivara, M.D., M.P.H. (remote)

Lesli Rotenberg

George R. Saade, M.D.

Timothy P. Shriver, Ph.D.

Sheila C. Zimmet, J.D.

Council members absent:

Michael Boninger, M.D.

Catherine Gordon, M.D., M.Sc.

Clifford Tabin, Ph.D.

Alyce Thomas

Department of Defense

Col. Teresa L. Brininger, Ph.D.

National Advisory Board on Medical Rehabilitation Research

Council Liaison

Richard K. Shields, Ph.D. (remote)

Ex officio members present:

Patricia Dorn, Ph.D.

Aaron M. Lopata, M.D., M.P.P.

¹ Members absent themselves from the meeting when the Council discusses applications from their own institutions or when a conflict of interest might occur. The procedure applies only to individual applications discussed, not to *en bloc* actions.

Others present:

Diana W. Bianchi, M.D., Director, NICHD

Catherine Y. Spong, M.D., Deputy Director, NICHD

Della M. Hann, Ph.D., Director, Division of Extramural Research, and Associate Director for Extramural Research, NICHD

Constantine Stratakis, M.D., D.Sc., Director, Division of Intramural Research, NICHD

Members of NICHD Staff

Members of NIH Staff

I. CALL TO ORDER AND INTRODUCTORY REMARKS

Dr. Diana Bianchi welcomed Council members, guests, and staff to the 165th meeting of the NACHHD Council and announced that the meeting would be open to the public for the morning portion and would be broadcast on the NIH videocast network.

Review of Confidentiality and Conflict of Interest

Dr. Della Hann reminded the Council that all members were required to read, agree to, and sign the confidentiality and nondisclosure rules for special government employees on the Council member website before evaluating any NIH grant applications. Council members at the meeting also received a conflict-of-interest certification form, which they were required to sign prior to the closed session of the review of applications. Dr. Hann also reminded Council members that if there were a specific discussion involving any organizations or universities for which they were in conflict, in addition to those listed on the Council Action document, they were required to recuse themselves from the discussion and leave the room. Council members are not allowed to serve on the NIH peer review panel while serving as Council members. It is NIH policy that individuals may not serve on both the first and second levels of peer review.

Council Minutes

Dr. Hann moved to approve the June 2017 meeting minutes. The minutes were approved unanimously as written.

Future Meeting Dates

Dr. Hann reviewed the future meeting dates:

January 18, 2018	(Thursday)
June 7–8, 2018	(Thursday–Friday)
September 13-14, 2018	(Thursday - Friday)

II. NICHD DIRECTOR'S REPORT AND DISCUSSION**Budget Update**

The government will be funded through a continuing resolution from October 1, which is the beginning of fiscal year 2018 (FY18), through December 8.

The Senate budget includes an increase of \$2 billion to the NIH FY18 budget. If Congress approved that increase and it was signed into law, NICHD would receive a \$50 million increase

(and \$1.426 billion total) for FY18. Both the House and the Senate have indicated that indirect costs for extramural researchers would not be capped.

The Research, Condition, and Disease Categorization (RCDC) system allows the public to see how tax dollars are spent. RCDC is a database that NIH has maintained since 2009 to report on funding in more than 280 topic areas.

21st Century Cures Act

The 21st Century Cures Act, signed into law in 2016, required the establishment of the Task Force on Research Specific to Pregnant Women and Lactating Women. The Task Force will advise the Secretary of the Department of Health and Human Services (HHS) of gaps in knowledge and research on the safety and effectiveness of medications taken by pregnant and lactating women. The Task Force met for the first time on August 21 and 22. This year, as part of the Task Force's work, NIH established "pregnancy" and "breastfeeding and lactation" as RCDC categories.

While most women have at least one pregnancy in their lifetime, an analysis of the research literature from 2006 to 2017 found that there have been few clinical trials and basic science studies to evaluate the effects of medication on pregnant women, lactating women, and their children. Because there is very little research, obstetricians and pediatricians cannot provide evidence-based advice on medications to pregnant and lactating women. Women must choose whether to take a medication that they need without knowing whether it could harm them or their child.

Section 2012 of the 21st Century Cures Act includes the Next Generation Researchers Initiative. This initiative invests in early stage investigators (ESIs; those within 10 years of obtaining their terminal degree but who have not received an R-type award) and in early established investigators (EIs; those within 10 years of receiving their first independent R-type award but who are in danger of losing their status because they do not have a second R-type award). Dr. Hann would present more on this initiative later in the meeting.

Staff Updates

Dr. Germaine Buck-Louis is leaving NIH for a position at George Mason University. Dr. Michael Weinrich is retiring from federal service.

Vision Update

The NICHD vision includes building bridges, communicating the message, and committing to the strategic planning process.

Dr. Bianchi and Dr. Collins have discussed NIH efforts on the opioid crisis with members of Congress and will also speak to the Women's Congressional Policy Institute. The long-term effects of fetal exposure to opioids are not known. NICHD, the Environmental influences on Child Health Outcomes (ECHO) Program, and National Institute on Drug Abuse (NIDA) are funding efforts to compare the effectiveness of different treatments for neonates who are born addicted to opioids. The effort will partner NICHD neonatal researchers with researchers from Institutional Development Awards (IDeA) program states where neonatal opioid exposure is higher.

NICHD organized the fourth annual Human Placenta Project meeting to build bridges with researchers in different fields, including bioinformatics and bioengineering.

Dr. Bianchi encouraged Council members and others to respond to the *All of Us* Research Program request for information (RFI) to name their highest precision medicine research priorities related to children.

The next strategic planning process will begin in 2018. NICHD will bring together about 50 people, including NICHD and external stakeholders, to do the planning.

Council Discussion

Dr. Saade said that the *All of Us* Research Program should include questions about pregnancy. Dr. Spong said that the Research Program is currently developing research questions. Dr. Bianchi suggested mentioning pregnancy, including how the prenatal environment affects a child's long-term health outcomes, when responding to the RFI.

Dr. Gilliam noted that many women who were pregnant and addicted to crack cocaine were prosecuted during the 1980s. She asked whether there was a way to prevent similar prosecutions during the opioid crisis. Dr. Bianchi said that this could be discussed more fully during concept clearance.

III. DIVISION OF EXTRAMURAL RESEARCH REPORT

Staff Updates

Dr. Hann introduced Dr. Tuba Fehr, an American Association for the Advancement of Science fellow who will join the Intellectual and Developmental Disabilities Branch.

Dr. Marita Hopmann of the Scientific Review Branch has retired from federal service.

Dr. Anne Zajicek of the Obstetric and Pediatric Pharmacology and Therapeutics Branch has moved to the NIH Intramural Research Program.

Next Generation Researchers Initiative

This initiative, part of the 21st Century Cures Act, was introduced by Dr. Bianchi earlier in the meeting. Dr. Hann said that the law calls upon NIH to increase opportunities and a path to earlier independence for ESIs and EEIs. The goal is to ensure an adequate pipeline of researchers for the future. To do this, ESIs and EEIs with meritorious grant application scores will be prioritized for funding. The goal was to fund 200 more ESIs and 200 more EEIs during FY17. The policy came out very late in FY17, but NICHD was able to fund 38 ESIs and 51 EEIs.

Progress in Clinical Trial Reforms

As of January 2018, all applications proposing clinical trials must be submitted through a funding opportunity announcement (FOA) that is specifically designated for clinical trials. NICHD will review existing FOAs to determine whether they accept clinical trials. NICHD has already published notices to communicate these changes. The Office of Extramural Research has released FAQs and is emailing clinical trial investigators to let them know that a renewal application may have to come in under a new FOA.

IV. ONCOFERTILITY: FROM BENCH TO BEDSIDE TO BABIES

Dr. Bianchi introduced Dr. Teresa K. Woodruff of Northwestern University, who heads the Oncofertility Consortium, an interdisciplinary team of biomedical and social science experts in oncology and fertility.

Dr. Woodruff said that her work on oncofertility began nearly two decades ago, when NIH challenged investigators to propose any study involving an intractable problem. She was interested in preserving fertility in girls and in women of childbearing age who had to undergo cancer treatmentS.

Dr. Woodruff's team formed the Oncofertility Consortium, which aims to hasten the pace at which basic science is translated to medical practice. The Consortium formed the National Physicians Cooperative and the Oncofertility Global Partners network. Dr. Woodruff discussed the work that her team has done to meet the long-term fertility and endocrine needs of adult and pediatric cancer patients. NICHD has funded much of her work.

Dr. Woodruff and the Oncofertility Consortium have cultured follicles in a bioengineered environment and, using a mouse model, have grown follicles in vitro, induced ovulation, and produced offspring.

The team has invented a device, [EVATAR™](#), that models the female 28-day reproductive cycle. The device enables the study of reproductive hormones on downstream tissues and may also allow researchers to study drug metabolism in women.

In research on the human egg that was conducted using nongovernment funding, Dr. Woodruff's laboratory discovered that the egg releases a "spark" of zinc at the time of fertilization. This "zinc spark" is a signature of human egg activation.

The team has developed a method to isolate healthy follicles from cancer cells in ovarian tissue and has developed a bioprosthetic ovary that led to the birth of a mouse. This prosthesis could one-day allow a pediatric cancer patient to go through a natural puberty and have normal reproductive health.

Ovarian tissue cryopreservation is now an option available through the National Physician Cooperative sites. Cryopreservation is for pediatric patients and for women who do not have the time to go through in vitro fertilization before beginning treatment. Eighty percent of the ovarian tissue is preserved for the patient to use later, and 20 percent is for research. Ninety children have been born from the use of ovarian tissue transplanted after the women have recovered from cancer.

The Consortium has also found that the fertility intervention can improve initiation and compliance with tamoxifen treatment in young breast cancer patients.

In summary, Dr. Woodruff said that NICHD funding has allowed her team to take their work from the bench to the bedside to babies.

V. VOICE OF THE PATIENT

Ms. Megan Connolly recounted her experience of being diagnosed with non-Hodgkin lymphoma at 20-years old. After 6 months of grueling chemotherapy treatment, she was in remission and returned to college.

Eight months later, the cancer returned, necessitating a second round of treatment that would include chemotherapy, radiation, and an autologous stem cell transplant. Ms. Connolly was referred to the NIH-funded Oncofertility Consortium before beginning treatment.

A patient navigator at the Consortium met with Ms. Connolly and explained that she could become infertile as a result of the upcoming round of treatment. Ms. Connolly said that this was an issue that had not even crossed her mind. But the patient navigator also listed the resources available to enable her to have children when she chose to do so.

“The fact that [the patient navigator] and my medical care team went above and beyond just treating my disease, but also giving me hope to preserve my fertility and thrive in survivorship, is astounding,” Ms. Connolly said. She opted for egg harvesting, which she referred to as “banking hope,” before treatment. The Consortium also helped her find funding to pay for the hormone stimulating drugs and a place to bank the eggs. All of this was completed within two weeks, so that her treatment would not be delayed.

After successfully undergoing a second round of treatment with chemotherapy, radiation, and a stem cell transplant, Ms. Connolly is now in remission six years later. She has been diagnosed with premature menopause but hopes to be able to have a biological family in the future.

Dr. Bianchi thanked Ms. Connolly for sharing her story, which she said aptly describes how research can be translated to health for the patients. She invited attendees with questions to meet with Ms. Connolly during the break.

VI. CONCEPT CLEARANCE REVIEW AND DISCUSSION

Dr. Hann said that there were 10 concepts to review.

The Prenatal and Childhood Mechanisms of Health Disparities

Dr. Stephen Gilman said that this initiative will investigate the developmental origins of health disparities by establishing a diverse cohort of pregnant women and following their offspring through the first year of life.

Council Discussion

Dr. Saade asked how the study would align with other NICHD pregnancy cohorts, such as the ECHO program. Dr. Gilman said that this project would work in parallel with other pregnancy cohorts such as ECHO.

Dr. Rivara asked whether this is a new cohort and how big the cohort would be. Dr. Gilman said that it is a new cohort that will enroll 2,000 pregnant women.

Dr. Shriver asked whether disabilities would be included as a health disparity. Dr. Gilman said that the initiative will aim for as diverse a cohort as possible, including women with mental health problems. Dr. Shriver asked whether women with developmental disabilities would be

included. Dr. Gilman said that the study will be as diverse as possible, including participants with developmental disabilities, and that he appreciated the comment.

The Council unanimously concurred with the concept.

Opioid Use Disorder in Pregnancy

Dr. Uma Reddy said that NICHD would solicit proposals for research on opioid use disorder in pregnancy. The research could include the studies of the maternal, fetal, and neonatal outcomes of medically supervised opioid withdrawal and studies of the pharmacokinetics and pharmacodynamics of medications to treat pregnant and postpartum women.

Dr. Gilliam asked whether the federal Interagency Pain Research Coordinating Committee had been involved. Dr. Reddy said that it has not, but the project will align with the Protecting Our Infants Act of 2015.

Dr. Pursley asked how long the study would follow the family. Dr. Reddy said that the R01 would be only five years. That is a gap, because even longer-term outcomes would be of interest.

The Council unanimously concurred with this concept.

Male and Female Contraceptive Development

Dr. Daniel Johnston said that the objective is to stimulate private-sector research to develop novel compounds or devices that provide safe and reversible contraceptive methods for men and women. The initiative would provide economic incentives to increase small business involvement.

Council Discussion

Dr. Kopf asked whether the program is linked to the Small Business Innovation Research program or the Small Business Technology Transfer program. Dr. Johnston said that it is.

The Council unanimously concurred with this concept.

Data Coordinating Center (DCC) for the NICHD Cooperative Multicenter Maternal-Fetal Medicine Units Research Network

Dr. Menachem Miodovnik said that the aim is to invite applications from institutions willing to participate as the data coordinating center.

Dr. Butte said that the current DCC has not submitted data to the Data and Specimen Hub (DASH) since 2012. He said that this FOA should require that the DCC submit their data to DASH. Dr. Miodovnik said that the DCC is working on submitting the data to DASH and that he would follow Dr. Butte's suggestion. Dr. Hann said that the 21st Century Cures Act requires that the data be publicly shared; there will be language in the FOA regarding the importance of this.

Dr. Spong said that it is possible to get access to the data from the DCC by clicking on the link and receiving directions via email. She also said that NICHD will ensure that the data in the current DCC remain publicly available, even if a new DCC is selected. However, NICHD cannot require that the data go to DASH.

Dr. Bianchi said that NICHD is committed to data sharing that is user-friendly. DASH is a work in progress, but more studies are being uploaded every month. NICHD is committed to having a user-friendly way to access de-identified clinical information and biospecimens.

The Council unanimously concurred with the concept.

Noninvasive Diagnostics to Improve Gynecologic Health

Dr. Candace Tingen said that the goal of this initiative is to support the development of new or improved noninvasive tools and devices for the diagnosis of endometriosis, adenomyosis, and uterine fibroids. The tools are meant to reduce delay in diagnosis of these conditions.

The Council unanimously concurred.

Safe and Effective Devices for Use in Neonatal, Perinatal, and Pediatric Care Settings

Dr. Tonse Raju said that this FOA seeks to foster collaboration between clinical and bioengineering researchers to develop, test, and optimize devices for use in neonatal, perinatal, and pediatric care settings. The FOA also would facilitate interactions with the Food and Drug Administration (FDA) early in development to bring products to market more efficiently.

Dr. Dorn asked Dr. Raju to expand on the work envisioned with FDA. Dr. Raju said that FDA has consortia to help get pediatric devices to the market and wants to encourage investigators to work with FDA staff in the early stages of development.

The Council unanimously concurred with this concept.

Collaborative Pediatric Critical Care Research Network (CPCCRN) and CPCCRN DCC

Dr. Valerie Maholmes presented two concepts together: to renew the CPCCRN, and to renew the CPCCRN DCC. The goal of the CPCCRN is to advance the science of pediatric critical care medicine. The DCC supports the CPCCRN's efforts by enhancing the design of clinical studies with cutting-edge technologies and by producing high-quality and robust datasets to advance the field.

Dr. Butte said that none of the datasets listed on the CPCCRN website have been placed in DASH. Putting all datasets into DASH will enable easy access to the research community.

The Council unanimously concurred with both concepts.

The Role of Stem/Progenitor Cells in the Pathogenesis and Treatment of Gynecologic Disorders

Dr. Lisa Halvorson stated that the aim of this FOA is to stimulate research into the role of stem cells in the pathogenesis and potential treatment of uterine fibroids, endometriosis, adenomyosis, endometrial polyps, and pelvic organ prolapse.

The Council unanimously concurred with the concept.

National Centers for Translational Research in Reproduction and Infertility

Dr. Stuart Moss said that the Centers form a network of translational research centers that emphasize high-quality reproductive, infertility, and gynecological health and disease research.

Council Discussion

Dr. Kopf asked whether the Centers encourage basic research. Dr. Moss said that the clinical research is aligned with the basic science research.

The Council unanimously concurred with this concept.

VII. NIH CLINICAL TRIALS POLICY AND IMPLEMENTATION

Dr. Michael S. Lauer, Deputy Director for Extramural Research, said that a study published in 2012 found that only 45 percent of NIH-funded trials had published their main results within 30 months of the study's completion. The FDA Amendments Act is meant to reduce the problem of non-reporting of clinical trials, but many trials are not covered by the Act. In these cases, no policies exist to ensure that the public has access to the results from NIH-funded studies that are not published.

Dr. Lauer said that NIH did its own study, looking at 244 cardiovascular trials funded by the National Heart, Lung, and Blood Institute (NHLBI) over a 10-year period. They found that most trials with primary clinical endpoints, such as premature death or myocardial infarction, were published within two years. However, less than 20 percent of the 244 studies had primary clinical endpoints. Of trials with surrogate endpoints, only 40 percent were published within two years.

Another study of leading academic institutions found similar problems in reporting the results of clinical trials.

Researchers who studied this issue concluded that the failure to share results is so pervasive that it appears to be a systems and culture issue, not an issue with individuals. Funders, investigators, academic medical centers, clinical research organizations, and journals share responsibility. According to Dr. Lauer, thought leaders have argued that not reporting results violates the principles of the scientific method, hurts patients and society, impedes scientific progress, and wastes research funding.

In March 2016, the General Accounting Office concluded that NIH must collect more data to enhance the stewardship of NIH-funded clinical trials.

Over the last four years, NIH has embarked on an extensive process to improve stewardship of its clinical trials investment. The work was led by the Office of Science Policy, with engagement of most NIH Institutes and Centers (ICs). In late 2014, NIH posted a revised definition of "clinical trial" that parallels the revised Common Rule; shortly thereafter the NIH requested comment on a proposed policy on dissemination of clinical trials information. The NIH reviewed approximately 240 comments, which came from individuals, organizations, and professional societies.

In September 2016, NIH finalized a rule that clinical trials must register within 21 days of enrolling the first patient (making others aware of the study) and that results must be reported within one year of trial completion.

NIH created a website with multiple resources to help investigators understand and meet the new requirements, including registration and results reporting. NIH has created a system to link the grant funding the study with its registration. If an institution has a trial and results are not

reported within a year of completion, NIH will withhold funding for future trials at that institution.

Council Discussion

Dr. Petrill asked for a clearer definition of “clinical trial.” Dr. Lauer said that a clinical trial is an experiment in which the investigator attempts to modify something about the human subject. Clinical trials include studies that measure biological or behavioral outcomes. Dr. Lauer acknowledged that there are gray areas. Investigators who could help further refine the definition should contact him at NIH.

Dr. Gilliam asked why Phase I study results must be reported. Some of these studies may not be publishable. Dr. Lauer said that “publishing” includes posting the results on clinicaltrials.gov. There is value in publicizing the findings of all publicly-funded experiments that are being done on people, even failed studies and small studies. The investigators have an ethical obligation to their participants to publish whatever they find.

Dr. Butte said that even failed experiments can produce new science, particularly if the data are made available for other investigators to use. NIH should also require that investigators release their raw data.

VIII. DIVISION OF INTRAMURAL RESEARCH (DIR) ANNUAL REPORT

Dr. Constantine A. Stratakis said that the DIR has 62 principal investigators who are conducting more than 80 clinical protocols. NICHD has one of the largest clinical programs within the NIH Intramural Research Program.

The DIR supports five medical training programs in pediatric and internal medicine including the Maternal-Fetal Medicine Fellowship Training Program, Medical Genetics Training Program, NIH Inter-Institute Endocrinology Training Program, Pediatric Endocrinology Inter-Institute Training Program, and Reproductive Endocrinology and Infertility Training Program. The Maternal-Fetal Medicine Fellowship is part of the Perinatal Research and Obstetrics Program, which is headed by Dr. Roberto Romero at Wayne State University.

Investigators are organized into 13 affinity groups. The Board of Scientific Counselors evaluates the research of the NICHD DIR and advises institute leadership on programmatic decisions and resource allocations. Drs. Vanessa Auld, Elizabeth Bonney, Deborah Johnson, and Martha Werler are international leaders in their respective fields and new members of the Board.

The FY17 DIR budget totals approximately \$181 million. Dr. Stratakis detailed where the funding is spent, including approximately \$54 million for personnel, approximately \$51 million in lab consumables, approximately \$29 million to the Clinical Center, and approximately \$36 million to overhead. The DIR renovation costs for FY17 are estimated to be approximately \$3.4 million as part of a years-long effort to provide new or renovated space to more than 80 percent of all DIR investigators. Over the past six years, the DIR has decreased its proportion of fixed expenses, giving the DIR greater flexibility in how its money is spent.

The DIR has a trainee population that currently stands at approximately 265, 70 percent of whom are postdoctoral fellows, but also includes post baccalaureate fellows, graduate students, and clinical fellows. The DIR has seen a decrease in the number of training positions, a trend that has happened across NIH.

Two senior investigators, Drs. Igor Dawid and Thomas Sargent, retired this fiscal year. Drs. Catherine Drerup, Claire Le Pichon, and Timothy Petros have recently joined the DIR as tenure-track investigators. The DIR is also recruiting in the areas of cellular and developmental neurobiology and in translational research. DIR is particularly interested in physician scientists.

Among many other honors to a number of DIR investigators, Dr. Gisela Storz received three awards in 2017: the Biomedical Research Exemplar award from Washington University in St. Louis, the Ruth L. Kirschstein Mentoring Award, and was named the 2017 Anita B. Roberts lecturer.

The DIR has been very successful at obtaining additional funding; examples include the NIH Bench-to-Bedside Program awards and the Opportunities for Collaborative Research at the NIH Clinical Center (U01). NICHD has received more Bench-to-Bedside awards between 2006-2015 than any other Institute proportionate to its size. In addition, DIR investigators received four of the 30 Deputy Director for Intramural Research Innovation Awards that were awarded recently. DIR investigators have won other competitive funding opportunities, including the NIH Intramural-to-Russia Program awards, the Office of AIDS Research Strategic Funding, and the Postdoctoral Research Associate Fellowships program. Finally, Dr. Stratakis sets aside about two percent of the DIR budget each year for competitive awards for intramural investigators through the NICHD DIR Director's Awards.

Dr. Stratakis finished his presentation by summarizing the DIR's efforts to increase diversity in all its ranks, and to promote communication of our scientific efforts. The DIR has supported programs such as the Scholars Developing Talent Program, the Fellows Recruitment Incentive Award, and by centrally funding 15 summer student positions for individuals from disadvantaged backgrounds or groups traditionally underrepresented in science. DIR provides fellows and graduate students with professional training in speech and presentation development.

The DIR's presentation ended with the video of Dr. Miranda Broadney, one of the finalists of the Three-Minute Talks: Science Communication Training and Awards Program.

IX. COATOPATHIES: GENETIC DISORDERS OF PROTEIN COATS

Dr. Bonifacino said that his laboratory studies the molecular mechanisms by which proteins and organelles are distributed within the cell and the role that dysfunction in distribution plays in diseases such as Hermansky-Pudlak syndrome and MEDNIK (mental retardation, enteropathy, deafness, neuropathy, ichthyosis, keratoderma) syndrome.

Transmembrane proteins possess sorting signals that are recognized by adaptor proteins. Adaptor proteins read the sorting signals and send the transmembrane proteins to the correct location within the cell. Dr. Bonifacino focused on one of the adaptor protein complexes, AP-3. His laboratory discovered AP-3, found the two types of sorting signals the complex recognizes, and made discoveries about its physiological function.

Dr. Bonifacino's team found that AP-3 mutations caused an autosomal recessive disorder, Hermansky-Pudlak syndrome, characterized by reduced pigmentation of the eyes and skin. People with this condition have poor vision, prolonged bleeding and bruising, fibrosis of the lungs, and inflammatory colitis. Lung fibrosis leads to early mortality.

When they tested skin fibroblasts from several patients with this syndrome, the researchers found AP-3 defects in two patients. However, Hermansky-Pudlak syndrome is a genetically heterogeneous disease, meaning that mutations in a variety of genes, including AP-3, can cause the condition. Mutations in AP-3 cause Hermansky-Pudlak syndrome type 2. Dr. Bonifacino has named these genetic diseases of protein coats “coatopathies.”

Dr. Bonifacino provided additional details about the discoveries his team has made regarding the molecular mechanisms of protein and organelle distribution within cells. Like many of the projects in DIR, his work started with the study of basic cellular and molecular mechanisms and then moved to application of that knowledge to the mechanisms of human disease. This approach has been repeated in other DIR laboratories.

X. GABRIELLA MILLER KIDS FIRST UPDATE

Dr. Lorette Javois, who serves as the Kids First Working Group Coordinator, provided an update on the Gabriella Miller Kids First Pediatric Research Program, which began in 2015. The program involves nine ICs and the Centers for Disease Control and Prevention. The program was established by a 2014 law that ended taxpayer contributions to presidential campaigns and moved part of the money to pediatric research. Congress authorized the NIH Common Fund to receive \$12.6 million of this money per year for 10 years. The first appropriation came in FY15.

Dr. Bianchi serves as one of the four Institute Director Co-Chairs. Dr. Javois and several other program staff serve on the Working Group Leadership team.

The aim of the Kids First program is to alleviate suffering from childhood cancer and structural birth defects by fostering collaborative research to uncover the etiology of these diseases and by supporting data sharing among pediatric researchers.

The major Kids First initiatives include:

- Identifying children with cancers and structural birth defects whose genomes could be sequenced at gene sequencing centers
- Developing the Kids First pediatric data resource to provide access to high quality genomic and phenotypic data. The aim is to facilitate research to identify DNA changes that cause or contribute to childhood cancers and birth defects
- Supporting data mining and data demonstration projects to understand the biology of childhood cancer and structural birth defects

Over the first three years, the Kids First program has selected 23 cohorts and about 18,000 genomes for whole genome sequencing. The cohorts selected for sequencing included groups with adolescent idiopathic scoliosis, cancer susceptibility, congenital diaphragmatic hernia, and disorders of sex development, among others. However, because of funding limitations, upwards of 34,000 genomes could not be sequenced.

The cohort investigators have exclusive use of the genomic data for six months. The data are entered into the database of Genotypes and Phenotypes (dbGaP) or the NCI’s Genomic Data Commons. The quality control process at dbGaP happens during this period, and then the data are released for the research community’s access.

The Kids First Pediatric Data Resource Center includes the public-facing data resource portal, the Data Coordinating Center to facilitate deposition of data, and the administrative and outreach core to develop policies and reach out to advocacy groups.

In addition to Kids First funding of the sequencing effort, six ICs, including NICHD, are providing R03 research grants to investigators who propose to analyze the data that is available. The grants are for up to \$200,000 over the course of two years.

Dr. Javois said that more information about the program is on the Kids First website. She encouraged Council members who work with Kids First relevant advocates and advocate organizations to direct them to this site. NIH is working closely with the advocate community on this program.

Dr. Bianchi closed the public portion of the meeting at 1:00 p.m.

XI. DIVISION OF INTRAMURAL RESEARCH CLOSED SESSION

The Scientific Director presented the confidential reviews of the Board of Scientific Counselors. The Council approved the report and had no questions on the presentation.

XII. DIVISION OF EXTRAMURAL RESEARCH CLOSED SESSION

This portion of the meeting was closed to the public in accordance with the determination that it concerned matters exempt from mandatory disclosures under Sections 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).

XIII. REVIEW OF APPLICATIONS

The session included a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions or other applications for which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect. The Council considered and approved 482 HD-primary applications requesting \$135,654,127 in direct costs and \$188,471,415 in total costs.

XIV. ADJOURNMENT

There being no further business, the meeting adjourned at 4:30 p.m. on Thursday, September 14, 2017. The next meeting is scheduled for January 18, 2018.

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.²

SIGNED

Diana W. Bianchi, M.D.
Chair, National Advisory Child Health and
Human Development Council
Director, *Eunice Kennedy Shriver* National
Institute of Child Health and Human
Development

11/28/17
Date

Kimberly A. Witherspoon
Committee Management Officer, *Eunice Kennedy Shriver* National
Institute of Child Health and Human Development

Attachment: Council Roster

² These minutes will be formally considered by the Council at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.