***Eunice Kennedy Shriver* National Institute of Child Health and Human Development**
Division of Intramural Research
BOARD OF SCIENTIFIC COUNSELORS
MINUTES
December 7, 2018
Building 31, Room 2A48

Members Present: Dr. Scott A. Rivkees (chair), Dr. Kate Ackerman, Dr. Elizabeth Bonney, Dr. Serdar Bulun, Dr. Dauer William (nominee), Dr. Frances Jensen, Dr. Deborah L. Johnson, Dr. Kojo A. Mensa-Wilmot, Dr. Yoel Sadovsky, Dr. Susan S. Taylor, and Dr. Martha Werler.

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

OPEN SESSION

The meeting convened at 8:00 a.m. Dr. Stratakis welcomed everyone before introducing Dr. Diana Bianchi, Director, NICHD, to provide the Director's Report.

Director's Report

Dr. Bianchi provided an outline of her talk which included budget updates, the strategic planning process, NICHD research initiatives, and staff updates.

For the first time in 22 years, NIH started the fiscal year on October 1st with the full fiscal year appropriation, which was passed in September as part of an "essential services" minibus that also included defense spending. NIH funding is therefore not affected by the current continuing resolution, set to expire later in December 2018. In FY18, the NIH appropriation increased by $3B to just over $37B, with NICHD receiving a $75M increase. NIH received a further $2B increase for FY19 to $39B, a 5.4% increase over the FY18 budget. NICHD's FY19 budget is $1.506B, an increase of approximately 4%. NICHD used some of the additional funding in FY18 to help more early-stage researchers, doubling the number supported from 29 to 61. Funding was also used to facilitate the PRGLAC task force efforts to support inclusion or pregnant and lactating women in research. In FY18, NICHD allocated an additional $30M for the Advancing Clinical Trials in Neonatal Opioid Withdrawal syndrome (ACT NOW) study, which aims to identify, treat, and care for babies exposed to opioids *in utero*. Finally, more than $39M was allocated to sustain existing research programs in preeclampsia, material mortality, and fertility and infertility and protect them from additional cuts. NICHD also paid a tap of approximately $1.5M to the Department of Health and Human Services (DHHS), which was used to support children separated from their parents at the US-Mexico border. Additional funding of $4M was added to the National Center for Medical Rehabilitation Research to improve the health, productivity, independence, and

quality of life for children and adults with physical disabilities. NICHD also increased funding by more than $2M for early-stage small businesses that seek to commercialize biomedical technologies, such as prosthetics and other assistive devices. Finally, in FY18, the NIH budget for research on Down Syndrome increased to $58M, compared to $35M in FY17.

Dr. Bianchi noted that NICHD has not had a strategic planning process in 18 years. She participated in the scientific visioning exercise led by Dr. Alan Guttmacher in 2012, which was not strategic planning but rather sought to identify priorities for the field and not specifically for NICHD as other institutes also fund pediatric research. Several things came out of the scientific visioning that were relevant to NICHD, including the Human Placenta Project and two new extramural branches: the Gynecologic Health and Disease Branch and the Pediatric Trauma and Critical Care Branch. The current strategic planning process will provide a global overview of NICHD's portfolio, an opportunity to refresh and refocus the science, and to align NICHD's $1.5B with the priorities that emanate, all with the goal of improving the health of the populations we serve. The majority of the year has been focused on analyzing the portfolio, collecting the data, and understanding the impact of the research that we fund. That information was presented to a variety of working groups, both externally and internally, and now, in December 2018-January 2019, the themes that have emerged will be consolidated before getting input from the public. The final strategic plan is expected to be communicated to the public before the Advisory Council meets in September 2019. The core principles of the strategic planning process have been transparency, stakeholder participation, and decisions informed by evidence.

The strategic planning process is important in determining the identity of the institute in the 21st century, deciding whether we want to continue to focus on health and development or shift priorities to specific diseases or conditions, determine the right balance of clinical, basic and translational research, and to integrate and align or broad areas of science with our many stakeholders. The portfolio analysis was done by looking at scientific domains, focusing on the methods that are being used to study the science, as well as into four main public health domains. Dr. Bianchi reminded the BSC that 6.5% of NICHD's budget is for the National Center for Medical Rehabilitation Research, which includes things like stroke rehabilitation for adults. The data was sourced from the NIH Research, Condition, and Disease Categories (RCDC) database and the NICHD Child Health Information Retrieval Program (CHIRP). Dr. Bianchi then presented the results of the analysis. The scientific domains were not mutually exclusive. Of the $1.376B in FY17, 59% supported basic sciences, 15% population/epidemiology, 14% screening/diagnosis, 19% biomedical interventions, and 1% non-specific training and infrastructure costs. When the FY17 budget was analyzed by public health category, the breakdown included 55% pediatrics and child development, 15% gynecology and reproduction, 14% pregnancy and maternal health, 18% intellectual, developmental, learning and physical disabilities, and 7% in other categories.

The strategic planning working group then met in October 2018 to look at the data and provide big picture ideas on where the research is going. Since October, the Division of Extramural Research (DER), and Division of Intramural Research (DIR)/Division of Intramural Population Health Research (DIPHR) working teams have been meeting to review the 50 or so scientific themes that were prioritized by the working group. One of the goals is to also find ways to align the DIR,

DIPHR, and DER. More information about the process is available on the NICHD website at https://www.nichd.nih.gov/about/org/strategicplan and questions or ideas can be sent by email to NICHDStrategicPlan@nih.gov. A formal Request for Information (RFI) will be sent out in early 2019.

The NICHD Young Investigators Conference was held on August 26-29th in Potomac, MD, with 140 participants attending. Chairs of Pediatric, OB-GYN, and Rehabilitation Medicine departments were asked to nominate attendees. The conference originally focused on clinical trials, but this year's conference also included a track for basic scientists. The meeting was held locally to give junior clinical investigators the opportunity to get to know program officers and intramural investigators and be informed about grant and career opportunities available at NIH that are not traditionally emphasized like the Lasker Program, the NIH Clinical Center Bench-to-Bedside Program, and the U-01 opportunity.

The INCLUDE program (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE), which includes 18 ICs, investigates conditions that affect individuals with Down syndrome and the general population, such as Alzheimer's disease/dementia, autism, cataracts, celiac disease, congenital heart disease, and diabetes. The program includes basic science that will translate to clinical studies, as well as supplements for investigators who are doing clinical trials on a population to incorporate a cohort of people with Down syndrome.

The Trans-NIH Pediatric Research Consortium (N-PeRC) was developed to address child health research across all of the institutes and centers at NIH after discovering that there is $4.2B going towards child health research. NICHD only funds 18% of NIH's child health research. N-PeRC is working on harmonizing efforts in child health research across the 27 ICs, identifying gaps and opportunities for collaboration, providing trans-NIH supported training to grow pediatric work force, enhancing communication between NIH, advocacy groups and Capitol Hill, and includes an outreach effort to encourage senior pediatric researchers to serve on review panels. If successful, the BSC recommended establishing a similar consortium on women's heath research.

The Medication Taken by Pregnant and Lactating Women (PRGLAC) Task Force has submitted their recommendations to the Department of Health and Human Services (DHHS). Their recommendations included changing the existing culture that has limited scientific knowledge of therapeutic product safety, effectiveness, and dosing for pregnant and lactating women. For example, protecting pregnant woman *through* research instead of *from* research and removing pregnant women as a vulnerable population through the NIH Common Rule. Other recommendations included expanding the workforce of clinicians and researchers with expertise in obstetric and lactation pharmacology and therapeutics and removing regulatory barriers. The full report is available online and was submitted to the DHHS Secretary and Congress in September 2018.

NICHD is supporting a National Academy of Medicine (NAM) study to look at safety issues related to birth setting, in follow up to a study done in 2013. NAM was tasked with providing an

evidence-based analysis of the complex findings in the research on birth settings, including, but not limited to definitions and assessment of risk factors; access to and choice in birth settings, especially in subpopulations of women, social determinants that influence risk and outcomes in varying birth settings; financing models for childbirth across settings; and the licensing, training, and accreditation issues impacting professionals providing maternity care across all settings. NICHD expanded the scope of the current study to look at other areas of interest like the effect of maternal obesity, race/ethnicity, and age on maternal morbidity and mortality.

Dr. Bianchi concluded her presentation with a couple of staff updates. Dr. Bruce J. Tromberg has been named Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB). Dr. Tromberg is a leader in the field of biophotonics and will have an intramural laboratory within NICHD. Dr. Helene Langevin, is the new Director of the National Center for Complementary and Integrative Health (NCCIH). The review of the Scientific Director, Dr. Stratakis was completed, and a formal presentation was made in September 2018 to National Advisory Child Health and Human Development (NACHHD) Council. Dr. Bianchi thanked the BSC for providing input as part of Dr. Stratakis' review. Also, former NICHD fellow Dr. Tasuku Honjo shared this year's Nobel Prize in Physiology or Medicine with Dr. James Allison "for their discovery of cancer therapy by inhibition of negative immune regulation." Dr. Honjo is well known for his identification of Programmed Cell Death Protein 1 (PD-1) and Activation-Induced cytidine Deaminase (AID). He was a postdoctoral research fellow under Dr. Phil Leder in NICHD from 1973 to 1974, staying on as a visiting fellow in 1975 and then again in 1977.

Questions followed. A propos of the strategic planning, Dr. Bianchi indicated that the goal is to determine what areas of research NICHD should focus on, taking a broad approach and then prioritizing so that NICHD isn't duplicating efforts already made by other institutes. Major changes to the DIR aren't expected but the strategic plan will inform future intramural recruitments. One group not well represented in clinical medicine is adolescent health and, in particular, adolescent gynecological health. Dr. Bianchi indicated that this is one of the goals of N-PeRC but noted that the DIR would be establishing a program in Pediatric and Adolescent Gynecology in the coming year. The BSC emphasized that NICHD is unique in being able to link early development and late impact and wellness across the lifespan, not just disease-oriented research. Dr. Bianchi indicated that one of the biggest challenges for NICHD is communicating that connection and changing the perception that pregnancy is a term-limited experience. The BSC said it's also important to stress that development doesn't stop at age 18 as well. One of the ways to address gaps in research is for institute directors to come together where their interests overlap, for example NICHD and NIDA are working together to look at neonatal opioid withdrawal syndrome to see the impact on the brains of fetuses, infants, and children. A propos of the intramural reorganization, Dr. Rivkees said that the positive impact of the structure in creating a rich scientific environment was evident in the site visit that occurred the previous day.

Scientific Director's Presentation

Dr. Stratakis noted that two BSC nominees withdrew from consideration due to regulatory issues: Dr. Vanessa Auld and Dr. Joseph Majzoub. **Dr. Petra Hüppi**, Group Leader of Child

Development Disorders at the University of Geneva, will join the BSC in June 2019. Dr. Stratakis welcomed new member **Dr. Bill Dauer**, Elinor Levine Professor of Neurology at the University of Michigan Medical School.

Dr. Stratakis reviewed the tasks of the BSC, including the main one which is to evaluate the research of NICHD DIR, our investigators, cores, and programs, and advise institute leadership on programmatic decisions and resource allocations. Dr. Stratakis stated that the goal of the intramural program is to promote high-risk, high-impact laboratory and clinical investigations, especially those that could not be readily supported in the extramural environment. The BSC meets twice a year, each June and December, to review site visits and advises us on the career course of our tenure-track investigators on an ongoing basis. The review policy is outlined in the NICHD DIR Guidelines for Site Visit Reviews.

Dr. Stratakis reviewed the NICHD DIR's organizational structure and noted that one change in previous years is that the Clinical Director now reports directly to Dr. Bianchi. Investigators are organized into six building hubs based on areas of science, that has resulted from the reorganization. All investigators are organized in 13 self-selected intellectual affinity groups. An important group for how the NICHD DIR functions is the Group of Senior Advisors (GSA). This group consists of Associate Scientific Directors (ASDs) most of whom head one of the building hubs. In addition, the GSA includes **Dr. Mary Dasso**, who serves as the ASD for Budget and Administration; **Dr. Tracey Rouault**, the ASD for Recruitment, Retention, and Diversity; **Dr. Chris McBain,** Deputy Scientific Director; **Dr. Forbes Porter**, Clinical Director of NICHD; **Ms. Francie Kitzmiller,** Deputy Director for Administration & Budget; and **Ms. Sara King**, Chief of Staff of the Office of the Scientific Director. Memberships of the GSA and affinity groups were presented.

In FY18, the DIR represented 14% of NICHD's total budget. Of the approximately $188M the DIR received for FY18, 22% was allocated for lab consumables, 34% toward personnel, 20% toward the NIH Office of Research Services to cover buildings, maintenance, etc., and 16% was paid in support of the NIH Clinical Center. Smaller portions of the budget go to central support of animal care, capital equipment, IT support, renovations, and various contract agreements. In addition to the discussed DIR allocation, DIPHR has a budget of approximately $9M. The DIR was also able to dedicate approximately $4.5M towards capital equipment in FY18. The space and renovation costs in FY18 are now much lower, following a years' long effort that began in 2012 to provide labs with new or completely renovated space. The total effort cost approximately $18M. The effort is now winding down, with just a few more moves pending, freeing this money for future recruitments.

The total number of DIR staff is 918, with 304 FTEs, and 614 non-FTEs which includes trainees and contractors. DIPHR has another 100 or so staff members. The trainee population includes 191 postdocs, 76 postbacs, 54 summer students in 2018, 14 of graduate students, and 2 clinical fellows.

Dr. Pedro Rocha, a newly recruited Stadtman Investigator who heads the Unit on Genome Structure and Regulation, will present to the BSC later in the agenda. Dr. Ryan Dale, the newly recruited Scientific Information Officer and Head, Bioinformatics and Scientific Programming Core will also present to the BSC. Dr. Dale's recruitment follows calls from site visit reviewers for stronger bioinformatics support. Dr. Stratakis thanked Dr. Bianchi for supporting the recruitment of Dr. Dale through the hiring restrictions. Dr. Fady Hannah-Shmouni has been recruited as the new Co-chief for Internal Medicine and NICHD's Associate Program for the Inter-Institute Endocrinology Training Program, and will hopefully start in early 2019. Dr. Hannah-Shmouni, graduated from the NIH Inter-Institute Endocrinology Training Program in 2017 and has since worked at Sick Kids at Toronto. Dr. Bruce Tromberg has been recruited as Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB). Dr. Tromberg will be the second institute director who will have a lab in the NICHD DIR. Dr. Matt Gillman, Director of the Environmental influences on Child Health Outcomes (ECHO) Program since July 2016, will be an adjunct investigator in both DIPHR and DIR, working with Dr. Enrique Schisterman and Dr. Jack Yanovski, respectively.

NICHD continues to support the Lasker Clinical Research Scholars Program. The goal of the program is to grow the diminishing pool of talented clinical/translational researchers. Candidates of the program are early stage clinical researchers, within 10 years of completing core residency, with the ability to conduct independent research. Lasker Scholars are able to come to the intramural program to conduct research for up to five years, and then may be funded for an additional three years either in the intramural program or at their home institution. At the end of the program Scholars may be recruited by the NIH Intramural Program as senior investigators.

Recent honors were highlighted including Dr. Mary Dasso's 2018 NICHD Mentor Award and election to AAAS. Dr. Miranda Broadney, Acting Director of the Pediatric Endocrine Fellowship Program won the Pediatric Endocrine Society Clinical Scholar Award. Dr. Todd Macfarlan, head of the Unit on Mammalian Epigenome Reprogramming, was awarded tenure by the NIH Central Tenure Committee on October 15, 2018.

NICHD DIR investigators continue to be successful in competing for funding. 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. BSC members were encouraged to advertise this program at their own institutions in an effort to have more extramural investigators take advantage of this program.

The NICHD DIR Director's Awards are in its third cycle. This competitive award was established following the recommendation from the 2013 Blue Ribbon Panel Report to foster new collaborations and support new research ideas. Applications are based on an R-21 and reviewed by a panel of NIH extramural reviewers, with successful awards receiving two years of funding. Approximately $3.2M in awards were made to investigators in FY18-19, and the 12 successful applications were presented.

Dr. Stratakis then reviewed the activities of the Office of Education. Dr. Yvette Pittman was appointed Director of the Office of Education in December 2017. The Office of Education continues to support trainees at all levels through a variety of activities, including a monthly newsletter, which celebrated its 100th issue in September, and an Annual Fellows Retreat. The 2018 Annual Retreat was held at the Smithsonian American Indian Museum and 120 fellows and trainees at all levels attended.

The Office of Education, along with the Scientific Director, support a number of initiatives to increase diversity. The Developing Talent Scholars program supported five recruitments at the postbaccalaureate level in 2018-2019. Three new alumni from the program started professional school in the fall with full scholarships. As part of the summer program, 15 centrally-funded students from groups traditionally underrepresented in science or from disadvantaged backgrounds were supported in 2018. The Fellows Recruitment Incentive Award, which supports fellows at the postdoctoral level, is currently accepting applications for the coming year. NICHD also has a number of international collaborations for training including the NICHD-Inserm Exchange Program and the Future Researchers Program which supports medical students from the Santa Casa de São Paulo School of Medical Sciences (Brazil) to train with NICHD investigators. Postbaccalaureate fellow medical and graduate school acceptances were presented.

The Office of Education is continuing initiatives aimed at public speaking, teaching, and grantsmanship, and career counseling. The DIR has vetted an extensive list of grant opportunities to confirm intramural fellows' eligibility for competitive funding from outside organizations. The Intramural Research Fellowship is an award opportunity for NICHD DIR postdocs and clinical fellows which will provide training on how to write an NIH grant. Awards will be for $30K for one year and applications will be reviewed by the BSC. Finally, the annual Three-minute Talks (TmT) Competition was held on June 28, 2018 to promote the effective communication of science. The competition now includes five institutes and Dr. Jakob Gutzmann from the Hoffman lab placed 3rd overall. Due to technical difficulties, the video of Dr. Gutzmann's presentation could not be shown.

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

Presentation on DIPHR

Dr. Grewal reviewed the mission of DIPHR, to conduct research leading to the promotion of population health and wellbeing. It includes 27 FTEs members organized into three branches: the Epidemiology Branch, the Biostatistics and Bioinformatics Branch, and the Social & Behavioral Sciences Branch. The Social & Behavioral Sciences Branch, formerly the Health Behavior Branch, was renamed following the appointment of Dr. Stephen Gilman as the permanent branch chief in April 2018. DIPHR's FY18 operating budget was $9M. This increase over previous years is the result of the expansion of the division to include the Contraceptive Development Program headed by Dr. Diana Blithe, which was previously part of NICHD's extramural program.

Three DIPHR investigators were awarded tenure in 2018: Dr. Stephen Gilman on April 16, 2018, Dr. Pauline Mendola of the Epidemiology Branch on March 5, 2018, and Dr. Zhen Chen, an investigator in the Biostatistics and Bioinformatics Branch, on May 21, 2018. A fourth investigator was scheduled to be reviewed by the NIH Central Tenure Committee on December 10, 2018. Dr. Enrique Schisterman, Chief of the Epidemiology Branch, received the Outstanding Contributions to Epidemiology in Methods Development Award from the American College of Epidemiology. Dr. Keewan Kim, a Research Fellow in the Epidemiology Branch, was recognized with the 2018 Student Paper Prize Award from the Society for Pediatric and Perinatal Epidemiologic Research. Dr. James Mills, a senior investigator in the Epidemiology Branch, received both the NICHD Lifetime Achievement Award and the 2018 NIDDK Director's Award for his work on Creutzfeldt-Jakob disease. Dr. Elizabeth DeVilbiss and Dr. Carrie Nobles, postdoctoral fellows in the Epidemiology Branch, were the recipients of the Trainee Poster Awards at the 31st Annual Meeting of the Society for Pediatric & Perinatal Epidemiologic Research and Dr. Andrew Williams, also in the Epidemiology Branch, was a runner-up for the Trainee Poster Award.

A propos of other epidemiology branches at NIH, NCI and NIEHS both have large epidemiology programs which, like DIPHR, are separate divisions from the rest of their intramural programs while other intramural programs have investigators conducting epidemiological studies in their DIRs. Like investigators in the DIR, DIPHR investigators are charged with doing high-risk, high-reward research that could not be easily done with extramural funding however, unlike DIR DIPHR investigators use a contract mechanism to collect the data they use. Dr. Werler noted that the impact of DIPHR's work in the field is huge.

Dr. Stratakis has been serving as acting director of DIPHR since October 2017. The search for a permanent director has not started yet as the strategic plan may have some impact on the administrative link between DIR and DIPHR. During this time, Drs. Grewal and Schisterman have represented DIPHR in the DIR's weekly administrative meeting and have shared a good collaborative relationship with the DIR. The DIR and DIPHR also held their first joint scientific retreat in September 2018 to foster interactions between the two groups.

A short break followed. Three members, Drs. Elizabeth Bonney, Kojo Mensa-Wilmot, and Martha Werler, departed for a parallel closed session presentation on the Contraceptive Development Program.

When the meeting resumed, Dr. Stratakis introduced the next speaker, Dr. Pedro Rocha. Dr. Rocha is a Stadtman Investigator, one of the newest recruits at the NICHD Division of Intramural Research, and head of the Unit on Genome Structure Regulation.

Scientific Presentations

Pedro Rocha, PhD, Stadtman Investigator & Head, Unit on Genome Structure and Regulation, NICHD

Organizing nuclei to shape up a blastocyst: The importance of 3D chromatin structure in early-cell fate decisions

Mammalian cells need to package two meters of DNA inside a nucleus of just a dozen microns in size, while at the same time ensure proper gene expression, replication, and maintenance of overall genome stability. It is therefore not surprising that in the past decade we have learned that the processes by which the DNA is organized inside the nucleus are far from random. In fact, we now know that the genome is folded in intricate, interconnected hierarchical levels.

At NICHD, the goal of the Unit on Genome Structure and Regulation, which Dr. Rocha leads, is to understand the biochemical and molecular mechanisms that regulate the formation of topological genome structures. In addition, the lab also aims to understand how DNA 3D structures contribute to the precise spatial-temporal cell-fate decisions that happen following fertilization and allow the cells in the embryo to differentiate into distinct lineages.

Fertilization is the ultimate reprogramming experiment where two highly differentiated cells (oocyte and sperm) fuse to form a zygote with totipotent potential. Within a few cell divisions, in the short time span of 72 hours the first cell-lineages are established and different gene-expression programs put into action. This makes the early embryo the perfect system to study how genome folding is established to control gene expression. In addition, the first lineage-fate decisions are essential to form the extra-embryonic tissues that allow mammalian embryos to implant in the uterus and support development. Even though we know what are the signaling pathways and transcription factors that allow these embryonic lineages to be determined, we still do not understand the regulatory mechanisms that initiate these differentiation programs. By using molecular and genetic tools to investigate the influence of 3D genome structure on these cell-fate decisions, the Rocha lab will begin to shed light into how these processes are regulated at the level of the genome, and how deregulation of these mechanisms can lead to problems in early animal development and ultimately contribute to fertility-related diseases.

Questions followed. The BSC commended Dr. Rocha for his interesting work and nice presentation.

Dr. Stratakis then introduced the next speaker, Dr. Anirban Banerjee. Dr. Banerjee was one of the first Stadtman Tenure-Track Investigators recruited by the NICHD DIR back in 2012. Dr. Banerjee is the head of the Unit on Structural and Chemical Biology of Membrane Proteins and had just been site visited the previous day.

Anirban Banerjee, PhD, Stadtman Investigator & Head, Unit on Structural and Chemical Biology of Membrane Proteins

Structural and Mechanistic Studies of Iron Transporters and Integral Membrane Enzymes that Catalyze Protein Lipidation

Research in Dr. Banerjee's laboratory is devoted to understanding the structure and mechanism of membrane embedded proteins. Since starting at the intramural program of NICHD, the lab has focused on two distinct areas – acyltransferases that catalyze posttranslational lipidation of proteins and transporters that move iron across membranes. Their work in the protein lipidation area has led to the first high resolution crystal structures of two members of the DHHC family of eukaryotic integral membrane enzymes that catalyze protein palmitoylation (Science, 2018). About 1000 cellular proteins are now known to be palmitoylated ranging from signaling proteins to ion channels, cell surface receptors and neuronal scaffolding proteins. In humans, there are 23 DHHC palmitoyltransferases and protein palmitoylation has been linked to, particularly, neuropsychiatric diseases and several forms of cancer. Yet there were no structures of these enzymes that severely thwarted progress in this field. Their work has provided a major breakthrough that will be the starting point for further mechanistic experiments as well as design of small molecule probes. In the iron transporter area, the Banerjee lab started focusing on Mitoferrin, the only known transporter of iron into mitochondria. In spite of the pervasive importance of iron in biology, there has been no robust reconstitution based proteoliposomal assay for iron transporters reported in literature. Recently the lab developed such an assay to show that Mitoferrin is a bona fide iron transporter. They also showed that Mitoferrin is a promiscuous transporter of first row divalent metal ions and identified candidate residues involved in iron binding and transport by Mitoferrin (JBC, 2018). They subsequently used this assay to reconstitute and demonstrate the iron transport activity of MavN, a highly conserved transmembrane effector protein of the intracellular bacterial pathogen, *Legionella pneumophila*. *Legionella* sequesters itself in an intracellular compartment termed the *Legionella* Containing Vacuole (LCV) where it survives and proliferates. It was proposed that MavN is inserted into the LCV membrane to hijack iron from the host. The lab's studies revealed that like Mitoferrin, MavN is also a promiscuous transporter of divalent first row transition metal ions. In collaboration with the lab of Ralph Isberg at Tufts University School of Medicine, a mutagenesis based dissection of MavN transport showed a striking correlation between transport activity in a reconstituted *in vitro* transport assay and Legionella growth in a cell-based assay.

Questions followed. A propos of his publications, Dr. Banerjee indicated that the lab was about to write up the paper on DHHC17, expecting to submit it within two or three months, and was anticipating that the paper on MB simulation would be ready for submission in about six months. While the lab had created a great assay for showing iron transport, Dr. Banerjee was cautioned to focus on his work on the mitoferrin and DHHC which he indicated that he intended to do.

Following a short break, Dr. Stratakis introduced the next speaker, Dr. Ryan Dale. Dr. Dale is the new Scientific Information Officer (SIO) at the NICHD DIR and head of the newly established Bioinformatics and Scientific Programming Core.

Ryan Dale, PhD, Scientific Information Officer and Head, Bioinformatics and Scientific Programming Core

Building and scaling bioinformatics support for NICHD

Starting in summer 2018, the NICHD Bioinformatics and Scientific Programming Core (BSPC) aims to meet and exceed the current and projected needs of the intramural program for bioinformatics with a strong focus on collaboration and to empower DIR researchers through training, infrastructure, and tool-building. Combining ideas from successful bioinformatics cores, the BSPC uses a hybrid approach of centralized and embedded bioinformaticians and an emphasis on training the next generation of scientists to build bioinformatics support from the ground up within labs. In its first few months, the BSPC has collaborated on projects with at least a dozen labs. In addition to performing these analyses and clearly communicating the results and their interpretation, we have identified commonalities in methods and are developing robust tools to be used across multiple research programs.

In addition to running the BSPC, as SIO Dr. Dale also serves as liaison between the institute's IT staff and intramural scientists.

Questions followed. The BSC was very impressed with Dr. Dale's presentation and strategy for having both embedded and centralized support. Dr. Dale clarified that each embedded bioinformatician works with a group of labs but that if a lab needed additional support, the core could help them find and train a dedicated expert for their individual lab. Across NIH, there is a bioinformatics special interest group as well as a single cell interest group which allows members of the BSPC to see how other people are tackling the same problems. In addition to supporting the DIR, the BSPC also supports DIPHR investigators.

Dr. Stratakis then introduced the final speaker, Dr. Karim Calis to speak about his role in the institute and the effort across NIH to merge the institutional review boards (IRB).

Karim Calis, PharmD, MPH, FASHP, FCCP, Director of Clinical Research and Compliance & Chair, Institutional Review Board, NICHD

Dr. Calis was recruited into his current role about a year ago but has served on the NICHD IRB since 1990, first as a member, then as vice chair beginning in 2007, and finally as chair. After his training, Dr. Calis had worked at two area hospitals before he was first recruited to NIH in 1989 as Director of the Drug Therapy Consultation Service and as a clinical specialist working with NICHD and NIDDK in endocrinology and women's health. In addition, he also served as the Program Director of an accredited pharmacotherapy post-doctoral residency in the Clinical Center and on data monitoring committees. Dr. Calis worked for the FDA in a number of roles between 2009-2017, continuing to serve on the NICHD IRB during that time. He has also maintained academic appointments as a clinical professor at both the University of Maryland and at Virginia Commonwealth University as well held a number of advisory committee roles including

serving on the FDA Drug Safety and Risk Management Advisory Committee. In his current role as Director of Clinical Research and Compliance, Dr. Calis oversees compliance with applicable regulations, ethical principles and scientific goals, in all of the processes and phases, review, conduct monitoring, and reporting of the clinical research.

As IRB Chair, he leads the review and monitoring of clinical research including ensuring the safety and welfare of human study participants. In January 2018, NIH changed its policy so individual investigators could no longer hold INDs, requiring that INDs instead be held by the institutes. Dr. Calis is assisting with these transitions and also with a policy to ensure adequate monitoring and compliance. Dr. Jonathan Green was recently appointed as head of the Office of Human Subjects Research Protections (OHSRP) overseeing the effort to consolidate and form a centralized NIH IRB. Under the current system, there are 12 separate IRBs across NIH which creates inefficiencies, inconsistencies, and variable quality in the system. The system that is being proposed is a single IRB with nine primary members but drawing alternates from a large pool of those who currently serve on the separate IC IRBs to allow for the right mix of expertise. This shift to a centralized IRB also coincides with the revision of the NIH Common Rule which will include changes to informed consent, exemptions, continuing review requirements, and broad consent.

Questions followed. A propos of how the new IRB will function, Dr. Calis indicated that there will be six subcommittees, each meeting once a week to cover the 1400 active clinical programs run at the NIH Clinical Center.

With that, the open session concluded at 12:15 pm.

Drs. Elizabeth Bonney, Kojo Mensa-Wilmot, and Martha Werler rejoined the meeting for the closed session.