

***Eunice Kennedy Shriver* National Institute of Child Health and Human
Development Division of Intramural Research
BOARD OF SCIENTIFIC
COUNSELORS MINUTES
December 1, 2017 Building 31,
Room 2A48**

Members Present: Dr. Scott A. Rivkees (chair), Dr. Kate Ackerman (nominee), Dr. Vanessa Auld (nominee), Dr. Elizabeth Bonney (nominee), Dr. Jeanne Brooks-Gunn, Dr. Serdar Bulun (nominee), Dr. Frances Jensen (nominee), Dr. Deborah L. Johnson (nominee), Dr. Kojo A. Mensa-Wilmot (nominee), Dr. Antonios Mikos, Dr. Yoel Sadovsky, Dr. Susan S. Taylor, Dr. Eric Vilain, and Dr. Martha Werler (nominee).

Federal Employees Present: Dr. Constantine A. Stratakis, Dr. Arlyn Garcia-Perez, Ms. Francie Kitzmiller, and at various times additional members of the NICHD staff participated in the meeting.

I. OPEN SESSION

The meeting convened at 8:05 a.m. Dr. Stratakis introduced Dr. Diana Bianchi, Director, NICHD, to provide the Director's Report.

Director's Report

Dr. Bianchi provided an outline of her talk which included a Congressional update, an update on her vision for NICHD, and an overview of some future activities.

The US government was operating on a Continuing Resolution through December 8, 2017. Only those extramural grants that scored extremely high are being funded, until the final budget is known.

Dr. Francis Collins recently presented an update to Congress on the 21st Century Cures Act, which was signed in December 2016. NICHD is involved in several areas, which Dr. Bianchi had previously presented. Research in pregnancy and lactation by the PRGLAC taskforce will focus on safe and effective therapies for pregnant women and lactating women. The issue of inclusion is another aspect of the 21st Century Cures Act. NIH held an Inclusion in Research Workshop June 1-2, 2017 to address issues of including children, older populations, women, and other minorities in research. In response to another clause in the act, the Next Generation Researchers Initiative aims to improve the grant-funding prospects for early- and midcareer investigators. Dr. Bianchi presented a chart showing the proportion of funding going to early-, mid-, and late career investigators from 1990 to 2015 and the worrying trend that an increasing proportion of funding is going to those late career investigators, while proportions to early- and midcareer scientists are falling. The Grant Support Index (GSI) had been proposed as a way to measure a PI's grant support using a point system, however, this is being rethought following tremendous pushback from the

research community. Early stage investigators (ESI) are those who have completed their degree or post-graduate training within the past 10 years and who has not previously competed successfully as a program director or PI for a substantial NIH independent research award. An early established investigator (EEI) is one who is within 10 years of receiving their first substantial, independent competitive NIH research award. NIH hopes to increase the number of ESI and EEI awardees as well as other investigators anywhere on the continuum who are at risk of not having any funding when their grant expires and falling out of the federal pipeline. NICHD made improvements in FY2017 but is looking at other ESIs and at risk-EEIs who scored within the 25% percentile to potentially fund, to improve further.

Dr. Bianchi then provided an update on NICHD's partnerships. Over the past 13 months since her arrival, she has been meeting with other IC directors and their program officers to target programs where partnerships can be enhanced. NICHD and the National Human Genome Research Institute (NHGRI) will be holding a joint workshop on preconceptional, reproductive, prenatal, and neonatal genomics which will be webcast in an effort to promote transparency. NICHD is also partnering with the National Institute on Drug Abuse (NIDA) on the Environmental Child Health Outcomes (ECHO) study to address issues related to neonatal opioid withdrawal syndrome. NICHD's current research on childhood obesity focuses primarily on behavior and is partnering with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) who funds most of the research on the topic to identify new areas to move into. With the National Institute on Aging (NIA), NICHD will be partnering to look at Down syndrome and NICHD will be working with the National Institute of Allergy and Infectious Diseases (NIAID) on the subject of perinatal infections looking at pregnant women and children under age 3.

In an effort to better communicate the impact of our research, NICHD will continue to include the "Voice of the Patient" in Advisory Council meetings and at other meetings and workshops. So far, Ms. Kristine Ribas spoke about her daughter who had a pituitary tumor and was seen at the Clinical Center, Ms. Tara Schafer presented at the Human Placental Project workshop to talk about her experience having a stillbirth, and Ms. Megan Connolly, a two-time cancer survivor, spoke about her participation in the NICHD-funded oncofertility research program at Northwestern University.

Dr. Bianchi and Dr. Stratakis visited the DIR's Perinatology Research Branch, headed by Dr. Roberto Romero, in August 2017 as they celebrated their 25th year anniversary in Detroit, Michigan. Congresswoman Debbie Dingell and Detroit Mayor Mike Duggan also took part.

NIH-Congress interactions are a great way for NICHD to promote what we do. In recent months, Dr. Bianchi has met with the Congressional Black Caucus, the Women's Congressional Policy Institute, and the Congressional Brain Injury Caucus. Acting Health and Human Services Secretary Eric Hargan visited NIH on November 28, 2017.

Dr. Bianchi then turned her attention to internal communications. She recently launched an online suggestion box where staff can ask questions or make a suggestion that will be addressed in an issue of the NICHD Director's Newsletter. The first question received was "*How does NICHD compare with other institutes and centers, now and in the past, in the number of female tenured, tenure-track and ACI investigators?*" Looking at NIH Leadership positions, women currently

occupy none of the five NIH Deputy Director positions, 7 of 14 NIH Associate Director positions, and 8 of 27 IC Director positions. Historically, only 1 of the 16 NIH Directors has been female. Across the intramural research program, 59 out of 265, or 22% scientific leadership positions are held by women. NICHD is one of only five ICs with 50% or more leadership positions held by women. Compared to the top 10 academic research institutions where women held 23% of tenured positions in 2013, NIH was at 20% in 2013 but saw this grow to 23% by 2016. The proportion of female tenure-track investigators and tenured investigators was presented for each IC and also compared to the national average. In 2015, NICHD was just below the national average of tenure-track faculty at 41.7% compared to 44% nationally and just above average for tenured investigators at 23% compared to 22% nationally. The NICHD DIR has seen an increase in the proportion of female tenure-track investigators since Dr. Stratakis was named Scientific Director in 2011. Over the same period, DIPHR had a decline in the number of tenure-track investigators due primarily to departures and successful awards of tenure. DIPHR has seen an increase in the proportion of female tenured investigators over the same period while DIR saw a decline, due to a disproportionate number of female senior investigators who have retired.

Next, Dr. Bianchi provided an update about NICHD's analysis of Training and Career Development or K Awards which she had presented at the June 2, 2017 meeting. The analysis showed that those who had received individual K awards, particularly physician scientists, were more likely to receive an independent NIH grant. The results of the analysis will be published in the January 10, 2018 issue of *JAMA Pediatrics*.

Another area of focus is data sharing and making resources available. The NICHD Data and Specimen Hub (DASH) is a publicly accessible online archive where researchers can store and access deidentified data from NICHD-funded studies to use for secondary research. Dr. Bianchi hopes to promote DASH as an opportunity for junior investigators to test hypotheses and start to show some productivity, without being delayed by the need to obtain IRB approvals and patient or sample recruitment. As of the time of the meeting, 52 studies have been registered in DASH and 9150 users from the United States and 906 international users have used the site. Studies will continue to be added and we hope to see interest continue to grow.

The Scientific Director, Dr. Stratakis, will undergo a regularly scheduled review by an external committee to evaluate his scientific vision, administrative style, training and mentoring, and his efforts with respect to promoting diversity. The review is tentatively scheduled for spring 2018. Dr. Bianchi is working with Dr. Rivkees to assemble the committee.

The NICHD will also be undergoing a strategic planning process in 2018. NICHD's last strategic plan was put in place in 2000. In 2012, the institute did go through a scientific visioning process to identify gaps in the science, but this was not a strategic plan. This effort will be much smaller and will focus on metrics to see what the impact is of research currently being funded. The process will include a group of about 50 people made up of both internal and external stakeholders. Planning is underway, and more information will be forthcoming.

Dr. Bianchi concluded her presentation with a couple staff updates. Dr. Germaine Buck Louis stepped down as the Director of DIPHR to become the Dean of the College of Health and Human Services at George Mason University as of October 1, 2017. Dr. Stratakis will be serving as the

Acting Director of DIPHR and Dr. Una Grewal will continue to serve as the Deputy Director. The search for a new Director has not begun yet due to the hiring freeze. Dr. Michael Weinrich, Senior Advisor for Device Development, Biotechnology and Bioengineering, retired at the end of September 2017. Dr. Weinrich previously served as Director of the National Center for Medical Rehabilitation Research from 2000 to 2014, a position currently held by Dr. Alison Cernich.

Questions followed. In response to a comment about the NICHD's portfolio, Dr. Bianchi indicated that the institute's core populations include children, reproductive couples, people with intellectual disabilities, and people with physical disabilities. She and Dr. Spong wrote a commentary, recently accepted for publication by *JAMA*, on the need to include these populations in research.

The BSC applauded NICHD's efforts in working with other institutes to leverage resources for shared interests. As part of the strategic planning process, Dr. Bianchi indicated that the institute will also look for ways the DIR, DIPHR, and the Division of Extramural Research can work together on certain high impact projects. In terms of the intramural program, Dr. Stratakis said that the DIR is quite integrated with other institutes in neuroscience where we are part of the Porter Neuroscience Research community at building 35, in the area of biophysics, and in translational research at the Clinical Research Center where NICHD investigators work closely with NCI, NIDDK, NIDCR, and others. The NICHD DIR Director's Awards are a two-year, competitive funding opportunity created to encourage DIR investigators to collaborate with each other and investigators in other institutes.

Discussion then turned to the data presented on female scientists. NIH has created a Gender Equity committee, chaired by NICHD's Dr. Gisela Storz, which will analyze salary and resource data for investigators across institutes on a routine basis. The DIR has also worked with the Deputy Director for Intramural Research to request exceptional pay increases to address existing inequities in compensation and also increased the number of women in leadership positions with the recent reorganization. Feeding the pipeline of female investigators and leaders continues to be a challenge facing both NIH and outside institutions. The applicants through NIH-wide Stadtman and Lasker programs have been noticeably more diverse in terms of women and underrepresented minorities. Dr. Bianchi noted that with the analysis of training awards, NICHD showed the timelines for MDs were unrealistic and a similar analysis may help with gender differences. Having strong male and female role models in leadership positions who promote diversity may also help women and underrepresented minorities in the career pipeline succeed. Another suggestion was made that increasing public awareness that childcare can be a healthy option may also help prevent women from falling out of the pipeline. The issue of unconscious bias will also be a topic of a later presentation.

Scientific Director's Presentation

Dr. Stratakis introduced and welcomed two new members of the BSC: **Dr. Vanessa Auld**, from the Department of Zoology at the University of British Columbia, and **Dr. Elizabeth Bonney**, director of research at the Department of Obstetrics and Gynecology at the University of Vermont. He also announced that **Dr. Rita Balice-Gordon**, an expert in the field of neuroscience, resigned from the Board in September 2017. Dr. Stratakis offered his congratulations to **Dr. Tony Mikos**, who was elected member of the Academy of Athens in Greece.

Dr. Stratakis then reviewed the tasks of the BSC to evaluate the research of NICHD DIR and advise institute leadership on programmatic decisions and resource allocations. The goal of the intramural program is to promote high-risk, high-impact laboratory and clinical investigation that could not be readily supported in the extramural environment. The BSC reviews site visits and tenure-track investigators on an ongoing basis, and meets twice a year, each June and December. The NICHD DIR Guidelines for Site Visit Reviews is a dynamic (i.e. continuously updated) policy document that has been in effect since 2010. Each investigator of the DIR is reviewed at least every four years utilizing ad hoc review committees chaired by members of the BSC. While the NICHD DIR uses a scoring system similar to that used in extramural study sections, the review of an intramural laboratory differs in that it covers the whole research portfolio of an investigator, not just a single project and that the main evaluation is retrospective, rather than prospective, at least for tenured investigators. Site visit scores allow for prioritization between laboratories, as well as between projects within a laboratory.

NICHD DIR's staff currently numbers around 950, including 57 tenured and 6 tenure-track investigators. More than 80 clinical protocols are run by NICHD, two-thirds of them at the NIH; five accredited graduate medical education programs train clinical fellows, some in collaboration with other ICs (e.g., Medical Genetics run by NHGRI).

The NICHD DIR's current organizational structure has been in place for two years, since October 1, 2015. Scientifically, the laboratories have self-assembled into intellectual affinity groups, with some having secondary affiliations in addition to their primary groups. Each group elects an Affinity Group Head but this individual does not have a supervisory or administrative role.

A number of Associate Scientific Director (ASD) positions were created to serve the needs of PIs such as managing maintenance contracts, shared equipment, and administrative staff within the six building clusters; ASDs do not participate in budget and personnel negotiations that take place between the SD and individual PIs. Thus, each investigator deals directly with the Office of the Scientific Director (OSD) for the purposes of administration and resources.

The ASDs represent their functional areas on the Group of Senior Advisors (GSA), which meets monthly. There are two additional ASDs, **Dr. Mary Dasso**, who serves as the ASD for Budget and Administration, and **Dr. Tracey Rouault**, the ASD for Recruitment, Retention, and Diversity. **Dr. Chris McBain** continues to serve as Deputy Scientific Director. Memberships of the GSA and affinity groups were presented. Leadership in the OSD and the Administrative Management Branch, led by **Ms. Francie Kitzmiller**, meet every Tuesday to review all personnel, budget, and space requests. Budget meetings are held in the summer with each investigator to review their budgets for the coming fiscal year.

The NICHD has an overall budget of more than \$1.3B, of which approximately 14% goes to supporting the DIR, including 5% for taps and 9% for operations. Of the approximately \$186M the NICHD DIR received for FY17, 33% was allocated toward personnel, 21% toward consumables, 20% toward the NIH Office of Research Services to cover buildings, maintenance, etc., and 15% was paid in support of the NIH Clinical Center. The DIR renovation costs for FY17 were approximately \$3.8M as part of a years-long effort to provide new or renovated space to more than 80% of the investigators which is expected to be complete by the end of 2018. Under the

FY17 appropriations bill signed by the President in May, the NICHD DIR received an additional allocation of \$2M over the FY16 budget which was used to support capital equipment and sequencing contract requests. A total of approximately \$6.3M was spent on capital equipment purchases in FY17. Animal care costs are currently approximately \$4.5M including ~\$2M in support of the nonhuman primate research program which will be closing in 2018.

The Perinatology Research Branch (headed by Dr. Roberto Romero) is supported by a \$15.5M contract with Wayne State University in Detroit, MI; the program receives an additional sum of approximately \$1.5-\$1.7M for operating costs from the DIR.

In addition to the discussed DIR allocation, DIPHR has a budget of approximately \$8.6M, including \$6.8M for operating costs and \$1.8M in assessments. DIPHR receives additional support in the form of contracts which are not included in their intramural budget.

For FY18, NIH is currently under a Continuing Resolution approved through December 8, 2017 and the final budget allocation for FY18 remains uncertain.

A number of staff changes were reviewed. Dr. Ida Owens, the first African American investigator at NIH, a true pioneer and celebrated biochemist, retired in August 2017. Another senior investigator, Dr. Chi-Hon Lee has announced plans to retire from NIH in February 2018 to go to Taiwan's Academia Sinica as head of their neuroscience program. As Dr. Bianchi mentioned in her presentation, Dr. Germaine Buck Louis, former Director of DIPHR, departed in September 2017 and Dr. Stratakis has assumed the role of acting director of DIPHR until her successor can be identified. He also shared the sad news that Dr. Kevin Catt passed away on October 1, 2017. Dr. Catt spent more than three decades at NICHD and served as Chief of the Endocrinology & Reproduction Research Branch where he made significant contributions to our understanding of hormone receptors, signaling and actions.

The NICHD DIR has recruited three new tenure-track investigators, between late 2016 and early 2017: Dr. Katie Drerup, a developmental biologist, Dr. Claire Le Pichon, a neuroscientist, and Dr. Timothy Petros, also a neuroscientist. Dr. Petros will present later in the meeting. The DIR also supported DIPHR in the recruitment of Dr. Fasil Tekola-Ayele in 2016 whose primary appointment is with DIPHR and he has a secondary appointment with the DIR. Recruitment efforts are ongoing through the NIH Stadtman Investigator search. NICHD also participates in the Lasker Program which provides support for 5 years at NIH followed by up to 3 years at an extramural research facility or continuation in the intramural program. Success with this program has been limited NIH-wide and NICHD has not had any successful candidates to date.

NICHD DIR investigators continue to be successful in competing for funding across the NIH intramural program. NICHD is the lead institute for the U-01 program, an effort to open up the NIH CRC to extramural investigators through collaborations with intramural researchers, now in its fifth cycle. There are currently two studies at the CRC with NICHD involvement supported by U-01s.

The NIH Bench-to-Bedside awards primarily supports intramural investigators who may also have extramural collaborators. For the FY17-FY18 cycle, three awards were made to NICHD

investigators: Dr. Jack Yanovski, Dr. Forbes Porter, and Dr. Constantine Stratakis, totaling more than \$900K. Between 2006 to 2015, NICHD investigators received 27 Bench-to-Bedside awards, on par with much larger institutes.

The DDIR Innovation Awards is a new opportunity to provide seed money for innovative and high-impact research, and to stimulate interactions among investigators across NIH's intramural research program. For the first award cycle in 2017, awards were made to four groups that included NICHD DIR investigators: Drs. Ajay Chitnis, Joshua Zimmerberg, Claire Le Pichon, and Todd Macfarlan.

The NICHD DIR Director's Awards are an opportunity that was created based on the recommendation of the Blue Ribbon Panel to foster new collaborations within the DIR or across NIH's intramural program, providing two years of funding. Two cycles have been completed and we anticipate the third cycle going forward for FY18-19, though the funding level has yet to be finalized. Successful awards from second cycle, FY16-17, were presented. The application was based on a modified R-21 and an external review committee of NICHD and NIH extramural staff conducted the reviews.

NICHD DIR investigators also had the opportunity to compete for NIH Intramural-to-Russia funding through the NIH Office of AIDS Research and for Office of AIDS Research Strategic Funding made available by the NICHD Office of the Director. The successful awards were presented.

Dr. Stratakis then introduced Dr. Una Grewal, Deputy Director of DIPHR, to provide an update on the division.

Presentation on DIPHR

The Division of Intramural Population Health (DIPHR) is focused on the health and wellbeing of populations. It includes 26 staff members and roughly three dozen trainees organized into three branches: the Epidemiology Branch, the Biostatistics and Bioinformatics Branch, and the Health Behavior Branch. DIPHR's FY17 operating budget was \$8.6M, less than 5% of NICHD's intramural budget.

In addition to the departure of Dr. Germaine Buck Louis, Dr. Danping Liu, a tenure-track investigator in the Biostatistics and Bioinformatics Branch recently left to join NCI. With the previous departure of the Branch Chief, Dr. Paul Albert, this leaves only three investigators in the Biostatistics and Bioinformatics Branch. The search for a new Branch Chief will commence after the new Division Director is named.

The Contraceptive Development Program, formerly part of NICHD Extramural Program, has now been incorporated into DIPHR. The program is led by Dr. Diana Blithe and includes two additional staff members, Dr. Jill Long and Dr. Min Lee.

Several scientific advances from each of the three branches were presented. In 2017, 11 press releases from DIPHR were viewed by more than 1.1 billion people globally.

Dr. Stratakis thanked Dr. Grewal. He then introduced the next speaker, Dr. Yvette Pittman, who has been serving as acting director of the Office of Education since Ms. Brenda Hanning's departure at the end of 2016.

Presentation on the Office of Education, NICHD

Yvette Pittman, PhD, Acting Director, Office of Education

The mission of the Office of Education (OE) is to support the training needs of the DIR's fellows and students at all levels through the development of academic support programs, complementing intramural lab mentoring, providing career guidance, and through the creation of new training initiatives. The DIR has a trainee population of about 310, including, 169 postdocs, 45 postbacs, 19 clinical fellows, 15 graduate students and 62 summer students in 2017.

In terms of career outcomes, approximately 30% of the DIR's trainees go on to academic faculty positions, higher than the national average of 15-20%. Academic research positions at 19%, government research positions at 17%, and industry research positions at 14% make up the next three largest categories.

The OE also tracks trainee progress while they are in the DIR. An Online Annual Progress Review System for postdoctoral and clinical fellows was launched in November 2015 giving fellows and their mentors the opportunity to report progress and set goals for the coming year. The system has also allowed the OE to collect data on the fellows' activities including conference attendance, writing abstracts and grant proposal submissions, as well as to evaluate mentoring for our investigators' site visits, and targeting educational programs to the fellows' needs. The data on the 277 reports collected to date was presented. A priority of the OE is to increase grant activities among the DIR's fellows. As part of the Annual Progress Review, fellows are also asked to complete a survey on their training experience with 95% indicating that they would recommend NICHD as a place to train. When asked about areas where training could be improved, nearly half indicated career development, giving feedback such as wanting more opportunities to mentor students, exposure to other careers and asking for more grant writing and college teaching opportunities. For postdoctoral fellows, the OE's key activities include public speaking, teaching, grantsmanship, publishing, and career preparation. One current initiative for those pursuing an academic career is a two-part workshop series on interviewing skills and chalk talks.

For the approximately 50 postbaccalaureate fellows, NICHD provides an annual course on a variety of professional development and mini scientific lecture topics. Fellows are also offered shadowing opportunities with a variety of clinical groups in the institute. Dr. Pittman also shared a list of medical and graduate school acceptances for NICHD postbacs in 2017.

The Three-minute Talks (TmT) Competition to promote the effective communication of science will be entering its fourth year in 2018 and will be expanding to include a total of five institutes.

Dr. Pittman highlighted a few of the other activities in the OE. She provides one-on-one counseling to fellows on a number of topics including mentoring challenges, career transitions, and grant writing. OE leads fellows' efforts in publishing their own monthly newsletter. The

NICHD Connection focuses on mentoring, careers, and academic programs for young scientists, and over 90 issues have been published thus far. DIR fellows also organize an annual retreat each spring. Along with investigator Dr. Gigi Storz, Dr. Pittman has worked on establishing a Responsible Conduct of Research (RCR) Training for NICHD DIR fellows to ensure they are receiving eight hours of training in their first two years, on par with extramural requirements. The DIR supports a number of initiatives to increase diversity at all training levels through the Developing Talent Scholars Program for postbacs and graduate students, the summer student program where 15 slots are centrally supported for individuals from disadvantaged backgrounds or groups underrepresented in science, and the Fellows Recruitment Incentive Award for postdocs. The NICHD-INSERM exchange program is an international collaboration where postdoctoral fellows have the opportunity to train with both French and US mentors, and the Future Researchers Program provides medical students from Brazil with the opportunity to train at NICHD.

In terms of grant writing, the OE has vetted 150 grant opportunities from NIH and outside organizations, providing a list of 76 for which intramural fellows are eligible to compete. Within NIH, the Postdoctoral Research Associate (PRAT) Fellowships administered by NIGMS is one such opportunity. Currently NICHD fellows hold 6 out of the 20 slots available across NIH. OE offers extensive guidance on grant writing and the application process, through both group training and one-on-one advising. With OE leadership, NICHD DIR recently completed the first cycle of its Intramural Research Fellowships, resulting in three fellow awards from the Burgess, Banerjee, and Bornstein labs. Dr. Pittman thanked the BSC members for their help in reviewing the applications.

Looking forward, the OE would like to expand its efforts around grantsmanship, career planning and readiness and exposure to a variety of science careers through both group sessions and individual activities. Individual orientation sessions will be held to make sure trainees are aware of the resources that are available to them. The OE also plans to expand its alumni tracking efforts and create an Endocrine Clinical Scholars Program. The “Explore” Series was launched to provide exposure to different career paths such as science policy, grants management, and technology transfer. OE has continued to sponsor individual training activities related to college teaching, project management, advanced English, GRE preparation, FDA careers, and participation in the NIH-Duke University masters program for clinical research. The *SciPhD* is a certificate program NICHD will begin offering, and it is designed to translate academic research skills into business-oriented qualifications.

Discussion followed. The BSC commended Dr. Pittman on her excellent work and presentation. A suggestion was made that the Office of Education may also want to address the topic of work/life balance for both men and women through discussion panels, so fellows can see how different people have dealt with the issue. A propos of the size of the office, Dr. Pittman indicated that it is currently just her and a program coordinator, but there have been discussions about increasing the staff, particularly to recruit two associate directors, one focused on GME and the other for postdoctoral and graduate education. Additional support for OE must be balanced against scientific positions and would need the approval of the GSA. It was clarified that NIH has a central Office of Intramural Training and Education that provides for general needs, and each institute has their own training office, meant to complement each other. There is some collaboration between IC training offices, but this may be one area where efforts could be expanded.

Drs. Stratakis and Pittman then introduced a video from Dr. Miranda Broadney, a finalist of the 2017 TmT competition. They reminded the BSC that this program was started in NICHD three years ago, then expanded to include NHGRI and NIDCR, and in 2018 will include a total of five institutes for its fourth cycle of competition. Dr. Broadney is a graduate of the Pediatric Endocrinology Fellowship Program and a Thrasher Research Fund Scholar, who also spent time with DIPHR.

Following a short break, Dr. Stratakis introduced the next speaker, Dr. Todd Macfarlan.

Scientific Presentations

Todd Macfarlan, PhD, Stadtman Investigator and Head, Unit on Mammalian Epigenome Reprogramming

The evolutionary functions of KRAB-zinc finger proteins in mammals

Krüppel-associated box zinc finger proteins (KRAB-ZFPs) are the largest family of sequence-specific DNA binding transcription factors in mammals, including humans. These proteins emerged in the last common ancestor of coelacanth, birds, and tetrapods and have expanded and diversified in the mammalian lineage. Several lines of evidence have suggested that KRAB-ZFP evolution is being driven by the need to bind and transcriptionally silence transposable elements (TEs), which also undergo continuous turnover in animal genomes. To gain insights into the developmental and evolutionary function of KRAB-ZFPs, the Macfarlan lab has undertaken systematic biochemical and genetic approaches that include mapping the genome-wide binding profiles of dozens of KRAB-ZFPs and knocking out hundreds of KRAB-ZFPs in mice using a newly developed CRISPR/Cas9 based strategy that allows us to remove clusters of KRAB-ZFP genes up to nearly ~3Mb. Their data demonstrates that the majority of recently evolved KRAB-ZFPs indeed bind and suppress TEs, but that this suppression is not essential for development. In contrast, more ancient KRAB-ZFPs play important roles in mammalian evolutionary adaptations. One such KRAB-ZFP, ZFP568, acquired a critical function in the embryonic suppression of a key growth signaling molecule in mammals, a placental transcript isoform of the insulin like growth factor 2 (Igf2), which was likely critical during the early evolution of mammals. This leads to a model where TE turnover drives the evolution of new KRAB-ZFPs, many of which decay as the target TEs decay by genetic drift, except in cases where the KRAB-ZFP adopts a new critical function. Dr. Macfarlan discussed the lab's ongoing work that seeks explanations for the continuous expansions of KRAB-ZFPs against TEs and identifies additional KRAB-ZFPs that contributed to adaptations that define the mammalian lineage.

Questions followed. The BSC commended Dr. Macfarlan for his great work and presentation.

Dr. Stratakis then introduced the next speaker, Dr. Alex Sodt, who had also presented at the site visit the previous day.

Alex Sodt, PhD, Investigator and Head, Unit on Membrane Chemical Physics

Building the next generation of membrane models to describe reshaping processes in the cell

A membrane reshaping process like clathrin mediated endocytosis uses a coat of proteins to reshape the membrane into a vesicle. The proteins interact with each other and with the membrane to bend the membrane into a “bud” shape. Various qualitative mechanisms have been proposed to explain how adsorbed proteins bend the membrane, including scaffolding, crowding, and induction of mechanical properties. With their detailed model, Dr. Sodt’s lab is turning these qualitative ideas into quantitative answers for how much force the cell can apply to reshape the membrane. An equally important question is: How much force is required to bend the membrane into a particular shape? They have discovered that lipids act collectively to change the “stiffness” of the membrane, an effect that breaks the textbook understanding of how lipid composition determines the shapes the membrane prefers. In his talk, Dr. Sodt explained how his lab uses experimental and theoretical information to discriminate between mechanistic hypotheses for membrane reshaping.

Questions followed.

After a brief recess, Dr. Stratakis introduced the final scientific speaker, Dr. Steve Suomi. Dr. Suomi’s work has had wide reach, impacting the fields of pediatrics, behavior, and mental health including our understanding of how the environment, in utero, at birth, and early experiences shape who we are. Dr. Suomi has announced plans to retire in 2018, following a 34-year career in NICHD that began in 1983.

Stephen Suomi, PhD, Senior Investigator and Head, Section on Comparative Behavioral Genetics

Dr. Suomi’s lab uses nonhuman primates, in particular rhesus monkeys, to study individual personality or temperament, the underlying biological substrates, and how genetic and environmental factors act and interact to shape individual developmental trajectories. The lab is based at the NIH Animal Center in Poolesville, Maryland and includes indoor/outdoor housing for the monkeys, a neonatal nursery, and a five-acre field site where the monkeys can live in naturalistic settings. This set up allows for behavioral studies in the normative social context of the monkeys which live in large social groups with dominance hierarchies that depend on matriline. Every member of the highest-ranking family including infants outranks every member of the next highest-ranking family and, within each family, younger daughters outrank older daughters.

Much is known about the early relationships between infant monkeys and their mothers. They spend the first month in intimate physical contact with their mothers, forming strong and enduring attachment bonds. After this time, the young monkeys begin to explore and have interactions with their peers, but the mother remains present in the immediate vicinity as a secure base and, if the mother isn’t nearby the infant quickly loses any motivation to explore. Throughout the first three years of childhood, the monkeys spent several hours everyday in active social play with their peers and it’s in the context of this play that virtually every behavior pattern that is going to be important for normal adult functioning is developed and practiced.

However, in about 10 percent of cases, the mother monkeys are neglectful or abusive to their offspring. This pattern of behavior tends to pass from generation to generation so if a monkey has a neglectful mother it will likely become a neglectful mother herself. The infants who grow up with neglectful mothers become preoccupied with trying to get access to their mothers and spend less time exploring their environment or playing with their peers, ultimately becoming more aggressive when they lack this secure attachment relationship. To further study this effect further, the lab has compared infant monkeys raised in a neonatal nursery by human caregivers with those who are raised in small groups with peers and their mothers. These nursery-reared monkeys and the mother- and peer-reared monkeys are later put together into larger social groups, around seven months of age. The nursery-reared monkeys become hyper-attached to one another and do not explore or reach the levels of play as seen in their mother-reared counterparts. As they grow up, the nursery-reared monkeys continue to be excessively fearful and anxious in novel situations, much like their counterparts with neglectful mothers. Other long-term consequences include higher levels of cortisol for at least the first two years of life, tendency to develop intense aggression, and they show dysfunction of serotonergic metabolism along with other biological effects. Neuroimaging studies show that the brains of the nursery-reared and mother-reared monkeys differ both structurally and functionally in terms of serotonin binding potential and lymphocyte telomere length.

Since his last site visit in 2012, Dr. Suomi has focused on studying the epigenetic changes associated with development and with early rearing effects. The results show that peer-reared monkeys are under-expressing genes associated with immunoglobulin production, interferon, antiviral responses, and overexpressing inflammation, cell growth, and differentiation and transcription control.

In collaboration with Dr. Moshe Szyf at McGill University, Dr. Suomi's lab has also shown that a number of genes that are differentially methylated between mother-reared and nursery-reared monkeys, but also shows that these differences, while still significant, decline as the monkeys get older. They have also shown that genome-wide patterns of methylation can differentiate infants from high-ranking mothers with those from low-ranking mothers. These same patterns of genome-wide methylation between high-ranking and low-ranking mothers are also shown in placentas gathered at birth suggesting that even in utero the infants are experiencing different environments based on their mothers' social status. Low-ranking status also affects access to resources, predictability of social initiations by others, leads to chronically high levels of HPA activity, higher injury rates, more immune system vulnerability, excessive inflammation, and high incidence of GI disorders.

The Suomi lab, notably staff scientist Dr. Annika Paukner, has also studied face-to-face neonatal mimicking in monkeys, given the importance of mother-infant interactions. This stimulation from their mothers, leads to distinct patterns of brain activity in the infants as shown through EEGs. Failure to imitate can lead to some developmental problems later on, including autistic-like behaviors and much lower levels of play, showing that these infant capabilities are predictive of later social competence and adaptation.

Dr. Suomi concluded his presentation by saying what a privilege it had been to spend the last three decades of his career at NICHD. He was appreciative of the extended withdraw, over two-and-a-half years, from the Poolesville facility which allowed time to place the monkeys at other facilities and finish some research activities. Data and samples from the lab will be made available to collaborators for further analysis, given the immense value of these resources. Dr. Stratakis and the BSC acknowledged the impact of Dr. Suomi's work on the field of behavioral pediatrics and thanked him for all of his contributions.

The BSC recognized Dr. Suomi with a standing ovation in recognition for his momentous contributions to the field and NIH.

Dr. Stratakis introduced the final speaker for the day, Dr. Anna Han, noting that this presentation is timely given the discussion earlier about the importance of diversity in the workforce. To help address the issue, it is important that BSC members, ad hoc reviewers who participate in site visits, and DIR staff, faculty, and trainees learn to recognize their own biases. The DIR will therefore be incorporating implicit bias training for into the scientific review process and Dr. Han's presentation will serve as a pilot.

Presentation on The Science of Diversity and the Impact of Unconscious Bias

Anna Han, PhD, Office of Scientific Workforce Diversity, NIH

Twenty years ago, when Dr. Han started her work, no one had heard of unconscious, implicit, and explicit memory. Outlining her talk, topics would include why diversity matters, how unconscious bias is a hurdle in judgements, decision making, and every day interactions, and what strategies can be used to mitigate the influence of unconscious bias.

Understanding implicit bias and having a diverse workforce are important in order to address health disparities, increase the effectiveness of the existing workforce to manage research teams foster creativity, innovation, and motivation, and to attract and retain talent in the workforce. Diversity broadens the scope of scientific inquiry, allowing solutions to be found for more complex problems. The literature shows that research teams that are ethnically diverse tend to publish in more higher impact journals and receive more citations and that gender and ethnically diverse teams produce more creative work that leads to better innovation. Studies also show that diversity leads to better decision making. For instance, juries that are more homogenous do not deliberate as long and are more prone to errors than more diverse groups. Likewise, groups of financial day-traders that are homogeneous are more likely to cause a bubble that bursts during simulations than more heterogeneous groups. In addition to having more deliberation, diverse groups also benefit from collective intelligence. An example is a study from 1904 where people were asked to guess the weight of a cow during a fair and, while no one person guessed correctly, when the guesses of the entire crowd were averaged, the average was within one pound of the cow's actual weight. Replication studies and similar studies have had similar outcomes. Diversity makes us better thinkers and deliberators as individuals and as a team.

We know however that our biomedical workforce is not diverse. Medical school applicants and graduates are close to 50-50 in terms of gender. However, as their careers progress, the proportion

of women who hold professorships and department chairs drops significantly; women make up only about 14% of department chairs. At the current rate of improvement, gender parity will take about 48 years. These figures are even worse if you look at racial differences. The demographics of tenured and tenure-track investigators the NIH Intramural Research Program show similar disparity.

So why is it so difficult to achieve diversity? For some disciplines, like computer science and physics, there is a gender disparity in the pipeline, but for most disciplines this does not account for problem. The disparities are also not from a lack of talent or lack of commitment or interest. Individuals may feel isolated or lack a sense of belonging and may feel taxed if they are always the token person representing their gender or race in a group. Implicit and unconscious bias, or the errors in judgement or decision making we make due to the influence of beliefs and attitudes we may not consciously be aware of, also have an impact.

According to Nobel Prize winning neuroscientist Dr. Eric Kandel, we are exposed to about 11 million pieces of information at a time and we can only handle about 40 of those consciously. To make up the difference, 80-90% of our mind works unconsciously, using mental shortcuts and past knowledge to make assumptions. These “mind habits” influence our thoughts, judgments, and interpretations of seemingly objective situations; we see what we look for and look for what we know. Every single one of us has these biases. As a demonstration, Dr. Han asked everyone to say “spot” out loud with her ten times before asking the question “What do you do at a green light?” Most of the audience immediately answered “stop”. She explained that we do this because we are cognitively lazy, it is easier to mentally travel to “stop” than “go”, and those who did get it right took a little time and effort to override the tendency to say “stop”.

Implicit bias is difficult to overcome because it challenges our core values that we are smart, objective people, our sense of morality, and our beliefs in a just world. Even the most well-intended person can have implicit bias or biases, and, if left unchecked, it can influence our judgments and decisions without our conscious awareness. In one study, a fake resume for a lab manager position, with either a male or female name on it, was sent to male and female faculty members to evaluate. Both male and female faculty members rated the male applicant as more competent, more hireable, more likely to offer mentoring, and on average offered a salary that was

\$3,700 more than for the identical female applicant. While this may not sound like a large salary difference, as the basis for promotion and salary adjustments, this can mean hundreds of thousands of dollars over the course of a career. In another study, 312 recommendation letters went through a qualitative analysis of content and found that not only did the letters for women tend to be shorter, about 84% as long as letters for males, the content was quite different as well. The letters for women were more likely to talk about training, teaching ability, the woman’s personal life and were more likely to raise doubts, while the letters for men were more likely to focus on their research skills, publications, and career potential. Similarly, in an analysis of NIH R01 application summary statements, males are more likely to be described as leaders, highly innovative, and the research described as highly significant while those for female applicants are more likely to describe their expertise and research environment. Even girls as young as five are more likely to describe a boy as brilliant than another girl, and this affect is exaggerated over time.

Dr. Han then discussed strategies to overcome potential bias. People tend to have a narrow definition of success, where characteristics of success are too narrowly defined and are often aligned with stereotypical traits of some groups. As an example, she showed the lack of diversity among the 2017 Nobel Prize winners, displaying the recipients' photos. Similarly, if you ask kids to draw a scientist, 58% of students in kindergarten-2nd grade will draw a male, 73% of students grades 3-5 draw a male, and 75% of grade 6-8 students draw a male. To overcome this, you can think about counter-stereotypical individuals, for example a wide array of successful scientists or famous women in history. We are also more likely to think people like us are better – people from our own institutions, our own disciplines, and our own fields – so we have to step back and reanalyze that. We also have to rethink indicators of success that are subject to unequal access and opportunities such as invited presentation, international collaborations, and editorial roles that are subject to biases.

Another pattern of potential bias is that some individuals are being held to a higher standard due to stereotypic assumptions of their social group membership, being held to a higher bar or to prove it again. For example, a male with lots of first authorship papers may be seen as an independent thinker while a female with just as many first author papers may be seen not as a good collaborator. As another example, neurobiologist Barbara Barres transitioned to male becoming Ben Barres and someone made the comment that he gave a great seminar and his work was “much better than his sister’s work” when they didn’t realize they were talking about the same person. To prevent this shifting standard, the most important criteria should be clarified and levels of performance calibrated before evaluation, ensure that the criteria are applied consistently, allow for anonymous voting, ensure you are able to articulate your evaluation with supporting evidence rather than vague praises or criticisms, and assign someone to play devil’s advocate to prevent others from just going along with a judgement.

The last pattern of bias that was discussed was performance attribution, when people use stereotypic assumptions to make causal inferences about an individual’s performance while overlooking situational factors.

In summary, bias can be interrupted by ensuring the committee composition is diverse, using a consistent set of interview questions and format for all candidates, being mindful of when you make a causal judgment and asking if there are other possible reasons, and sticking to criteria and performance evidence that can be observed.

Questions and suggestions were invited. A propos of how diversity is defined, Dr. Han indicated that it is really cognitive diversity, or having different backgrounds and experiences, that matters. As this is difficult to qualify and study, gender and race are used to approximate. The BSC thought the presentation was great and also recommended the Harvard’s implicit bias test as a complement to this training. Dr. Stratakis proposed using the presentation Dr. Han gave today as training for ad hoc reviewers going forward. Dr. Han provides this training to other organizations, such as scientific societies. The BSC also recommended that this training be provided to graduate students and trainees, who may be more receptive at their stage than faculty. In response, Dr. Han said you can’t always make people receptive but hopes that a cultural change will happen with time.

With that, the open session concluded.