***Eunice Kennedy Shriver* National Institute of Child Health and Human Development**
Division of Intramural Research
BOARD OF SCIENTIFIC COUNSELORS
MINUTES
December 4, 2015
Building 31, Room 2A48

Members Present: Dr. Jerome F. Strauss (chair), Dr. Rita J. Balice-Gordon (by phone), Dr. Jeanne Brooks-Gunn, Dr. P. Michael Conn (nominee), Dr. Laurinda Jaffe, Dr. Frances Jensen (nominee), Dr. Antonios Mikos, Dr. Tarun B. Patel, Dr. Scott A. Rivkees (nominee), Dr. Yoel Sadovsky, Dr. Lilianna Solnica-Krezel, Dr. Joan A. Steitz, Dr. Susan S. Taylor (by phone, closed session only), Dr. Eric Vilain (nominee), and Dr. Michelle A. Williams.

Federal Employees Present: Dr. Constantine Stratakis, Dr. Catherine Spong, Dr. Arlyn Garcia-Perez, Ms. Brenda Hanning, and at various times additional members of the NICHD staff participated in the meeting.

Ad Hoc Reviewers Present (open session only): Dr. Terri Beaty and Dr. Timothy Thornton.

I. OPEN SESSION

The meeting convened at 8:14 a.m. Dr. Constantine Stratakis thanked the members of the BSC for their service. He welcomed two ad hoc reviewers, Drs. Terri Beaty and Timothy Thornton, who joined the open session to assist in the review of Dr. Ruzong Fan, a tenure-track investigator in the Division of Intramural Population Health Research (DIPHR). Dr. Stratakis then invited Dr. Spong, Acting Director, NICHD, to provide an update on the institute to the BSC.

Acting Director's Remarks

Dr. Catherine Spong presented several NIH-wide updates:

- Dr. Walter Koroshetz was appointed Director of the National Institute of Neurological Disorders and Stroke in June 2015. He previously served as Deputy Director and then as Acting Director, following the retirement of Dr. Story Landis.

- Dr. William Riley was named Director of the NIH Office of Behavioral and Social Sciences Research and Associate Director of NIH for Behavioral and Social Sciences in August 2015.

- Dr. Kay Lund joined NIH in August 2015 as the inaugural Director of the Division of Biomedical Research Workforce Programs, a position created in response to the 2012 report of the NIH Biomedical Research Workforce Working Group.

- Dr. Michael Lauer is the new Deputy Director for Extramural Research, following the departure of Dr. Sally Rockey in September 2015.

- Dr. Thomas Insel stepped down as the Director of the National Institute of Mental Health on November 1, 2015 to lead a new effort focused on mental health as part of the Life Sciences team at Alphabet. Dr. Bruce Cuthbert will serve as Acting Director while a national search is conducted.

- Dr. Spong was named Acting Director of NICHD following the retirement of Dr. Alan Guttmacher. Dr. Spong began in the intramural program of NICHD and served as the Pregnancy and Perinatology Branch Chief of NICHD's extramural program before serving as the inaugural NICHD Associate Director for Extramural Research and the Director of the Division of Extramural Research. Dr. Spong is an expert on maternal and child health, emphasizing prematurity and the basic science of Down Syndrome and fetal alcohol syndrome. A national search is being conducted to identify the next permanent NICHD Director. BSC members were encouraged to apply and to submit names of potential candidates for the NICHD Director position.

- NIH was tasked with creating a 5-year NIH-wide Strategic Plan in order to advance its mission to support research in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce illness and disability. A Request for Information went out inviting comments and suggestions on a framework to articulate approaches and opportunities looking forward, and the plan will be presented to Congress on December 16, 2015.

- The Precision Medicine Initiative will generate scientific evidence to take into account people's individual variations in genes, environment, and lifestyle in the prevention and treatment of diseases in clinical practice. The first push has been to apply precision medicine to adult and pediatric cancers. A longer-term goal of the project is to create a research cohort of more than one million volunteers who will be actively engaged and share genetic data, biological samples, and diet/lifestyle information. A director is being recruited for the Precision Medicine Cohort Program and interested candidates were encouraged to apply by December 24, 2015.

- The National Children's Study (NCS) has been terminated but $165M of FY15 funding remained available to support the mission and goals of the original study. The timeframe for redirecting the funds was short, with planning beginning in January 2015 and awards made in September 2015. Several initiatives were supported in FY15 including (1) the development of tools to enhance the study of environmental influences of pediatric diseases; (2) the study of the influence of environment on in utero development with the goal of identifying the "seeds" of future diseases and conditions; and (3) expanded examination of environmental influences on later child development by leveraging extant programs.

- Should funding continue to be available in FY16, a proposal has been put into place called the Environmental influences on Child Health Outcomes (ECHO) program to

leverage extant cohorts to investigate the longitudinal impact of prenatal, perinatal, and postnatal environmental exposures on pediatric health outcomes with high public health impact. The four outcome focus areas are upper and lower airways; obesity; pre-, peri-, and post-natal outcomes; and neurodevelopment. A director of the ECHO project is being sought and applications are due December 18, 2015.

- Funds from the NCS will also be redirected to the NIGMS Institutional Development Award (IDeA) Program, which supports faculty development and research infrastructure enhancement to increase competitiveness where NIH success has been historically low. With the additional funds, NIH plans to create an IDeA States National Pediatric Clinical Trials Network to address access gaps for rural children by utilizing the existing IDeA network.

- The Common Fund's Gabriella Miller Kids First Pediatric Research Program began in FY15, providing $12.6M per year for ten years, to the NIH Common Fund to be used for pediatric research. The program will focus on pediatric cancers and structural birth defects with leadership by NICHD, NHLBI, NHGRI, and NCI. The program will develop a data resource for the pediatric research community of well-curated phenotype and sequence data.

Dr. Spong continued her update to the Board with NICHD news:

- The Human Placenta Project (HPP) is a collaborative effort involving multiple researchers, institutions, and funding sources, with the ultimate goal to understand human placental development, structure, and function in real time. The HPP received some of the funds redirected from the National Children's Study in FY15. Three Requests for Applications (RFAs) went out in FY15 to leverage existing technologies and to develop new tools and technologies to study the human placenta, resulting in 19 awards totaling $46M. In FY16, two RFAs have gone out to use 'omics to define human placental development and function across pregnancy. The 3rd Human Plancenta Project Meeting will be held April 14-15, 2016 in Bethesda, MD focusing on imaging, bioinformatics,and technology. This has been an international effort and NICHD has participated in the China Human Placenta Project Meeting and the Provocative Ideas on Human Placental Biology Meeting in India over the last several months.

- PregSource is a crowd-sourced, interactive mobile app that details the natural history of human pregnancy, provides accurate information about pregnany to women from trusted sources, and lets pregnant women know about opportunities to participate in targeted research. NICHD currently has 20 partner organizations as part of this effort. The goal is to get a better picture from women about normal and abnormal pregnancy in order to develop strategies for improving research and care. A propos of how many people have signed up to date, Dr. Spong indicated that the app is expected to launch in early 2016.

- The NIH Medical Rehabilitation Coordinating Committee is developing a comprehensive plan for the conduct and support of rehabilitation research to identify current rehabilitation research activities at NIH, gaps in and opportunities for additional research,

and priorities for future research. An RFI is out and responses are due by December 11, 2015. A meeting will be held May 25-26, 2016 entitled "Rehabilitation Research at NIH: Moving the Field Forward" in Bethesda, Maryland.

- The NICHD Data and Specimen Hub, N-DASH, will provide a centralized resource for researchers to store and access de-identified data from NICHD-supported studies.

In legislative news, the Congressional Neuroscience Caucus Briefing was held on December 1, 2015 and included presentations by BSC member Dr. Frances Jensen as well as intramural investigators Drs. Peter Basser and Carlo Pierpaoli. The FY16 budget has not been set and NIH is opertating under a continuing resolution through December 11, 2015.

Dr. Spong then invited questions. A propos of the Enhancing Reproducibility through Rigor and Transparency notice, a number of changes will be implemented into the grant applications and review process to enhance reproducibility as of January 2016. Some other institutes are currently involved in piloting this in review panels. Extramural MIRA R-35 awards are an effort by NIGMS to reduce the application and reviewing load. NIGMS currently limits the number of awards it gives to a single investigator to one, though the investigator can receive funding from other institutes. NICHD has been discussing how to optimize their pay lines and decided to see how the R-35 mechanism works out in other institutes before trying to implement it in NICHD. A propos of how to ensure that volunteers for initiatives such as Precision Medicine and PregSource are representative of the most vulnerable and high-risk populations, Dr. Spong indicated that this issue has been discussed extensively. PregSource was designed as a mobile app since it was recognized that cell phones are common across socioeconomic strata. For the Precision Medicine Initiative, a variety of healthcare facilities will be targeted in an effort to reach communities that may otherwise not be represented. Other suggestions from the BSC were welcomed. The BSC suggested that the PregSource population could prove to be a valuable resource if it could be tapped by the Precision Medicine Initiative. Dr. Strauss raised concern challenge of accessing data and working to harmonize established cohorts with investigators' needs in other large-scale initiatives such as the Vaginal Microbiome Project and the Maternal Fetal Medicine Network. Dr. Spong noted that the Maternal Fetal Medicine Network data would be made available through the N-DASH system. Regarding training programs, a subcommittee of NICHD's Advisory Council is currently looking at the current training portfolio to see whether we are investing in the right proportions, places, and mechanisms, and whether people are ultimately successful. Compared to other institutes, NICHD has a large portion of institutional K-12 training programs. Overall, the percent of NICHD's budget going toward training has been consistent over the past decade and is consistent with most other institutes. Dr. Spong noted that it is difficult to establish pay lines under the continuing resolution without knowing what the final budget will look like. The impact to programs like 21st Century Cures is not known as it is not yet finalized.

Scientific Director's Presentation

Dr. Stratakis began his presentation by welcoming new members **Dr. Eric Vilain**, a molecular and human geneticist from the University of California, Los Angeles, and **Dr. Frances Jensen**, a

neurologist from the University of Pennsylvania. He 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 visit reports and tenure-track investigators on an ongoing basis, each June and December. The NICHD DIR Guidelines for Site Visit Reviews is a dynamic policy document that has been in effect since 2010. 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. Site visit reviews allow for prioritization between laboratories but also between projects within a laboratory.

Dr. Stratakis then reviewed the tenure process. For tenure consideration, both site visit and BSC reviews are required. If both are positive, an individual will move forward for review by the insitute's Tenure and Promotions Committee. Finally the case is reviewed by the NIH Central Tenure Committee. This process will be followed for the review of Dr. Ruzong Fan, from DIPHR. Dr. Stratakis added that to maintain the vitality of the DIR, existing resources need to be reallocated to allow for the recruitment of new tenure-track investigators. All investigators are encouraged to apply for outside funding opportunities.

NICHD DIR's staff currently numbers around 1000, including 61 tenured and 4 tenure-track investigators. More than 100 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 Perinatalogy Research Branch, headed by Dr. Roberto Romero, is supported by a $15.5M contract with Wayne State University in Detroit, MI and the program receives an additional sum of approximately $1.5-$1.7M for operating costs from the DIR. The NICHD has an overall budget of more than $1.3B, of which approximately 14% goes to supporting the DIR. Of the $177M the NICHD DIR received in FY15, 33% was allocated toward personnel, 21% went toward consumables, 21% went towards the NIH Office of Research Services to cover buildings, maintenance, etc., and 15% was paid in support of the NIH Clinical Center. While the NICHD DIR budget decreased from $179M in FY11 to $177M in FY15, the school tax the DIR pays to the Clinical Center has increased from $23M to $26.5M over the same timeframe. The BSC pointed out that the Clinical Center does not provide the infrastructure necessary to support the Perinatalogy Research Branch, requiring the institute to support this program with additional funding through a contract to Wayne State University. Since FY12, the DIR has undertaken the huge effort to co-localize laboratories into five or six research hubs around the Bethesda NIH campus. The cost of these renovations and moves was approximately $5M in FY15 and an additional $5-6M in FY16 is expected before the costs taper off the following year.

As the purchasing power of the NICHD DIR has decreased over the past several years, the number of personnel has also decreased. The total staff has decreased from 1132 in FY11 to 996 in FY15. A number of senior investigators have retired and been appointed as scientists emeriti including most recently Dr. Owen Rennert and Dr. David Klein. Dr. Mark Mayer will be retiring at the end of December 2015 and will also be nominated as a scientist emeritus jointly by NICHD and NINDS. Dr. Mayer will present to the BSC later in the agenda. A propos of what

happens to permanent support staff following the closure of a lab, Dr. Stratakis indicated that while some are placed in other NICHD DIR laboratories, others move on to opportunities in other institutes or outside NIH or choose to retire. The OSD works with individuals to identify new positions and supports retraining.

Dr. Stratakis then presented a number of personnel changes.

- Dr. **Maya Lodish** was appointed Director of the Pediatric Endocrinology Training Program at the beginning of 2015 after serving as Deputy Director since 2009.

- Dr. **Michael T. Collins**, a tenure-track investigator in the National Institute of Dental and Craniofacial Research (NIDCR), was appointed the Associate Director for the Inter-Institute Endocrine Training Program for NICHD. He will retain his lab within NIDCR but his new administrative role will be within NICHD.

- Dr. **Jenny Blau** was hired as a staff clinician who will serve as Co-Chief of the Internal Medicine Ward as well the Assistant Deputy Program Director, Inter-Institute Endocrinology Training Program.

- Dr. **Andrew Demidowich** was hired as a staff clinician who will serve as Co-Chief of the Internal Medicine Ward and will also serve as NICHD Liaison to the NIH Medical Research Scholars Program.

Several honors and awards were also presented.

- Dr. **Harold Burgess** was awarded tenure on September 21, 2015 by the NIH Central Tenure Committee. Dr. Stratakis reminded the BSC that investigators get additional resources once they receive tenure.

- Dr. **Todd Macfarlan** received a 2015 Office of the Director Honor Award to the Scientific Initiatives Core Group on IRP Long-term Planning for providing creative scientific ideas and leadership in defining new research directions for the IRP.

- The second annual Three-minute Talks (TmT) Competition was held to promote the effective communication of science. In 2015, NICHD postdocs and graduate students participated in a live competition with trainees from NHGRI and NIDCR. The winner was Dr. **Kathryn Tabor**, a postdoc in the laboratory of Dr. Harry Burgess. The BSC encouraged the institute to circulate the winning videos more broadly.

An update was provided on the efforts to open up the NIH Clinical Center to extramural investigators through collaborations with intramural researchers. NICHD continues to participate, having made two awards during both the first and second cycles. Awards for cycle 2 included (1) Antiretroviral Therapy in Aicardi Goutieres Syndrome, with Dr. Rohan Hazra from extramural NICHD in collaboration with staff from NHGRI, NINDS, and NIAMS, and (2) Choroid Plexus-Directed Gene Therapy for Alpha-Mannosidosis in collaboration with Dr. Stephen Kaler.

As part of the Human Placenta Project, the NICHD Office of the Director allowed intramural investigators to compete for funding. A total of four awards were made to (1) Dr. Amir Ganjbakhche for Real Time Oximetry of Anterior Placenta Using Near Infrared Spectroscopy, (2) Dr. Sergey Leikin, Dr. Peter Basser, and Dr. Roberto Romero for Imaging Extracellular Matrix in Human Placenta, (3) Dr. Jennifer Lippincott-Schwartz and Dr. Carolyn Ott for Integrated Cellular Changes Drive Synciotrophoblast Differentiation, and (4) Dr. Erin Wolff for MRI-Elastography Ultrasound Fusion (MR-eUS fusion) Characterization of Normal and Abnormal Human Placentation. This research will be presented at the Human Placenta Project Meeting in April 2016.

Investigators also had the opportunity to compete for the NICHD DIR Director's Awards, which provided two years of funding, FY14-FY15. A total of $3M was awarded supporting 10 different projects. This opportunity was created based on the recommendation of the Blue Ribbon Panel to foster new collaborations within the DIR. The application was based on a modified R-21 and the NICHD's Division of Extramural Research organized an external review committee. Another competition will be held for FY16-FY17 and at least $1M will be set aside for awards.

Two additional NICHD awards provide funding to encourage the recruitment of trainees from groups traditionally underrepresented in science or from disadvantaged backgrounds. The Fellows Recruitment Incentive Award (FRIA) provides $25K per year for two years to support a postdoctoral fellow. The Developing Talent Award covers the stipend of a postbaccalaureate IRTA or Pre-IRTA, and is renewable for a second year. Selections for both awards are made through the Task Force for Diversity in NICHD DIR.

The NICHD DIR is currently recruiting for up to four tenure-track or mid-level investigators in the areas of clinical and translational research in pediatric or women's health, cell/development biology, and basic or translational neuroscience. One tenure-track investigator, Dr. Alexander Sodt, has already been recruited and will present to the BSC later in the agenda. The Lasker Clinical Research Scholars Program was established in 2011 to create career research opportunities for physician-scientists. BSC members were asked to encourage prospective candidates from their institutions to apply for both NICHD's recruitment as well as for the Lasker Program. The long time commitment for a Lasker Scholar, 7 years at NIH followed by 3 years at their home institution, was seen as a drawback by the BSC and this comment will be transferred back to the Deputy Director for Intramural Research (DDIR).

The NICHD DIR's new organizational structure was approved and has been in place since October 1, 2015. A number of Associate Scientific Director (ASD) positions were created to serve the needs of PIs such as managing maintenance contracts and shared equipment, but ASDs will not participate in budget and personnel negotiations. The ASDs represent their functional areas on the Group of Senior Advisors (GSA), which meets monthly. Scientifically, the laboratories have self-assembled into intellectual affinity groups, with some having secondary affiliations in addition to their primary groups. Support staff has also been reassigned to meet the needs of the new structure. Membership of the GSA and affinity groups was presented. Dr. Stratakis pointed out that half of the ASDs are women, a substantial improvement over the

former structure in which there was only one female program head. The BSC was invited to make suggestions on how best to evaluate the performance of the new structure.

Dr. Stratakis then introduced Dr. Germaine Buck Louis to provide an update on the Division on Intramural Population Health Research (DIPHR).

DIPHR is made up of 29 staff and 38 trainees organized into the Office of the Director and three Branches, the Epidemiology Branch, the Biostatistics and Bioinformatics Branch, and the Health Behavior Branch, that use a team science approach. Two new staff scientists have been recruited: Dr. Stefanie Hinkle, whose work focuses on gestational diabetes, and Dr. Rise Goldstein, who is interested in the early origins of mental health. Dr. Kaigang Li, a former Research Fellow in DIPHR, was recently recruited as an Assistant Professor in the Department of Health and Exercise Science at Colorado State University. In partnership with the NICHD DIR and Division of Extramural Research, DIPHR hosted a Workshop "Is Human Fecundity Changing?" on September 10-11, 2015, which took into account population health, demography, social science, and clinical perspectives on the issue.

The members of DIPHR have also received numerous honors in the past six months. Dr. Emily Mitchell, a postdoc in the Epidemiology Branch, received the Student Prize Paper Recipient at the Joint Statistical Meeting in August 2015. Dr. Buck Louis became the Chair of the NIH Office of Management and Budget Clinical Exemption Committee.

A few recent research findings were then highlighted. In a paper published in Biometrics, researchers in the Biostatistics and Bioinformatics Branch described new prediction methods for binary outcomes for longitudinal biomarkers or repeated biomarkers that are not normally distributed. A recent study in the Epidemiology Branch found that recent air pollution exposure increases the risk of eleveated blood pressure at admission for labor and delivery. From the Health Behavior Branch, Dr. Stephen Gillman published a paper in the *International Journal of Epidemiology* finding that children raised in socioeconomically disadvantaged households were more likely to exhibit neurologic abnormalities in infancy and early childhood. Research under the Office of the Director found that there are racial/ethnic differences in optimal fetal growth and that individualized standards are needed for white, Hispanic, Asian, and African-American women. Dr. Williams commended DIPHR on its attention to sampling and demographic representation in their work.

Dr. Stratakis thanked Dr. Buck Louis.

A short recess followed. During this time and the subsequent presentation, Drs. Williams, Beaty, and Thornton met with the DIPHR Director, Dr. Germaine Buck Louis, and Dr. Paul Albert, Chief of the Biostatistics and Bioinformatics Branch.

Scientific Presentations

Dr. Alexander Sodt, Stadtman Tenure-Track Investigator Recruit, Integrative Molecular, Membrane, Cell, and Tissue Pathophysiology Group

Dr. Stratakis introduced the first speaker, Dr. Sodt, who has been recruited by the NICHD through the NIH-wide Earl Stadtman Tenure-Track Search.

Biophysics of membrane remodeling and protein-lipid coupling from computer simulation

Molecular computer simulations apply the laws of physics to obtain predictive power on the scale of atoms and molecules, where experimental techniques can approach only under controlled conditions. There are limits, however, imposed by the molecular model quality as well as by short length- and time-scales. Dr. Sodt described how he uses simulations to build coarser models and theory that provide valuable insights into biological processes, such as membrane remodeling (e.g., clathrin mediated endocytosis) as well as how transmembrane proteins function in and couple to the lipid bilayer.

Questions followed.

Drs. Williams, Beaty, and Thornton rejoined the meeting.

Dr. Ruzong Fan, Tenure-Track Investigator, Biostatistics and Bioinformatics Branch, DIPHR

Dr. Albert introduced the next speaker, Dr. Fan, who came to DIPHR in 2011 as a tenure-track investigator. This presentation served as his mid-cycle review.

Statistical Genetics and Bioinformatics: Theory and Applications

Since the 2012 site visit, Dr. Fan has published 11 papers, with one additional paper submitted with revisions, and has released 9 R packages with over 5000 downloads to date in 2015. Dr. Fan outlined five new projects: (1) Genetic Factors in Cushing's Disease: Whole Exome Sequencing, and (2) Genetic Factors in Birth Defects-Genomic Testing, both in collaboration with Dr. Jim Mills of DIPHR, (3) Investigating the Role of Ldb1 Transcription Complexes in T Cell Acute Lymphoblastic Leukemia and in Normal T Cell Development, with Dr. Paul Love in NICHD DIR, (4) Offspring Genome Wide DNA Methylation Patterns at Birth and the Intrauterine Environment in the EAGeR Trial, with Dr. Edwina Yeung in DIPHR, and (5) the Pregnancy Eating Attributes Study, with Dr. Tonja Nansel in DIPHR. His methodological research focuses on functional regression models for gene-based association studies of complex disorders, longitudinal analysis and stochastic dynamic models, association analysis of using both triads and parent-child pairs, and gene-gene and gene-environment interactions. The functional regression models for gene-based association studies can be used to analyze quantitative, dichotomous, and survival traits. Based on population genetics theory, statistical theory of fixed and mixed models, real data analysis, and simulation studies, the functional regression models can be used to analyze rare variants, common variants, or a combination of the two.

Following a few questions, Dr. Fan met with Drs. Williams, Beaty, and Thornton in an adjacent room to finish their discussion. Drs. Williams, Beaty, and Thornton then met in an executive session. During this time, the BSC heard from the next two speakers.

Dr. Mark Mayer, Head, Section on Neurophysiology and Biophysics

Dr. Stratakis then introduced, Dr. Mayer, who is retiring at the end of December 2015. Dr. Mayer will be nominated as a Scientist Emeritus supported by both NINDS and NICHD.

What's in a name? Glutamate receptors in ctenophores and flies

The well-accepted role of glutamate as the major excitatory neurotransmitter receptor in the human brain begs the question of how did glutamate receptors evolve? Decades of work on the mammalian CNS have produced a rich tool box of ligands used to dissect iGluR function, and it is tempting to use these as tools to investigate the role of AMPA, kainate and NMDA receptor iGluR subtypes in model organisms such as Drosophila, C. Elegans, and zebrafish. Recent genome sequencing projects have revealed the presence of iGluRs in ctenophores, controversial candidates for the earliest branch of metazoan life, and similar to other model organisms, Ctenophore iGluRs were classified based on sequence homology. Using a combination of biochemical, electrophysiological, and crystallographic approaches to study iGluRs from model organisms, we discovered unexpected breakdowns in the iGluR classification scheme, and identify the molecular mechanisms underlying this. We have found ctenophore "kainate" receptors that bind glycine, but not glutamate; Drosophila AMPA receptors that do not bind AMPA; and Drosophila kainate receptors for which NMDA acts as an antagonist. Obviously caution is required when investigating iGluR function in vivo in these model organisms.

Questions followed.

Dr. Pamela Stratton, Staff Clinician

Dr. Stratakis introduced the final speaker, Dr. Stratton. Dr. Stratton was briefly reviewed as part of her program's 2011 site visit and was asked to present to the BSC as she was due to be reviewed again under NICHD's staff clinician review policy. Since 1999, she has served as part of the Gynecologic Consult Service in the NIH Clinical Center.

Translational Gynecologic Research in the Intramural Program: Gynecology Consult Service Research Collaborations, Endometriosis and Chronic Pelvic Pain Studies, and Studies in Women after Hematopoietic Stem Cell Transplantation

The NICHD Intramural Program provides support for women's health in studies at the Clinical Center through the Gynecology Consult Service. A major focus of Dr. Stratton's clinical collaboration is in the setting of hematopoietic stem cell transplant. The NIH consortium spans four institutes, and the Chronic Graft versus Host Disease Study Group and Late Effects Consortium supports this work through transplant teams and some organ-specific specialties. As part of these efforts, Dr. Stratton recently published

guidelines to standardize an approach to menses suppression and contraception at the time of transplant. The NIH Chronic Graft versus Host Disease Study Group has taken the lead nationally and internationally to develop consensus guidelines for the diagnosis, grading, severity, and developing of novel treatments for chronic graft versus host disease (GVHD). The evaluation is comprised of nine core assessments and six additional assessments, as needed. GVHD is a major post-transplant complication of cell transplantation. Dr. Stratton's initial work was focused on developing severity scoring for genital GVHD, which can affect the vulva or the vagina. While vulvar GVHD typically occurs 7-10 months after transplant, vaginal GVHD can develop years later. Treatment of vulvar GVHD will not prevent development of vaginal GVHD and genital GVHD must be distinguished from menopausal changes. Overall, one-third of women are asymptomatic, underscoring the importance of considering GVHD and performing gynecologic assessment, even when there are no symptoms displayed. Human papillomavirus (HPV) occurs in between 20 and 50 percent of healthy reproductive-age women. Ninety percent of cases clear within two years. Within 15 years post-transplant, 10 percent of women will have a second cancer and the risk is 18.5-fold higher in women over the age of 34. The topical immunosuppression for GVHD is associated with a flare in HPV disease. This has led to a multi-institute bench-to-bedside award to investigate the safety and immunogenicity of quadrivalent HPV vaccine in women after transplant. The association with extensive chronic GVHD or genital GVHD in transplant likely represents HPV reactivation and suggests a role for immune dysregulation. Based on the results of immunogenicity studies, the team will look at strategies to incorporate HPV vaccination into post-transplant care. The role of local estrogen in treating genital GVHD is also being explored.

Questions followed.

The open session concluded.