Network of Minority Health Research Investigators 10th Annual Workshop
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health

Bethesda Marriott at Pooks Hill
Bethesda, MD
April 19 - 20, 2012

Summary Report

THURSDAY, APRIL 19, 2012

INTRODUCTIONS

Juan Sanabria, M.D., M.Sc., F.R.C.S.C., F.A.C.S., Assistant Professor of Surgery and Nutrition, Case Western Reserve University, Cleveland, OH

Lawrence Agodoa, M.D., Director, Office of Minority Health Research Coordination (OMHRC), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD

Dr. Sanabria, Chair of the Network of Minority Health Research Investigators (NMRI) 10th Annual Workshop, welcomed the attendees and thanked Dr. Lawrence Agodoa and Ms. Winnie Martinez for the success they have had in promoting and organizing the NMRI for the past 10 years. He asked that everyone introduce themselves and tell how many years they have belonged to the NMRI and how many annual workshops they have attended. After the introductions, Dr. Sanabria asked Dr. Agodoa to say a few words about the NMRI.

Dr. Agodoa welcomed the participants and said that the NMRI has had two meetings per year: an Annual Workshop in the spring and a Regional Workshop in the fall. The Regional Workshops are held to recruit young investigators into the NMRI. He said that he was pleased to see so many senior NMRI members who have supported the Network in the past decade. He recognized Dr. Jacqueline Tanaka, chair of the first NMRI Annual Workshop in 2003.

WELCOMING REMARKS

Gregory Germino, M.D., Deputy Director, NIDDK, NIH, Bethesda, MD

Dr. Germino welcomed participants and passed along greetings from Dr. Griffin Rodgers, Director of the NIDDK, who had a prior commitment and could not attend. He announced that on the previous day Dr. Rodgers, a champion of the NMRI, was inducted into the 2012 class of the American Academy of Arts and Sciences, a prestigious group that is more than 200 years old and includes George Washington, Benjamin Franklin, and many other legendary figures from American history as past members.

Dr. Germino congratulated the NMRI on its 10th Anniversary and said that it was established and has been supported by the NIDDK because of the commitment to overcoming the challenges involved in increasing minority participation in research. He provided background on the NMRI and data collected as part of its evaluation process. The goals of the NMRI include the following:

- To encourage and facilitate biomedical research within NIDDK mission areas by its members.
- To recruit new investigators from these communities to biomedical research in NIDDK mission areas.
- To promote dialogue between NMRI members and the NIDDK.

The NMRI is dedicated to increasing the number of minority researchers and furthering research on health disparities. This effort is led by the NIDDK's Office of Minority Health Research Coordination (OMHRC) and its Director, Dr. Lawrence Agodoa, who was tapped to head an initiative of the National Institutes of Health (NIH) Director at the time, Dr. Harold Varmus, to address these issues. Dr. Varmus worked with then-NIDDK Director Dr. Allen Spiegel to support Dr. Agodoa in establishing the NMRI. Dr. Agodoa began by enlisting minority senior investigators as "owners" of the Network. Membership in the

NMRI required that an individual have a postdoctoral level or higher degree and be a member of an underrepresented minority group; at the occasion of its 10th Anniversary, the NMRI has more than 200 members, 20 percent of whom are senior members; 80 percent have faculty appointments. Throughout the years, more than 300 investigators have attended NMRI annual or regional workshops.

The NMRI began collecting member information through the online NMRI Questionnaire in 2008 (see http://nmri.niddk.nih.gov/membership/questionnaire.aspx). Data collected from 2008 to 2011 indicate what would be expected from a high-energy group such as the NMRI. During that time, there have been 16 promotions/appointments, 34 members have received grants (28 from the NIH), 23 members have received honors or awards, 170 publications have been generated by members, and members have been responsible for 93 poster presentations at national and international scientific conferences.

The NMRI is only one of the NIDDK's efforts to address health disparities, which disproportionately affect racial/minority groups as well as other underrepresented populations. The NIDDK has coordinated research efforts on obesity, type 2 diabetes (T2D), and kidney diseases, each of which are major health problems among underrepresented/disadvantaged populations. The estimated annual cost of these three conditions is $150 billion for obesity, $174 billion for T2D, and $27 billion for kidney diseases. Obesity—a significant risk factor for T2D, which in turn is the most significant risk factor for kidney diseases—is increasing in the United States and internationally and is likely to become the world's most significant health problem within decades.

Dr. Germino recounted the successes of NIDDK clinical trials that have special significance for minority populations, including the following:

- **The Diabetes Prevention Program (DPP).** This program showed that the risk of developing T2D could be reduced by 58 percent through lifestyle changes, compared with 31 percent through treatment with metformin. The DPP oversampled for minorities, and results indicated that these reductions were equivalent among minorities and Caucasians. The DPP followup study showed that the reduction in the risk of T2D has continued after the end of the trial.

- **LookAHEAD.** This randomized clinical trial study, which ends in 2014, compares intensive lifestyle interventions with conventional diabetes education among individuals who are obese and have T2D. LookAHEAD also oversampled for minorities. Preliminary results at Year 4 indicate that participants in the intensive lifestyle intervention arm of the study experienced improved fitness, glucose and blood pressure control, improved high-density lipoprotein (HDL) levels, and less use of medication. It is hoped that this study will have positive impacts not only on T2D and obesity, but also on cardiovascular disease (CVD) and mortality.

- **The African American Study of Kidney Disease and Hypertension (AASK).** The AASK study tested the hypothesis that an intervention with strict blood pressure control could delay the progression of chronic kidney disease (CKD). Results indicated that an angiotensin-converting enzyme inhibitor (ACEi) was more effective for blood pressure control among African Americans than calcium channel blockers and beta blockers. This was an unexpected finding. Other findings included a reduced rate of CKD progression among participants with a urinary protein/creatinine ratio of greater than 0.22, and that African American participants with hypertensive kidney disease had progressive CKD despite aggressive blood pressure control. The study authors commented that although aggressive blood pressure control slowed the rate of progression, it did not stop or reverse progression. This indicates the need for more effective therapies for CKD in this population.

- **Basic Science at the NIDDK.** Because approximately one-third of CKD cases in the United States are in the African American population, the search for understanding remains a priority. The NIDDK has supported genetic admixture studies to identify genetic risk factors for CKD among African Americans. A locus on chromosome 22 of African American CKD cases, but not controls, was 93 percent associated with African American ancestry. The gene *APOL1* was identified as a risk factor for CKD. Interestingly, individuals with the G1 and G2 variants of *APOL1* were found to have a 10-fold increased risk of focal segmental glomerulosclerosis (FSGS) and a 7-fold increased risk of end-stage

renal disease (ESRD). The high prevalence of this variant in individuals of African descent is similar to what had been reported for sickle cell variant in the hemoglobin gene. The latter was thought to confer evolutionary advantage by affording protection against malaria. ApoL1 may have similarly arisen through selective pressure as it seems to protect against *Trypanosoma brucei rhodesiense* infection.

- **Study of Latinos (SOL).** This National Heart, Lung, and Blood Institute (NHLBI)-funded epidemiological study is investigating Hispanic groups in the United States for a variety of health indicators. The NIDDK is one of many co-sponsors of the study, which began in the past year.

The NIDDK also is committed to communicating research findings to those communities that can benefit the most. The Diabetes Education in Tribal Schools (DETS) project has developed and implemented a grades K-12 school-based diabetes curriculum that supports the integration of American Indian/Alaska Native culture and community knowledge with diabetes-related scientific knowledge. Similarly, the National Kidney Disease Education Program (NKDEP) has developed a faith-based community program known as "Kidney Sundays" to provide African American communities with the information they need to increase awareness of kidney diseases.

Dr. Germino related the challenges ahead for reducing health disparities in the United States. The first challenge is illustrated by a graph of prevalence rates of ESRD from 1980 to 2008, which shows that ESRD rates continue to dramatically rise in each minority population except American Indians. Many of the diseases that fall within the NIDDK research mission, and which are fast increasing in their prevalence, disproportionately affect minority populations. We also face important gaps in the balance of our workforce composition and in their relative success rates. A recent analysis of minority participation published in the *Journal of the American Medical Association* showed that not only is the number of black applicants low but that their success rate is much below that of all other racial and ethnic groups. For example, of the approximately 83,000 grant applications analyzed in the study, only 185 awards were made to African American applicants, more than 10 percentage points below whites who received NIH funding. To draw attention to this concern, a recent issue of *Science* published a "Call to Action" for minority men in science, with data showing that approximately 25 percent of male African American and Hispanic high school students drop out of school between the 9th and 10th grades. In addition, among those enrolled in college and studying in the science and math fields, nearly 35 percent work 20 hours per week to make ends meet. The time constraints make it even more difficult for students to do both. Therefore, it is not surprising that although African Americans, Hispanics and Native American men accounted for 35 percent of the college population in 2008, only 12 percent graduated with science and math degrees. Proposed solutions include encouraging more minority faculty members and scientists to become actively engaged in mentoring undergraduates and providing adequate financial support so that students can focus on their academic pursuits. The NIDDK is addressing the pipeline problem through its Diabetes Education Curriculum in K-12 Schools Program (DECK-12) program. The goal of DECK-12 is to educate at-risk youth about healthy living and risk reduction strategies for preventing diabetes while exciting them about the power of science to improve health. Increasing the numbers of students who choose science-related careers is one of the goals of DECK-12.

For the NMRI, challenges for the future include retaining senior members who can become mentors for young investigators. As Dr. Agodoa wrote in the most recent issue of the *NMRI News*, an NMRI publication, "the NMRI belongs to its members, and their hard work and enthusiasm for the program will dictate success or failure. The challenge will be to keep the good work of the past moving forward in the future."

The final and possibly the most critical challenge for the NMRI is how to exist in a time of budgetary austerity. The NIDDK budget from 2007 to 2011 rose by a small amount, but given the added expense of biomedical inflation, there is less money to support the same level of funding for all programs. The real buying power in 2011 has returned to the real funding levels of 2001. Examining data on the percentage of grant applications funded during the past decade provides a way to illustrate what may be expected in the future: the percentage of grants funded in 2011 was at its lowest level than during any year other than 2006.

Dr. Germino concluded by congratulating the NMRI for 10 years of excellence and thanked the group for the opportunity to speak on this occasion.

Discussion

Dr. Lincoln Edwards commented that the burden of mentoring created by the lack of senior minority investigators presents another challenge for senior minority investigators who currently are in the academic setting. In addition, academic institutions generally do not recognize mentoring as a significant activity when individuals are evaluated for promotion. Dr. Germino noted that this problem can be overcome only by having institutions recognize the value of mentoring and having adequate numbers of minority faculty members serve on promotion committees. The NIH sometimes faces a similar problem with its review committees when they review applications from minority individuals or institutions; therefore, it is important that minority grant awardees be willing to serve on review committees when offered the opportunity

Dr. Kwami Osei asked about the relationship between the NIDDK and the National Institute on Minority Health and Health Disparities' (NIMHD) Research Centers in Minority Institutions (RCMI), headed by Dr. John Ruffin. Dr. Osei also asked if the NIH needs to make structural changes to encourage minority researchers. Dr. Agodoa noted that as part of Congressionally-mandated consolidation in 2012, the RCMI was moved from the National Center for Research Resources, which was dissolved, to the new NIMHD (which was elevated from a Center to an Institute in 2011). Dr. Germino addressed the comment on structural changes. He said that efforts should be made to ensure that the NIH grant review process includes a broad-based group of reviewers who appreciate the science without looking at the institution or past success of applicants in receiving grant awards. This would include reviewers who understand the context of the science included in the application and that the results of the project address something that will improve the health of all populations. He challenged those present to become involved in the NIH review process to offer their experience and perspective.

KEYNOTE ADDRESS: CHANGE AND CONTINUITY: LATINOS IN THE FUTURE OF AMERICA
Luis Ricardo Fraga, Ph.D., M.A., Associate Vice Provost for Faculty Advancement, Russell F. Stark University Professor, Director, Diversity Research Institute, Professor, Department of Political Science, University of Washington, Seattle, WA

Dr. Fraga began by relating his experience as a high school student in the sciences and being chosen for a National Science Foundation summer research institute in the Jackson Laboratory in Bar Harbor, ME. He recalled the importance of that experience in setting him on the path to an academic career.

He added that the United States is changing demographically, and this is a time for critical choices. Shifts in Latino demographics can be viewed through the lens of change and the consequences that come from these demographic shifts. Many people feel threatened by this demographic shift, and this should be addressed by the political system. Community leaders have a responsibility to describe and support tradeoffs that must occur to ease the effect of the demographic shift and make it acceptable to a majority of the people in the United States.

Population data from 1970 projected through 2050 show a dramatic demographic shift that is likely to continue. By 2050, the percentage of the U.S. population that identifies itself as a specific race will change among whites (84.1% to 46.3%), African Americans (10.6% to 11.8%), Latinos (4.5% to 30.2%), and Asians (0.7% to 7.6%). At the state level, California is the largest state and sends the most legislators to Washington, DC. California recently became a minority-majority state (i.e., the total number of minorities surpassed the total number of whites); Texas and Hawaii also are states that soon will be minority-majority states. Dr. Fraga characterized the changing demographics as an example of "linked fate and destiny" in describing the tradeoffs that will be needed in the future.

Since 2002, the source of growth in the Latino population has been among those born in the United States (62.6%), with 91.7 percent of those under the age of 18 years being native born. Both immigrant and native-born Latinos are important in today's population, but the future will belong to those who are

native born. The Latino population has a significant regional concentration, with New Mexico having the highest percentage of Latinos (46.3%). The pattern of Latino population dispersion in the United States from 1980 through 2008 shows that Latino population growth is spreading to the South and Northwest, but growth continues in traditional Latino areas such as the Southwest, California, New York, and Chicago. New areas of Latino growth are in states that traditionally have a history of poor race relations. Approximately one-fifth of all students enrolled in public schools in the United States are Latino, with higher rates in Texas (50.3%) and California (49.3%). These changes have occurred over a relatively short period of time, and have led to a perception of threat, loss of control, and a national identity crisis as one of the responses to these changes.

Dr. Fraga related his experience of trying to raise funds for a comprehensive survey of Latino perceptions, which garnered little support among funding agencies. When funds finally were acquired, the survey, which was the first state-stratified national survey of the U.S. Latino population, provided data on Latino attitudes about a wide range of issues relevant to the ongoing debate in the United States on immigration. The survey included both participants who were citizens and illegal immigrants and assessed the views of more than four generations. Survey findings included the following:

- Overwhelming majorities, especially in the first generation, felt that it was very important or somewhat important to learn English. It was noted that there is a large gap in the United States between the number of people who want to learn English and the number of publicly sponsored programs that provide this service.
- Majorities across generations felt that it was important to maintain the ability to speak Spanish, although by the third generation few survey participants had maintained that ability; the aspirational choice is to maintain both.
- More survey participants chose to identify themselves as “Hispanic” rather than “Latino,” indicating a pan-ethnic identity regardless of country of origin. This is borne out by survey participants simultaneously identifying with pan-ethnic, country of origin, and American identities.
- Across the four generations, those who identified with their home country decreased from the first to the fourth generation; the opposite occurred from the first to fourth generation for identification as Americans.
- For maintaining cultural identity, survey participants felt that it was important to assimilate but also to maintain the distinct culture of their home country.
- There was a clear aspiration for educational attainment among survey participants, which shows cultural convergence with a general American value. When asked how far they expected their children to go in the educational system, there were high expectations, but by the third and fourth generation there were fewer parents who expected their children to achieve a college or graduate degree. This may be indicative of the realities of the debt load at those levels.

The survey also included questions about political association or identification. This should be important to the scientific community because politics drives scientific funding, mentoring programs, and the research agenda. These are central questions that will impact academic institutions and, ultimately, the research community.

Data from the U.S. Census Bureau (2009) indicate that one-third of Hispanic children live in poverty; the national figure for all Americans is 20.1 percent. Approximately two-thirds of Hispanic and African American high school students attend schools that are 90 percent segregated. Not being able to read or complete high school are key indicators for entry into the prison system in the United States. These data show that the futures of minority children are being limited.

Dr. Fraga concluded with a quotation from Roberto Unger and Cornell West in their 1998 book, *The Future of American Progressivism*:

> *“To understand your country, you must love it. To love it you must, in a sense, accept it. To accept it as it is, however, is to betray it. To accept your country without betraying it, you must love it for that in it which shows what it might become.”*

Dr. Fraga said that choices await us concerning the type of future we want in the United States. Immigrants come here for a better life and have faith that their children's lives will be better than their lives have been. Dr. Fraga ended by saying that the choices we make should be made in the context of the legacy we want to leave for our children. He asked that the choice be for a future of linked faith and common destiny, and noted the tough choices that will have to be made to achieve such a future.

Discussion

Dr. Fraga clarified that "first generation" in his survey includes those not born in the United States, which may differ from other sociological or political definitions. As for defining ethnic and racial background, the U.S. Census began including a category of "mixed race" in 2000; 3.9 percent of Americans have chosen this category. This is not the same as ethnicity or ethnic identity. Regarding the issue of women in science, Dr. Fraga commented that there is a dysfunctional system of academic promotion in this country. It seems that an individual's value often is appreciated only when that employee notifies the institution that he or she is leaving. Loyalty to the institution seems to be undervalued. The standard in research institutions should be to value those who can bring diverse racial and ethnic perspectives to the scientific enterprise.

Population growth and birth control are significant issues in the immigrant community. A participant asked how the politics of religion and birth control will impact the population. Dr. Fraga indicated that birth rates among Hispanics are decreasing in both the United States and Latin America. The number of years of education is the highest predictor of number of children, with access to birth control as another critical factor. As educational levels increase in Latin America, it is expected that birth rates will decrease. In the United States, first generation Latinos are overwhelmingly Catholic, but there are marked declines with each generation. There does not, however, appear to be an impact of religion on birth control, which may sound contradictory.

PANEL DISCUSSION: ARTICLE IN *SCIENCE* ON RACE, ETHNICITY, AND NIH AWARDS
Ann Bonham, Ph.D., Chief Scientific Officer, Association of American Medical Colleges, Washington, DC
Kwame Osei, M.D., F.A.C.E., F.A.C.P., Director, The Ohio State University College of Medicine, Columbus, OH
Walter Schaffer, Ph.D., Senior Scientific Advisor, Office of the Director, NIH, Bethesda, MD

Dr. Schaffer
Dr. Schaffer began by describing the context from which the Ginther et al., paper on race, ethnicity, and NIH awards arose. The study was designed at the NIH and conducted by a contractor. The NIH, which has had diversity-related programs in place for nearly 40 years, has a unique and compelling need to promote diversity in biomedical research. Diversity improves the quality of education and training, broadens perspectives in research priorities, improves the ability to recruit subjects from diverse backgrounds, and improves the Nation's ability to address health disparity issues.

Drs. Schaffer and Raynard Kington launched a series of studies to provide credible evidence that would change the nature of the discussion about this issue. A study of women showed a steady increase of women in research programs. Currently, the number of women receiving doctorates is slightly more than one-half, and women receive approximately 30 percent of research project grants (RPGs). Women have almost identical success rates to men on Type 1 applications, and their retention as faculty and as individual investigators (R01 pool) remains the same. However, the situation with racial and ethnic minorities is more disparate: approximately 12 percent of the population is Hispanic or Latino; 10 percent is black or African American; 3 to 6 percent is Asian. The trends since 2000 show an increase in the number of Asians obtaining research project grants but the proportion of Hispanics and African Americans serving as Principal Investigators has changed little.

Dr. Schaffer described studies of education and funding trends. One paper (Pohlhaus JR, et al., Sex differences in application, success, and funding rates for NIH extramural programs. *Acad Med* 2011;86:759-767) examined application, success, and funding rates. A second paper (Ginther DK, et al. Race, ethnicity, and NIH research awards, is available on the Social Science Research Network at

http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1677993) considered the percentage changes in representation across career stages. It showed that Hispanics and African Americans were much less likely to go to college than whites or Asians, and a further decrease was seen from college to graduate school. The study also showed a significant increase in the number of Asians obtaining advanced education.

The Ginther et al. paper published in the journal *Science* showed a significant difference in the success rates among white, Asian, and Hispanic NIH grant applicants compared with African Americans, who were much less successful in receiving grant awards. These differences are seen across almost every field of science: African Americans receive lower application scores in a pervasive and persistent way. This trend in success rates also is seen in applications from top-ranking institutions.

Three additional studies are under way. One focuses on disparities among M.D.s. Dr. Schaffer noted that the disparity among M.D.s is not as large as with Ph.D.s, and that all applicants who work in medical schools experience better outcomes on NIH grants. Further studies will try to distill additional information from applications beyond what was available in the structured datasets on the individual applicants. In addition, the Diversity Workgroup of the Director's Advisory Committee held a workshop to discuss experimental techniques that could be used in the pre-application setting as well as during review to determine if biases are a contributing factor.

Dr. Bonham
Dr. Bonham said that the Diversity Workgroup (DW) report is due to the NIH director in June. As the Chief Scientific Officer of the American Association of Medical Colleges (AAMC), Dr. Bonham works with research policies and programs that interact with federal agencies involved with academic medicine. The AAMC is concerned about health equity and improving the quality and quantity of research to address problems of health equity and inequity. The organization recently hired Dr. Philip Alberti as its Director for Health Equity Research and Policy.

Dr. Osei
Dr. Osei was born in Ghana, trained in science in the 1970s, and completed his internship and fellowship in the United States. During the past 30 years, he faced challenges similar to those faced by today's younger investigators, but he persevered and received funding through NIH mechanisms. He has participated on multiple study sections, was part of RCMI, and has conducted work with the NIDDK.

Panel Questions and Discussion
Twenty-four questions were selected by a committee, based on responses to a premeeting solicitation via email for questions that participants wanted to hear answered. Panelists discussed the questions as time permitted.

Question #1: *How did you prepare the represented investigators to submit a more competitive and successful application?*

The panelists indicated that mentorship, grantsmanship, networking, and institutional resources are important components in this process. Dr. Schaffer said that education is an important factor. A survey of institutions showed that those whose investigators achieved the best success rates used strong internal review procedures ("pre-view") that provided constructive, critical feedback and allowed investigators to make substantive changes before submitting their application to the NIH. Dr. Osei commented that internal procedures are needed, particularly pre-review from researchers who have served on study sections. However, incentives (e.g., financial rewards or points toward promotion for faculty) are needed to encourage faculty to participate in this pre-review process. This pre-review phase must be institutionalized to be successful, and young investigators must have mentors. Dr. Bonham added that, in addition to mentoring and procedures, other key elements of grantsmanship are networking and pre-grant assistance (i.e., not related to the science) before beginning to write the grant application. The institutional resource list is an example of a pre-grant resource. Dr. Osei agreed that institutional infrastructures are critical to sustaining a grant, and a scientific writer can help ensure that the text conveys the science accurately.

Discussion of Question #1

Shay Lewis, Baylor College of Medicine, asked how applications from small institutions that do not have core facilities are considered and whether it is helpful to describe access to resources at other institutions. Dr. Bonham said that the best approach is to provide a statement from the other institution(s) with documentation about access and use of their core facility. Dr. Osei agreed and encouraged inclusion of a letter from the external institution indicating the researcher's knowledge and use of the facility.

A participant raised concerns about equity in grant awards, noting a long-term trend of larger universities receiving larger grants. Dr. Osei said that applicants should strive to submit the best application possible, and he encouraged pre-views of the grant before submission. Dr. Schaffer added that persistence is a virtue, and unsuccessful applications should be revised. He noted that having publications is an advantage, particularly if a member of the review committee has cited an applicant's paper. Dr. Bonham wondered about establishing a process for new investigators to interact with the review committee, and a participant suggested that interviews by the committee would provide a new approach. Dr. Germino said that NIDDK program staff are particularly attentive to applications from new investigators, and their R01 applications are considered under different paylines. He encouraged applicants to submit the right grant to the correct NIH grant category and to make sure that the program officer gets to know him/her. The panelists also recommended mentorship of first-time investigators.

Alexis Drenaham, Georgia Health Sciences University, described unsuccessful experiences of preparing and submitting $1.5 million in proposals during the past year and several attempts to find pre-reviewers. She asked about NIH plans to fund grant proposal mentoring to help facilitate relationships between senior and junior scientists and improve success rates for minority applicants. Dr. Bonham acknowledged that the DW considers this an important issue, including what would constitute a successful, targeted mentoring program, as well as issues of unconscious bias in processes and across institutions. She suggested that investigators could approach their institution's president for assistance in this area.

Question #2: *How can we position investigators to be viewed more favorably in the review process, including trying to diminish, eliminate, or address any unconscious biases?*

Dr. Bonham said that the DW is strongly committed to developing an evidence base for managing bias and unconscious bias during the peer review process. In terms of institutional bias, its recommendations will cover ideas to gather data and encourage mitigation. Dr. Osei commented that one approach is to omit investigator and institutional names from applications in review. This approach has been unsuccessful in the past, however. Dr. Osei suggested that investigators thoroughly proofread their applications prior to submission, as grant applications with grammatical errors are poorly received by review committees.

Discussion of Question #2

In premeeting comments, participants suggested that study sections do not always include a diverse membership and wondered whether junior researchers who do not have grants could serve on study sections. Dr. Schaffer said that younger investigators can participate as early career reviewers.

A participant expressed appreciation for the DW's desire for an evidence base for bias, commenting that the Endocrine Society had recommended an ethnographic or social science-based study on the operations of the review committees. To help shift peer review decisions, which often seem to be made on an investigator's "pedigree," clearer guidance may be needed regarding how closely the science meets the goals of NIH research, and there may need to be a separation between more mundane, needed studies versus exploratory science. Dr. Schaffer said that the NIH has a two-stage review process—the study section to identify the applications with the highest scientific merit, and selection by Council and program offices—with the funding decision made elsewhere. Dr. Bonham added that the issue of health disparities could be addressed at the funding level; health-equity related research should be given a higher priority in the broader biomedical community.

Deirdre Crews of The Johns Hopkins University asked whether personal statements on the NIH biosketch might affect bias about the applicant and how revealing the statement should be. Dr. Osei said that the statement should reflect passion for health disparities, and Dr. Bonham suggested that applicants include the following statement from former Surgeon General David Satcher: "The diverse team of researchers will be more likely to ask and pursue the appropriate questions in the appropriate manner, whether in basic, clinical, or health services and behavioral research, that affect their own group."

The question of whether diversity should be an NIH criterion was raised. Dr. Schaffer replied that this information is on the application under race/ethnicity, but the information is not provided to the reviewers.

A participant noted that, to be successful in today's fiscally strained environment, investigators must look for mechanisms of success, including emphasizing interdisciplinary teams, including a translational research component, displaying business sense, and adopting an altruistic approach, along with significant networking. The panelists were asked what else could be done if success was not achieved despite following the above advice. Panelists replied that collaboration is necessary, and that all possible sources of funding—foundations, industry—should be sought.

A participant commented on the very high percentage (98%) of foundation money that his institution receives as opposed to that received by the laboratories. Dr. Bonham observed that most institutions spend about 30 percent more from institutional funds for each $1 received through an NIH grant; state funds likely will be reduced, clinical margins are fragile, and contributions from philanthropy are never guaranteed. Dr. Schaffer added that, because of the potential for a substantial reduction in NIH funding, institutions are seeking additional funding sources. Strategies to adapt to reduced funds are needed; one idea is to fund applications through a lottery system.

Panelists were asked how the research community could best learn to develop creative solutions. Dr. Osei said national priorities for public health should be considered in the allocation of the budget. Dr. Bonham responded that this could be considered in terms of whether the research should benefit everyone or some citizens; in the clinical setting, the lupus drug shows great benefits for whites, but the drug's benefits for African American and Hispanic minorities, whom lupus affects the most, are unknown.

A participant asked how health disparities are considered and reviewed in study sections and whether the review panels understand health disparities. Dr. Osei agreed that it is important that health disparity applications be reviewed by the right people. Dr. Schaffer reflected on the NIH review process and commented that literature about health disparities may be relegated to second-tier journals. The grant application's cover letter should suggest specific review committees.

One participant related an anecdote about a researcher who, unable to obtain NIH funding, approached his university with the idea of forming an after-hours nephrology group that the university would help fund; he never had to write another NIH grant. Dr. Osei said that universities are becoming creative and have other businesses beyond academia, such as setting up companies to assist with grant applications. Institutions can support many different types of activities, provided that conflicts of interest are avoided.

A participant wondered how the constitution of study sections is determined. Dr. Schaffer said that every Scientific Review Officer (SRO) is cognizant of the need for diversity on his/her committee and actively recruits for this. The review pool is restrictive, however. NIDDK staff pointed out that, for committees that are chartered (i.e., most of the NIH Center for Scientific Review study sections), there is a legislative requirement for diversity in terms of gender, minority status, geography, etc. Dr. Bonham said that the DW received a suggestion to review the success rates of applicants to determine if there is a link between a more diverse group of reviewers and the success rate for minority awards.

A participant observed that young investigators face criticisms from review boards and institutions about too few publications and the lack of publications in first-tier journals; however, young researchers have not had the funding to conduct studies and publish many articles, and most health disparities science is not published in the first tier of publication journals. Dr. Schaffer said that the NIH is considering changes

to the biosketch to shift emphasis from the number of publications to "what have you done?" The NIH will issue an RFI to solicit feedback on this, and thus reduce the tyranny of "single-word" journals.

Because of time constraints, all questions were not answered. Dr. Sanabria said that the meeting Planning Committee would investigate a method to address the other questions, either by email or through the NMRI website.

LUNCH ADDRESS: CAREER DEVELOPMENT: LEADERSHIP FOR MID-CAREER PROFESSIONALS

Jasjit S. Ahluwalia, M.D., M.P.H., M.S., Associate Director, Clinical and Translational Science Institute (CTSI); and Director, Center for Health Equity (CHE), University of Minnesota Medical School, Minneapolis, MN

Dr. Ahluwalia encouraged participants to attend the upcoming "Summit on Science of Eliminating Health Disparities," a multi-agency conference that will be held October 31 to November 3, 2012, at National Harbor, MD.

Dr. Ahluwalia discussed successful career trajectories in academics. Success can be defined differently, based on what is most important: family, professional, work promotion, etc. He referred to Ginther's article (*Science*, Aug 2011), which showed that percentage points (for NIH R01 awards) were dramatically lower for African American Ph.D. scientists. The denominator—that is, the number of applications received from African Americans or Hispanics—may be a contributing factor. This will be interesting to watch during the next 10 years.

In pursuing success, it is important to be assertive and persistent, be inspired, encourage hard work, seek opportunities, emphasize personal and professional balance, and increase one's "people currency." There will be "ups and downs" in an individual's career path; it is a marathon without shortcuts. Younger investigators should focus on the road to excellence rather than worry about the outcome (e.g., tenure).

Who you know matters a lot—this is known as "people currency." Dr. Ahluwalia shared examples of his networking experiences, including greeting new acquaintances at restaurants, in airport lounges, and on airplane flights. He takes advantage of his service on National Advisory Councils and Board of Director positions for some of his networking. He encouraged participants to feel empowered to network, as the payback is significant though often intangible.

Dr. Ahluwalia shared his career trajectory from his early years through medical school and into several phases of his professional life. During the formative years, the experience of mentors should not be underestimated; his early mentor was his father. He completed combined M.D./Ph.D. degrees, with inspiration from many people along the way at Tulane Medical School, internal medicine residency at the University of North Carolina at Chapel Hill, and during fellowship in clinical epidemiology at Harvard. During this time, he had no abstracts or papers and almost quit his research trajectory. Through second jobs, he paid back his $100,000 student loan debt in 7 years. He also became involved in grant reviews and encouraged participants to do the same.

Mentorship is critical for success in the fellow-to-faculty transition. He was hired at Emory University with some support for protected time for research; 50 percent of his time was devoted to the walk-in clinic, which provided a laboratory for his first research projects. Bilateral mentor-mentee relationships were formed with colleagues working together on each other's projects. Dr. Ahluwalia also networked while attending many national meetings. His time at the University of Kansas was marked by "academic entrepreneurship." This included a randomized controlled trial of the nicotine patch for smoking cessation. He networked with Ed Riley, Marion Merrell Dow, Inc., which manufactured nicotine patches, and eventually received $175,000 in grants from the company to support a smoking cessation clinical trial. He received a number of small and then somewhat larger grants ($15,000-$25,000 to $40,000), including those from the Cancer Research Foundation of America, to conduct focus groups or pilot test interventions. These grants can build the basis for larger studies in the future. "Club membership" grants,

such as from the American Cancer Society and Robert Wood Johnson Foundation, provide additional funding along with their respective grantee annual meetings, which were an excellent networking forum.

Dr. Ahluwalia moved to the University of Kansas and served as Vice Chair and then Chair of the Department of Preventive Medicine, despite the caution expressed by his Chair at Emory that such a move would be "career suicide." It turned out to be an incredible 8 years of his professional life. He garnered leadership skills and helped colleagues grow their careers. However, events do not always happen as they are planned—the main outcomes paper of a major trial took him 9 years to submit, with the help of many others.

His first R01 grant focused on bupropion as a smoking cessation aid for African Americans. Receipt of an R01 is a career tipping point. There is an incremental drop of 50 percent between the first and second R01s, and again between the second and third R01s. Anyone with an R01 award should leverage it to obtain additional grants. Applications for smaller grants should be strategically focused to leverage the next award; Dr. Ahluwalia received three R01s that originated from small grants. Infrastructure grants provide support for helping other people become successful, and co-investigator mentoring provides additional opportunities on other investigators' R01 awards, both within and external to one's own institution.

Associate professors have a myriad of opportunities for career development, including: study sections, editor positions and editorial boards, reviewer/study sections, visiting professorships, scientific and pharmaceutical advisory boards, academic committees, community activities, and mentorship. Investigators should continually seek new opportunities and have grants in the pipeline. One way to address potential overfunding issues is to modify the level of effort at the onset and close of a grant. Another important component is team science. As clinical research commences, there is an initial delay in preparing papers. In time, though, the amount of research and ensuing literature increases.

Dr. Ahluwalia went to the University of Minnesota. He applied for and was awarded an NIH center grant which established the Center for Health Equity. He briefly reviewed his awards, noting that downtimes are followed by successes, such as the Herbert W. Nickens Award (2009), ASPO Joe Cullen Award (2010), APHA ATOD Lifetime Achievement Award (2011), and PCF – Cancer Prevention Laureate (2012). He was also is the Founding Chair, NIH Health Disparities Study Section, and is currently a National Advisory Council member for the National Institute on Minority Health and Health Disparities.

Dr. Ahluwalia encouraged attendees to strive for balance and stability in their personal and professional lives, exercise, and focus on activities they consider to be important. He recommended that participants read *Time Tactics of Very Successful People,* by B. Eugene Griessman (McGraw Hill, 1994).

MOCK STUDY SECTION

During a breakout session, participants attended one of three Mock Study Sections. Each session covered different types of NIH awards: R01/R03, K-Awards, and F-Awards. Session leaders were given sample grant applications (some from meeting participants) to review and provide critical feedback. The SRO led a discussion of the feedback sessions. One of the most useful activities during the session was the grading of the sample applications by "study section" participants, with direct feedback on why they would have scored the application as they did. The three study sections were comprised of a Chair and SRO, as noted below. Each mock session included experienced researchers who had submitted successful grant applications; they provided real-life experiences about their quest for funding, often after being unsuccessful in their first attempts. Discussion sessions were scheduled to allow participants to ask specific questions after hearing about the process and grading scale. These sessions were invaluable at this time because of the difficulty in winning awards due to budgetary reductions.

Study Section 1: R01/R03 Awards
SRO: *Lakshmanan Sankaran, Ph.D., Scientific Review Officer, NIDDK, NIH, Bethesda, MD*
Chair: *Susanne Nicholas, M.D., Ph.D., M.P.H., Associate Professor of Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA*

Study Section 2: K Awards
SRO: *Barbara Woynarowska, Ph.D., Scientific Review Officer, NIDDK, NIH, Bethesda, MD*
Chair: *Sylvia Rosas, M.D., Assistant Professor, Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA*

Study Section 3: F Awards
SRO: *Michele Barnard, Ph.D., Scientific Review Officer, NIDDK, NIH, Bethesda, MD*
Chair: *Carlos Isales, M.D., Associate Director, Professor, Department of Orthopaedic Surgery, Georgia Health Sciences University, Augusta, GA*

ROLE OF SCIENTIFIC SOCIETIES AND PROFESSIONAL ORGANIZATIONS

American Society of Transplant Surgeons

Jonathan Bromberg, M.D., Ph.D., Professor of Surgery, and Microbiology and Immunology Head, Division of Transplantation, University of Maryland School of Medicine, Baltimore, MD

The American Society of Transplant Surgeons (ASTS) is a nonprofit organization with a mission of being the authoritative resource in the fields of organ and cell transplantation by advocating for comprehensive and innovative solutions in the fields. ASTS promotes training and career-long education of transplant surgeons. More information about ASTS is available at http:\\www.asts.org.

The ASTS grant program was established in 1985 and awards $600,000 in grants annually; more than $8 million in grants has been awarded to more than 200 individuals in the past 20 years. Applications are received online, and more than 108 applications were received for 2012. The peer-review process is rigorous and similar to the NIH review process. Dr. Bromberg presented a list of criteria that are scored during the review process, members of the review teams, and those who were recipients of the grants for 2011. Dr. Bromberg noted that he was awarded a collaborative scientist award, which allows him to provide opportunities for transplant scientists to talk with scientists outside the field to develop innovative collaborative research. For example, Dr. Bromberg has been able to investigate the microbiota, a field of study he may never have been able to study without this collaborative grant.

Because of the increased number of applicants, the chance of receiving an ASTS grant is similar to that of the NIH. An advantage is that the grant application is generally about three pages in length. The types of grants available are for faculty, resident or trainee, and recognition. ASTS wants to make these grants available to a wider range of scientists, but there must be some application to transplantation.

Discussion

During the discussion period, Dr. Sanabria noted that ASTS is one of many professional societies and organizations that are of interest to NMRI members.

SCIENTIFIC PRESENTATIONS

Cirrhosis and Cognitive Impairment

Charmaine Stewart, M.D., Associate Professor, University of Minnesota, Minneapolis, MN

Dr. Stewart reviewed her K award-funded research involving the neuropsychological (NP) profiles of individuals with cirrhosis. She focused primarily on hepatic encephalopathy (HE), which ranges from no psychological impairment to coma. The primary neurotoxin underlying pathogenesis is ammonia, which is present in high amounts in cirrhosis patients because of poor systemic shunting (i.e., blood does not efficiently circulate through the liver, the primary site of ammonia detoxification), changes in gut flora, and impaired renal and liver function. Minimal hepatic encephalopathy (MHE) lacks overt clinical signs and requires NP testing for diagnosis. MHE affects a patient's overall productivity, quality of life, and ability to drive safely. Up to 60 percent of cirrhosis patients are not fit to drive, but this varies significantly by study.

In this study, comparisons between the driving performances of cirrhosis patients versus controls were conducted using a driving simulator. Cirrhosis patients drove slower, experienced more pedestrian collisions, exhibited slower reaction times, and were less able to follow map instructions. Upon NP testing, slow speed was found to be correlated with motor deficits, and impaired map abilities were correlated with impaired visual-spatial function. Practitioners are reluctant to make strong recommendations about driving; however, they do recommend that patients undergo on-road testing until the simulator is validated for testing in these patients.

Patients with any chronic disease exhibit a stronger tendency for depression, which is associated with poor cognitive function. Dr. Stewart designed a test battery with six domains to evaluate the NP effects in depressed (Beck Depression Index [BDI] >14) and nondepressed cirrhosis patients. The BDI scores correlated inversely with learning, attention, processing speed, and visual perception. Overall, cognitive function worsened as depressive symptoms worsened, indicating that a subset of cirrhosis patients may benefit from antidepressant therapy.

Factor analysis uses levels of significance to determine if a test is applicable to a particular disorder and if the disorder is present in a patient or population. Using a standardized battery developed with all three factors, Dr. Stewart was able to determine premorbid conditions of patients, assess typical HE findings, and evaluate memory and learning. The battery includes tests on global intellectual function (patient function prior to chronic illness), psychomotor speed, and learning and memory.

In summary, cirrhosis patients have been shown to exhibit cognitive impairment, which leads to poor performance in a driving simulator, which correlates with impaired attention/concentration and visual-perceptual function. Cirrhosis patients with comorbid depression demonstrate worse cognitive performance than patients without depression. Finally, cirrhosis patients display a particular pattern of cognitive impairment. A standard battery of tests for these patients currently is under evaluation.

Discussion

A participant asked if the extent of cognitive impairment is related to the cause of cirrhosis. Dr. Stewart said she had not found this to be the case, but she did note a correlation between NP impairment and patient survival. A question was asked regarding functional magnetic resonance imaging (fMRI) and other structural studies on cirrhosis. Dr. Stewart replied that others are using fMRI to investigate blood flow and have discovered impaired blood flow to the brain and increased blood flow to subcortical regions in patients with cirrhosis. A nephrologist noted many similarities regarding the NP impacts of depression on patients with either cirrhosis or kidney disease. Finally, a participant involved in rehabilitation and occupational therapy suggested several other potentially useful tests, for example motor-free visual perception and Dynavision tests.

A Decade of Diabetes Research Among Native Hawaiians: Experiences From Hawai'i and Beyond
Marjorie Mau, M.D., F.A.C.P., Professor, Center for Native and Pacific Health Disparities Research, John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, HI

Dr. Mau indicated that when she started her career, there were very few publications on diabetes in Native Hawaiians, but there are lessons from this population that may be applicable to others. She presented data on the incidence, causes, and health outcomes of T2D in Native Hawaiians, comparing them to those of other ethnic groups in Hawai'i as well as the general population. Native Hawaiians were aggregated with Pacific Islanders in the 2007 Office of Management and Budget racial/ethnic designation "Native Hawaiian/Pacific Islander," but their political history and self-perception are distinct from Pacific Islanders and likely affect their health. Despite the Native Hawaiian diaspora, most Native Hawaiians still live in Hawai'i. The age-adjusted mortality rates of Native Hawaiians are comparable to those of African Americans and higher than those of whites. Of the causes of death for Native Hawaiians, heart disease is the primary one, but diabetes ranks fourth.

As recently defined by the NIMHD and Agency for Healthcare Research and Quality (AHRQ), a health disparity is a health difference that is "closely linked with social, economic, and/or environmental

disadvantage," and a health disparity population is a group that has significant disparity compared with the general population in overall rates of disease incidence, disease prevalence, morbidity, mortality, or survival rates. Health disparities science and research study the differences in health that are biologically unavoidable and those that arise from disadvantage and injustice. Ideally, Dr. Mau said, the results of this research inform the health policies that address these disparities.

Research on health disparities shows that, compared with whites, Native Hawaiians have high incidences of T2D (20%), impaired glucose tolerance (15%), central adiposity (for all categories of BMI), metabolic syndrome, and cardiovascular outcomes. Many of these elevated risks are shared by the other minority ethnic groups (Japanese, Chinese, and Filipino), particularly Filipinos that reside in Hawai'i.

Studies of the risk factors for health disparities for Native Hawaiians have failed to show a correlation between Native Hawaiian ancestry and BMI or waist-to-hip ratio (WHR), although BMI and WHR were correlated. Adherence to traditional cultures and beliefs among Native Hawaiians has been linked to elevated diabetes risk. Native Hawaiians were found to have a comparatively healthy diet but had the highest total energy intake of all of the Hawaiian ethnic groups (including whites). High fat/meat dietary patterns were associated with diabetes risk in all minority populations.

The prevalence of ESRD is increasing in Hawai'i, as is ESRD caused by diabetes. This rise is occurring despite advances in diabetes treatment and prevention. In Native Hawaiians, compared with other Hawaiian ethnic groups, ESRD is overwhelmingly due to diabetes. Ethnic differences in CKD incidence indicate a need for programs that target particular groups. Native Hawaiians have disparities in other diabetes-associated outcomes as well, including lower extremity amputations and CVD.

Community-based lifestyle interventions show promise as the most effective approach, both in cost and outcome, to address the problem of diabetes in Native Hawaiians. An example is the PILI 'Ohana Project, in which community members identified the primary health problem (obesity), delivered culturally relevant interventions, and collected the data. Participants successfully improved and maintained improvement in their weight, fitness, and physical activity levels. Dr. Mau concluded by saying that engaging the community is a lifelong journey that can improve scientific research, and be an effective approach to translating science into communities. Our next challenge is to convince policy makers of such an approach that works and that can be applied across many health disparate diseases and populations at high risk.

Epicatechin Rich Cocoa to Treat What Ails the Type 2 Diabetes, Heart Failure Patient
Francisco Villarreal, M.D., Ph.D., Professor, Department of Medicine, University of California, San Diego, La Jolla, CA

Cacao has been used by Mesoamerican Indians since pre-Columbian times for its health benefits, including for the treatment of fatigue, heart problems, breathing difficulties, and emaciation. The special qualities of cacao were recognized by the Spanish Conquistadores. Cacao has the highest concentration by weight of any fruit or vegetable of flavanols, a family of flavonoids. The most abundant flavanol in cacao is (-)-epicatechin. Inspired by studies of the effects of green tea-derived catechin (another flavanol) on mouse exercise capacity, Dr. Villarreal and his colleagues evaluated the impacts of epicatechin and exercise, as well as their combination, on exercise capacity, heart and skeletal muscle structure, and mitochondria in mice. In a proof-of-principal clinical trial, he and his research team also explored the effects of chocolate and cocoa beverages on patients with heart disease and diabetes.

In the mouse study, the researchers found that 15 days of epicatechin treatment increased skeletal muscle, mitochondrial volume, and cristae abundance in the heart and skeletal muscle. In addition, epicatechin, as well as epicatechin combined with exercise, elevated markers of mitochondrial biogenesis. Treated mice had improved exercise capacity, which Dr. Villarreal demonstrated in a video clip of the mice running on treadmills.

In the clinical trial of five patients with Stage II heart failure and type 2 diabetes, patients underwent blood tests as well as skeletal muscle biopsies at baseline and after 3 months of epicatechin treatment, during

which no adverse reactions to chocolate consumption were observed. At baseline, patients had symptoms of fatigue and diminished physical capacity, in addition to exhibiting highly disrupted skeletal muscle mitochondrial structure. The cocoa/chocolate treatment increased cristae abundance and density, improved skeletal muscle mitochondrial structure, and elevated markers of mitochondrial biogenesis. Dr. Villarreal also discussed unpublished data on the destructive effects of the disease on dystrophin associated complex members and the striking recovery of these proteins with treatment as well as of various markers of muscle regeneration. He presented putative mechanisms by which epicatechin might act to increase ATP production, improve metabolism, decrease oxidative stress, and enhance endothelial function, thereby improving skeletal muscular and cardiac function, lung capacity, and ultimately, quality of life in patients with heart disease.

Dr. Villarreal concluded by saying that the optimal dose of epicatechin for building human muscle capacity is about 5 grams per day—the equivalent of a "Hershey's Kiss" worth of 70 percent cacao chocolate.

MARCO CABRERA POSTER AND NETWORKING SESSION—OVERVIEW
Judges: *Drs. Carmen Sceppa, Luis Cubano, and Trudy Gaillard*

Participants were invited to see the posters submitted to the NMRI Annual Workshop. This year, 33 posters were submitted in three categories: Basic Science, Clinical Science, and Translation. During the poster review, judges observed the posters and chose winners for each category; the awards were given to recipients on the second day of the workshop. This was the highest number of posters yet submitted for an NMRI Annual Workshop.

DINNER ADDRESS: MAKING PROGRESS IN UNDERSTANDING THE CAUSES OF HEALTH INEQUALITIES
Thomas LaVeist, Ph.D., Director, Hopkins Center for Health Disparities Solutions, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Dr. LaVeist addressed the issue of health inequalities during the NMRI 10th Anniversary Dinner. He began by announcing development of a documentary film on health disparities that will be available in the spring of 2013. The promotional materials include the statement that "African Americans live sicker and die younger than any other ethnic group in the United States. Why is this?" This is the core focus of Dr. LaVeist's research at The Johns Hopkins University (JHU). He used the example of disparity in those saved in the 1912 Titanic disaster: the chance of survival by class of accommodations indicated that 97.2 percent of first-class passengers survived, compared with the 54.7 percent of third-class passengers who survived. This example can serve as a reflection of the disparity in the U.S. health care system.

The 2002 report of the Institute of Medicine (IOM), which was not the first report on health disparities, finally raised awareness of the issue in the medical and research community. One reason this IOM report had an impact was that it reviewed only high-quality, peer-reviewed studies of patient-reported outcomes (PRO) and access to care among patients who had health insurance. The scientific rigor of the 2002 report made it acceptable to the medical community and put the issue on the agendas of health policymakers.

In discussions among Dr. LaVeist's colleagues at JHU, it was determined that calling for initiatives to address health inequities based on social justice and the fact that this would be the moral choice for the United States would not be sufficient to encourage political backing; a more fact-based argument was needed. This led to the writing of a report that used the monetary impact of health inequality on the U.S. health care system as a basis for developing strategies to address the issue. Three factors were readily apparent using data from 2003 to 2006: the direct medical care costs of health inequality were $229.4 billion; the indirect costs of disability and illness were $50.3 billion; and the costs of premature death were $957.5 billion. The total costs for health inequality from 2003 to 2006 were $1.24 trillion in 2008 inflation-adjusted dollars.

Dr. LaVeist presented data that show that African Americans with insurance have disparate access to procedures compared with white patients. An example is that African American patients are referred for

coronary angiography approximately 25 percent less than white patients with the same symptoms. In the Veterans Administration (VA) health care system, African Americans are referred for coronary revascularization at a rate that is approximately 50 percent less than that for whites. The VA system has no differences in physician salaries or differences in cost to the patient. At its core, this is what health disparity is about.

Dr. LaVeist offered different factors to account for health inequalities. For example, it is timely to provide a genetic rationale to explain diseases or treatments. The drug BiDil®, a heart failure drug that was FDA-approved for use in African Americans, is a good example. Dr. LaVeist suggested that this approval was based entirely on the wrong hypotheses because this drug addresses a genetic factor that only 8 percent of African Americans have, which means that 92 percent do not. However, because the FDA wanted to do what it thought was addressing a health disparity, the drug was approved for use in African Americans. Dr. LaVeist cited similar thinking and types of studies that can discount the fact that social status or income level are responsible for health inequities. For example, he used the 2005 National Health Interview Survey (NHIS) to construct a theoretical study that showed that income and race were not correlated with activities of daily living, which is an indicator of disability. For education, he showed pictures of four Baltimore-area high schools from different socioeconomic backgrounds to illustrate that any student who graduated from any of these schools would be counted as a "high-school graduate" in surveys, although it is clear that the quality of the education probably is not the same. In fact, few conclusions can be drawn about high school graduates in Baltimore without accounting for the students' different environments.

The critical point from the previous examples is that, for those who design and conduct such studies, segregation dramatically confounds health disparities research. The United States is racially segregated. Although everyone lives in the same country, we all experience it differently. National statistics have little meaning without the context of those experiences. Race is just one of the factors that are included in the experience. To conduct health disparities research studies that move beyond the confounding of segregation or SES, Dr. LaVeist began to look for communities of equivalence; communities that were racially integrated and did not have differences in income or education. The goal was to find these communities and replicate the study done by the NHIS to build models to determine if health disparities exist when people are living under similar conditions. Dr. LaVeist described the design of the study entitled Exploring Health Disparities in Integrated Communities (EHDIC). Researchers found 425 of the 168,000 census tracts in the United States that met the criteria of 35 percent African Americans and whites and black/white median income and percent of high school graduation ratios of 0.85 to 1.15. Many of these tracts were in Maryland, and two were in Baltimore. The Baltimore tracts were chosen for use in the EHDIC study. After replicating the NHIS methods, procedures, and analysis, the EDHIC results did not show the same level of health disparity as found in the NHIS, regardless of the variable included in the model. For example, the NHIS disparity for diabetes was 61 percent greater for African Americans than whites, but the disparity was only 7 percent greater in the EDHIC study; obesity among women was 87 percent to 25 percent in favor of the EDHIC. Neither of these was statistically significant. The significance of these results suggests that health disparities research needs to account for the type of environment being studied. Clearly, the complexity of the lives of individuals has an impact on their health.

In conclusion, to make a point about the need to look behind the statistics to confirm conventional perceptions, Dr. LaVeist asked how many people had heard the statistic that there are more black men 20 to 29 years of age in prison than in college. (Almost everyone said they had heard this.) Dr. LaVeist recounted that he also believed this, but he decided to investigate this perception by going to the U.S. Department of Justice website and educational websites to confirm it. He found that the perception is wrong; in 2006, there were 310,000 black men in prison and 480,000 in college. However, an individual can be in prison and in college during the same year, and some colleges offer courses in prison. What may be happening is that some individuals are being counted more than once in the survey. Dr. LaVeist asked participants to help him dispel the myth that more black men are in prison than are in college.

Discussion

A participant mentioned that some communities are being transformed as African Americans are being supplanted by Latinos and Asians, and he wondered how this impacts health disparities. Dr. LaVeist responded that the communities he studies in the EDHIC also have changed over time. For example, the Baltimore communities were established during World War II, when whites moved from West Virginia and blacks moved from North Carolina to the same community to take jobs in the manufacturing sector. Although some have moved to the suburbs, these communities have had the same level of integration for more than 50 years. This is different than the gentrification that is occurring in some inner city neighborhoods. These are stable working-class neighborhoods in southwest Baltimore.

A participant asked if there is a place for faith in combating health disparities. Dr. LaVeist strongly affirmed his belief that there is a place for everyone, including those from the faith community as well as those from the atheist community. At a time when many people are disengaging from their churches, individuals must adapt in ways that are relevant to the new generation; this also should include changes in the churches.

A participant noted that she studies health disparities in Alzheimers disease (AD). She noted that individuals of African heritage in the United States have a higher rate of AD than whites, but those of African heritage living in Brazil appear to be protected from AD. This supports Dr. LaVeist's position that context must be considered when researching health disparities.

A question was posed regarding the drug BiDil®, and whether this was an attempt to help poor people. Dr. LaVeist responded that the drug was a combination of two generic drugs and the new drug was not sold as a generic, which raised the price and actually goes against the idea that it was approved to help poor people. Everything we know about the drug is that it is effective, but the company that sold it has not done well. This is an example of science, politics, and policy coming together, and in these cases science will lose. If science was the primary force behind the production of the drug, it would have been made available to everyone. Once politics and policy became involved, the primary force became something different and eventually led to the failure of the company that produced the drug.

Because it appears that factors other than race are at the root of the health disparity issue, a participant asked what the new strategy should be for addressing them. Dr. LaVeist corrected the questioner by saying that his point was not that race should not be studied, but that race should be used carefully in the context of place (i.e., lifestyle, risk exposures, protective factors). This is the context for studying health disparities. He added that looking for the "racial gene" is not the right approach. In addition, admixture is a reality in the African American community if individuals have been here for more than three or four generations. If there ever were genes that affected one racial or ethnic group, they probably are irrelevant in today's world. This does not mean that there may not be gene variants that are important in some groups, but this is a nuance that is not likely to lead to results that impact large numbers of people.

FRIDAY, APRIL 20, 2012

BUSINESS MEETING AND COMMITTEE REPORTS

Oversight Committee Report

Charmaine Stewart, M.D., Associate Professor, Department of Internal Medicine/Gastroenterology, Hepatology, and Nutrition, University of Minnesota, Minneapolis, MN

Dr. Stewart, Chair of the NMRI Oversight Committee, provided an overview of NMRI activities during the previous year. She reviewed data presented by Dr. Germino the previous day and highlighted that there were approximately 200 active members of the NMRI and the list of accomplishments presented earlier.

The Oversight Committee was working to update the NMRI website with links to provide resources for members, including sections on completing grant applications and resume updating for junior members. The focus next year will be to collect as much information as possible from members on promotions, publications, and grants submitted and awarded. This will be facilitated by the revised online NMRI Questionnaire that can be accessed from the following URL: www.scgcorp.com/NMRIQuestionnaire. Dr. Stewart encouraged participants to complete the questionnaire following the meeting or during the meeting at the desktop stations in the corridor. It is critical that the NMRI have these data to show the value of the Network. It is anticipated that data will be published once there is enough to develop statistically significant results.

Dr. Stewart thanked Dr. Shirley Blanchard for chairing and hosting the 2011 NMRI Midwest Regional Workshop in November at Creighton University, Omaha, NE. A highlight was a session with more than 40 students from Omaha high schools, who spent an afternoon learning about scientific research and careers. Dr. Blanchard reported that after the session she received telephone calls from Omaha-area teachers requesting that additional sessions be scheduled for students who could not attend the November session.

Dr. Stewart announced that Dr. José Romero, Brigham and Womens Hospital/Harvard Medical School, Boston, MA, will be the 2013 Chair for the NMRI Annual Workshop. She thanked members of the current Planning Committee for their support during the past year in planning and organizing this workshop.

NMRI Mentorship Program

Virginia Sarapura, M.D., Associate Professor, Department of Medicine/Endocrinology, Anschutz Medical Campus, University of Colorado Denver, Aurora, CO

Dr. Sarapura reported on the NMRI Mentorship Program, which has been growing each year. The goals of the program are to identify willing mentors for a mentee in need and to create a framework to help accomplish the mentee's goals. At the current time, there are 23 mentor-mentee pairs; she requested that mentors and mentees provide her an update on whether these pairs are still active.

Dr. Sarapura asked that those who want a mentor or mentee visit the NMRI website at http://nmri.niddk.nih.gov/mentor/index.aspx and complete the appropriate Mentor or Mentee form. There also are questions about mentoring on the NMRI Questionnaire, specifically questions 11, 12, and 13.

Planning Committee Report

Dr. Sanabria

Dr. Sanabria thanked those who served on the workshop Planning Committee. He also thanked past Chair, Dr. Blanchard, next year's Chair, Dr. Romero, Dr. Agodoa, and Ms. Martinez for their support. He asked the attendees to increase their participation on the NMRI standing committees and to help Dr. Agodoa in his fight to maintain funding for the NMRI.

Dr. Sanabria asked participants to affirm that they liked the format of this workshop and if they were planning to attend in 2013 and bring someone with them. Overwhelming majorities affirmed this. He then

asked if some would be willing to pay one-half of their own way so that more people could attend; approximately one-half of the attendees said that they would consider paying one-half of their expenses next year. If the Network grows, it will become more successful.

MARCO CABRERA POSTER AWARDS
Carmen Castaneda-Sceppa, M.D., Ph.D., Associate Professor, Health Sciences Department, Northeastern University, Boston, MA

Dr. Castaneda-Sceppa thanked judges Drs. Luis Cubano, Trudy Gaillard, Sylvia Rosas, and Carlos Isales, and those who submitted posters. The following were determined to be winning posters in the categories of Basic Science and Clinical Translational Research.

Basic Science Poster Award
Dr. Lincoln Edwards, Loma Linda University, Loma Linda, CA
"Moxonidine and S43126 Enhance Glucose Uptake and Insulin Release in Cells"

Clinical Translational Research Poster Award
Drs. Alicia Mangram and James Dzandu, John C. Lincoln Health Network, Phoenix, AZ
"Increased A1C Level in Acute Care Surgical Patients Is Associated With Increased Risks of Infections at Admission, Hyperglycemia, and Prolonged Hospital Lengths of Stay"

POSTER SESSION ORAL PRESENTATIONS

Glycoxidative Modification of DNA (dC) and RNA (C) in Relation to Diabetes: Estimation of Carboxymethyl-2′-Deoxyadenosine (CMdA) and Carboxymethyl-2′-Deoxycytidine (CMdC) in Fasting Human Urine
Zeenat Lila, Ph.D., Kamika Manzano, Gabrielle Jenkins, Tatreka M. Polite, Miranda Williamson, Rafida Idris, Ph.D., and Mahtabuddin Ahmed, Ph.D.*, South Carolina State University, Orangeburg, SC*

According to the Centers for Disease Control and Prevention (CDC), more than 26 million people in the United States suffer from diabetes, with an estimated annual treatment cost of $174 billion. In South Carolina specifically, 348,000 people suffer from diabetes, with an annual cost of more than $2.7 billion. The objectives of Dr. Lila's study with others (pending publication: Dr. Mahtabuddin Ahmed, PI 1890 Project) were to identify uniquely modified deoxyribonucleic acid (DNA) nucleosides *in vitro*, identify modified DNA nucleosides in urine samples from fasting humans, and investigate the involvement of DNA in glycoxidation reactions that have implications in several diseases.

Minimal previous work has been done on this topic; however, studies that have been conducted indicate that N2-carboxymethyl-2′-deoxyguanosine was identified in cells exposed to induced glyoxal modification, and carboxymethyl-2′-deoxyadenosine (CMdA) was identified from glycoxidation reactions in DNA and urine. In the structure of DNA and RNA, there are four nucleosides that are susceptible to the glycation reaction: cytidine, deoxycytidine, adenosine, and deoxyadenosine. A glycation reaction is a nonenzymatic addition of a sugar molecule into protein, DNA, and/or lipid, causing damage and contributing to aging.

For this study, experiments isolate, identify, synthesize, detect, characterize, and quantify modified nucleosides in urine samples using liquid chromatography mass spectrometry (LC-MS), high-performance liquid chromatography (HPLC), a spectrophotometer, and a rotary evaporator.

The LC-MS spectra of 2′-deoxycytidine (dC) and 2′-deoxyadenosine (dA) with D-glucose, D-ribose, chloroacetic acid, and a control were visualized. The LC-MS spectra of CMdC and CMdA in urine samples of humans who were fasting also were examined. It was found that the concentration of CMdC and CMdA in urine samples from fasting humans increased with increasing patient age.

These data suggest that CMdC and CMdA in human urine are formed by degradation of glycated proteins *in vivo* and increase with patient age. Additionally, glycoxidation is involved in modification that leads to

CMdC and CMdA having implications in diabetes. It is hoped to mitigate disease suffering in the future by determining a mechanism to prevent or block the changes that occur in DNA and RNA molecules.

Discussion

A participant questioned the figure illustrating modified DNA and RNA as a ratio to urine creatinine that increases with age. This number may be increased artificially because creatinine (the ratio denominator) actually decreases with age. Dr. Lila affirmed that creatinine decreases with age; however, she confirmed that the modified compound increases with age. In this experiment creatinine was used as an internal standard (per unit of creatinine), not total creatinine, and estimation of CMdC and CMdA contents in fasting urine specimens using creatinine present therein as an internal standard indicate increasing amounts of CMdC and CMdA in human subjects within higher age groups compared with younger age groups of people investigated.

Responding to a question, Dr. Lila said that CMdC and CMdA can be utilized as biomarkers for early detection or to understand the extent of the disease in humans (due to the DNA damage indicated by the presence of CMdC and CMdA). A participant questioned the clinical utility of this biomarker because it requires a patient to have fasted. Can it be used if a patient arrives at a clinic after having eaten a hamburger? Dr. Lila responded that it was developed in fasting humans. More samples must be analyzed to achieve better quantification for such clinical applications. But to maintain a standardized situation, it was developed in fasting conditions to get the baseline value that is not influenced by a recent meal.

N-3 PUFA, Fatty Liver, and Inflammation

Moises Torres-Gonzalez, Ph.D., Department of Medicine, University of California, San Diego, La Jolla, CA

Dr. Torres-Gonzalez and colleagues investigated the effects of omega-3 polyunsaturated fatty acids (ω-3 PUFA) on nonalcoholic fatty liver disease (NAFLD) and inflammation. As obesity rates have increased, NAFLD, defined as excessive lipid accumulation in the liver, has become the most common cause of liver disease in developed countries, affecting 75 percent of obese and 100 percent of morbidly obese individuals. Twenty-five percent of the U.S. population has NAFLD, a hepatic manifestation of the metabolic syndrome that ranges in severity from simple fatty liver (steatosis) to nonalcoholic steatohepatitis (NASH); 30-40 percent of individuals with simple fatty liver progress to NASH. A “2-hit” hypothesis provides a possible explanation of the development of NASH in obesity: metabolic changes in the liver and adipose tissue caused by hyperinsulinemia/insulin resistance are followed by more severe effects (including mitochondrial dysfunction, oxidative stress, increased inflammation, cytokine production and release, and stellate cell activation), leading to liver fibrosis. These effects are difficult to reverse; therefore, efforts have been directed toward decreasing incidence through improved diet and increased physical activity. In the long term, however, maintaining these changes is difficult. Increased dietary intake of ω-3 PUFA (in particular eicosapentaenoic and docosahexaenoic acids) is an alternative strategy for reducing *de novo* lipogenesis, increasing fatty acid oxidation, and decreasing inflammation to protect against NAFLD.

Dr. Torres-Gonzalez examined the effects of ω-3 PUFA (i.e., fish oil) on hepatic function in a mouse model (LDL-R KO) of dietary-induced obesity and fatty liver. For 12 weeks, 3 groups of mice (8/group) were fed either standard chow or high-fat/high-cholesterol diets supplemented either with olive oil (HO) or fish oil (HF). The researchers determined that fish oil did not protect against obesity or hyperglycemia, but mice in the HF diet had reduced plasma triglycerides, cholesterol, apolipoproteins B and C (ApoB and ApoC3), and nonesterified fatty acids (NEFA). In liver tissue, mice fed fish oil had lower levels of markers for fatty liver.

In addition, the researchers showed that fish oil altered the expression of some of the transcription factors controlling *de novo* lipogenesis and mono-unsaturated fatty acid (MUFA) synthesis. Fish oil also reduced the expression of enzymes involved in liver triglyceride formation but not those that govern cholesterol metabolism. In addition, fish oil had anti-inflammatory effects that were not mediated by the NFκB pathway. Finally, hepatic fibrosis was reduced in fish oil-fed mice.

Dr. Torres-Gonzalez concluded from these results that dietary ω-3 PUFA can protect against some but not all of the metabolic abnormalities associated with NAFLD and NASH.

NIH/NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES
M. Roy Wilson, M.D., Deputy Director for Strategic Scientific Planning and Program Coordination, National Institute on Minority Health and Health Disparities (NIMHD), NIH, Bethesda, MD

Dr. Wilson discussed the importance of health disparities research and offered advice on career development in academia, drawing on his own experiences in navigating the academic ladder to success. Although disparities exist throughout the United States, a study published in October 2011 highlighted state-level variations in life expectancy. The District of Columbia has the largest gap in life expectancy in the country: a 14-year difference between white and African-American males. Health disparities in the United States are a problem for all Americans because the health of the Nation as a whole will not improve while these disparities exist. In addition, Dr. Wilson observed, the existence of racial disparities in health is an issue of morality and justice.

Disparities in African-American versus white life expectancy arise from multiple causes, including: (1) inequitable access to health care; (2) inequitable quality of health care received; (3) differences in disease manifestation, responsiveness to drugs and other therapies, and other biological/physiological considerations; and (4) racial variations in the social determinants of health. The importance of access to health care is illustrated by higher-than-expected life expectancies for African Americans in states with broader eligibility requirements for Medicaid and lower life expectancies for whites in states with more restricted Medicaid access.

Not only is access to health care unequal, but racial bias has been documented in the quality of care. One study compared the type of heart care recommended for people of different sexes and races under simulated conditions that controlled for socioeconomic status. African-American men were less likely than white men to be referred for appropriate care, and women were less likely than men to receive such referrals. These results received widespread coverage in the popular press, including *The New York Times*.

Historically, the NIH's strength has been more on investigations of the biological and physiological basis of health and less on social determinants. Social determinants of health include the conditions under which an individual is born, lives, works, and ages. These determinants are rooted in the societal distribution of resources, money, and power—all of which are affected by public policies.

The NIH, with NIDDK being among the leaders, has devoted significant resources to health disparities research. The NIMHD recently held a symposium on social determinants of health disparities and is committed to focusing attention and resources on this topic in the future. In 2011, the NIMHD issued two requests for applications (RFAs) for research on health disparities that used the R01 grant mechanism. One of these RFAs was for basic research, and the other was on the social determinants of health disparities.

Dr. Wilson offered advice for the early stages of an academic career. He advised seeking good mentors, ideally including someone from outside an individual's department or institution, to help with grant writing, the tenure process, institutional politics, and general career development. He also stressed the importance of being selective and committing only to those activities that further an individual's career.

Dr. Wilson discussed the disproportionately small number of research investigators who are members of minority groups. Over a 7-year period (2000-2006), the proportion of applications for NIH R01 grants that were submitted by investigators who are African-American or Hispanic/Latino was approximately 10 times lower than would be expected from their representation in the general U.S. population. In the fields of the biological sciences, chemistry, and physics, African Americans and Hispanics/Latinos are underrepresented in the number of B.A. and B.S. degrees received. The discrepancy is even greater in the number of doctoral degrees awarded. Dr. Wilson emphasized that despite its small size, the community of minority researchers represented at this Workshop is of vital importance to the Nation. One

of the keys to success for members of this community is to help each other, rather than compete with one another.

Discussion

A participant asked whether an unwelcoming work environment might be a factor that discourages African Americans from pursuing academic careers. Dr. Wilson responded that the working group established by the Advisory Committee to the NIH Director on funding disparities was aware of this issue but had not yet issued its recommendations.

Participants raised the questions of why such large disparities in health care exist in the United States, given that U.S. spending on health care is so high relative to other developed nations; and what the role of minority research should be in addressing the disparities. Dr. Wilson answered that it is a complex question and that cultural differences in spending priorities (i.e., high spending on end-of-life versus preventative care in the United States) as well as issues of morality and social justice are important. He called on minority researchers to interact with society so that their research is informed by societal needs, noting that community participatory programs provide a mechanism for this.

A participant lauded the NIHMD's support of health disparities research through its educational loan repayment program and asked about the NIMHD's future plans to foster career development using the K grant mechanism. Dr. Wilson explained that in the past, many NIMHD resources fell under congressional mandate but now that it is an NIH Institute, it is likely that future discretionary funding levels will increase.

An attendee said that the subject of her research, which uses a mouse model, is the role of stress hormones in diabetes, and asked about the potential for using animal models to study health disparities. Dr. Wilson cited the beneficial interactions between epidemiologic and basic research and said that it is likely that researchers will be able to make such connections with animal models.

PARALLEL INTERACTIVE WORKSHOPS

Attendees participated in two of three parallel interactive workshops during this session.

<u>Workshop 1</u>: Community-Based Participatory Research/Community Engagement, Research, and Research Scientists

This workshop had three speakers who addressed community-based participatory research (CBPR), and how to engage the community in research. Each speaker presented a brief overview of his/her topic; a discussion period followed the three speakers.

A. Community Engagement, Research, and Research Scientists
Beth Furlong, Ph.D., J.D., R.N., Associate Professor, Center for Health Policy and Ethics, Creighton University, Omaha, NE

Dr. Furlong related a story from her first meeting on the Council of Public Representatives (advisory to the NIH), when a consumer member from Arkansas told several pivotal stories based on a helicopter metaphor regarding the belief that outside researchers swoop into a community, conduct their research, and leave without follow-up. She recognized that community engagement is a necessary component of every research endeavor and provided a definition of CBPR:

> "Community engagement in research is a process of inclusive participation that supports mutual respect of values, strategies, and actions for authentic partnership of people affiliated with or self-identified by geographic proximity, special interest, or similar situations to address issues affecting the well-being of the community of focus."
>
> (Ahmed and Palermo, 2010, p. e4)

The rationale for including community engagement is multifold: research is tax-funded and society should demand accountability and respectful treatment of individuals who are affected by the research program; participants typically wish to receive feedback on the research results; community engagement enhances research outcomes by contributing to the need, design, execution, and analysis of the research; and the NIH has specified that translational CBPR is a high priority. In addition, engaging the community is viewed as beneficial to the common good and likely attracts more participants for future research endeavors.

A number of barriers work against community engagement. Dr. Furlong provided an argument and a counterargument for each of the points she listed in her rationale above. For example, private-sourced funding removes accountability related to tax support, although scientists may be accountable in other ways in privately funded research. With regard to respect for research participants, scientists often view that as covered by having participant sign consent forms, although participants often do not understand the agreement they signed. A significant barrier for researchers is a general lack of experience or understanding of community engagement; this challenge can be addressed by developing training programs aimed at researchers to increase their ability to engage communities. The argument that research is for the common good has no counterargument.

Dr. Furlong concluded by asking attendees to think about their research efforts and goals and to consider how their approach engages research participants, and she asked them to identify potential barriers and opportunities.

B. Black Family Health and Wellness: How to Organize an Annual Community-based Wellness Program

Wayne Houston, M.P.H., North Omaha Community Liaison, Center for Reducing Health Disparities. College of Public Health, University of Nebraska Medical Center, Omaha, NE

Mr. Houston spoke about the origins of the Black Family Health and Wellness Association (BFHWA). The idea of the program came to him in 1998 when a first-year medical student asked if he could help him develop a cancer presentation for the African American community. After many discussions, they decided to hold a health fair and provide lunch to all participants to gain community interest.

Mr. Houston listed several specific principles of community organizing:

- Insist that community leaders and all participants focus on the planned activity and not on their own agendas.
- Increase publicity by identifying sponsors who will support activities that occur early in the process, particularly in the case of a large community event.
- Create a theme for the event, for example, “A Healthy Family is the Heart of the Community.”
- Create a name for the organizing group, especially if events will recur. For example, Mr. Houston’s group branded themselves as the BFHWA.
- Build confidence through consistency; do not stretch resources too thin. For example, BFHWA health fairs always focus on health screenings and education, which gives the effort staying power.

Mr. Houston reported on the 2011 Health Fair Summary Report, a summary of the results from self-reported medical questionnaires completed by participants. The areas assessed included medical history; doctor and dental visits; return visits to the BFHWA health fair; lifestyle issues (e.g., smoking and inactivity); and screening results for blood pressure, cholesterol, triglycerides, BMI, and glucose.

C. The Community Nurse Perspective

Ira Combs, B.S.N., Community Liaison Nurse Coordinator, College of Public Health, University of Nebraska Medical Center, Omaha, NE

Mr. Combs provided a perspective on community nursing and highlighted a unique program he designed as an educational tool for the African American community in Omaha. He told a story about a previous discussion with physicians on the reasons why African American men tend to forgo prostate digital-rectal

exams. Although conventional wisdom implies that the physical discomfort related to the exam was the main barrier, Mr. Combs showed them that the real issue was cost. This discussion led to a job offer for Mr. Combs in the SELECT study, a prostate cancer study that required the recruitment of large numbers of African American men.
Mr. Combs helped to design a brochure and a community project to help overcome the barriers to the accrual of men in the African American community.

Mr. Combs played several videos representing a particularly significant component of the education program—a series of public service announcements based on a puppet known as "Dr. Jesse," who talks about the importance of research for the African American community with "Prevention Man" (seen on YouTube). This campaign has succeeded both in increasing the number of men who receive screenings and in encouraging young people to learn more about participation in research studies.

In conclusion, Mr. Combs said that CBPR is critical to building research in communities. He said that one serious problem with the research agenda is the tendency of researchers to pursue grant money without necessarily determining or considering community needs or wants.

Discussion

Mr. Combs said that his educational model initially was intended as a marketing strategy. Several individuals suggested that he partner with others to enable duplication of the effort and outcomes elsewhere. Mr. Combs was commended for the creative use of puppets as authoritative figures, versus their common patient-based use in pediatrics.

Mr. Combs said that recruitment often is overlooked in budget plans, which has become an ongoing problem for universities and other institutions.

Mr. Houston indicated that no formal needs assessment was conducted to determine community needs before the health fair, but the events are highly publicized. He has found ways to track individuals with abnormal readings between health fairs.

Workshop 2: Comparative Effectiveness Research
Ann Bonham, Ph.D., Chief Scientific Officer, Association of American Medical Colleges, Washington, DC

The Patient-Centered Outcomes Research Institute (PCORI) was congressionally mandated in 2010 to conduct research to provide information about the best available evidence to help patients and their health care providers make more informed decisions. PCORI's research is intended to give patients a better understanding of the prevention, treatment, and care options available, and the science that supports those options. PCORI specifically calls for Comparative Effectiveness Research (CER)—also called comparative clinical effectiveness research—to evaluate and compare health outcomes and the clinical effectiveness, risks, and benefits of two or more medical treatments and services.

Dr. Bonham stressed the value of networking and had participants list their contact information so that they could develop contacts with others interested in the same topic(s).

Understanding the intersection between basic science and partnering with clinical researchers in health disparities research is important. For example, a research question that asks how a signaling pathway differs among racial and ethnic groups would contribute to the understanding of disease inequities among groups. Dr. Bonham used the example of research in the Gullah Islands of South Carolina to illustrate CBPR investigations for diabetes. The research was based on genetic differences identified in the population that accounted for the incidence of diabetes.

Dr. Bonham provided information on PCORI funding and the types of investigations that are expected to be awarded funding. PCORI is a product of the first legislation that mandated a semi-independent funding organization with appropriated funds, generally from Medicare and insurers. The first call for grant applications for PCORI will be May 23, 2012.

What makes PCORI different from conventional clinical trial research is that patients must be involved at every step of the granting process. They also must be involved in disseminating the results to the community. This might include point-of-care studies, CBPR, and pragmatic trials, but all must have some value to the people in the "real world," not just those who have met inclusion criteria in a randomized clinical trial. Other important facets of PCORI include that patients must come from underserved populations, and a dissemination (implementation) plan must be included.

The types of studies that can be conducted under PCORI include prevention strategies, prevention versus interventions, diagnostics, health care delivery mechanisms, outcomes mechanisms, and comparing therapeutics. The main focus of the research will be to improve outcomes of historically underserved communities.

The PCORI Board meets regularly; Dr. Joe Selby, formerly of Kaiser Permanente, is the Director. PCORI is accountable to the U.S. Congress, and its Board includes members from other federal agencies.

Dr. Bonham concluded by stressing that in developing a PCORI RFA for submission, participants should present evidence of engagement with patients and the community. The best way to approach a study is to develop the needs to be met, design the experiment with patients and the community in mind, and create a dissemination plan based on the results.

Discussion

A participant asked if preliminary data would be required when applying for PCORI funding. Dr. Bonham responded that she did not know, but that this would be specified in the RFA to be released in May 2012. As noted above, requirements were expected to include involving the community and patients in designing, conducting, and disseminating the results of the experiment to the community. The PCORI was not expected to use the same review mechanism as the NIH R01 process. The criteria were expected to be different, although the review process was expected to be rigorous, as is the NIH review process. The PCORI was expected to have individual and team-based awards.

A participant asked if a feasibility study would be required, and if foreign investigators would be eligible. Dr. Bonham did not know if the feasibility study would be required and referred the participant to the RFA instructions. As for the eligibility of foreign investigators, she did not necessarily think they would be restricted from applying.

Workshop 3: Employing Multi-level Genomic Strategies to Profile Aggressive Hepatocellular Carcinoma

Anuradha Budhu, Ph.D., Staff Scientist, Liver Carcinogenesis Section, Laboratory of Human Carcinogenesis, National Cancer Institute, NIH, Bethesda, MD

Dr. Budhu studies multilevel genomics in the context of liver cancer, a common and deadly disease. Hepatocellular carcinoma (HCC), the most common type of liver cancer, is partly attributable to a viral infection with hepatitis. HCC is most prevalent in Asia and Africa; however, its incidence is increasing in developed countries due to obesity and alcoholism, among other factors.

Various "omics" can be used to delineate critical pathways that occur in advanced cancers. The hope is that by examining all of the information that is provided by "omics" approaches, the entire "interactome" can be understood. "Omics" also provides a route to personalized medicine that can be used to improve cancer outcomes.

The current study identified patient populations with "extreme" phenotypes (e.g., an extremely good or extremely bad characteristic). Metastasis, stemness, and gender were the factors examined via observing genomic gains and losses through DNA analysis, and by combining metabolomic with transcriptomic findings.

The first study example is metastasis, which is a significant problem in liver cancer patients. Tumor and microenvironment tissue are important features to examine. Using a copy DNA (cDNA) microarray, tumor tissue from two patient groups (metastatic lesion versus none) could be differentiated. This result has been validated (153 gene signature) and is related to patient outcome. This result is different from that obtained with other cancer types. The gene signature can be combined with clinical markers to substratify patients to determine high versus low risk of metastasis.

The microenvironment tissue was compared on the same platform as the tumor tissue, and 454 genes were found to be different in their expression in metastatic patients versus not. Bioinformatic work refined the 454 gene signature to 17 genes, all of which are related to the inflammatory system. These 17 genes could correctly predict patient groups (metastasis or not) with 92 percent accuracy.

These results led to the model that there is an imbalanced network in the immune system that may promote metastasis-related relapse, and particular elements in the microenvironment or tumor push the cytokine profile in the metastatic direction. This “opens a therapeutic window” so that interferon or other inflammation-related molecules may be used to shift patients toward the nonmetastatic condition.

As it is inherently difficult to decide on relevant targets based on interrogation of a large number of genes in a clinical setting, microRNAs (miRNAs) were examined. miRNAs are one of the largest classes of gene regulators and account for 1 to 4 percent of all expressed human genes. miRNAs bind to messenger RNA (mRNA) sequences and alter their stability, degradation, and translation. The expression of miRNAs is altered in many cancer types and can function as oncogenes or tumor suppressors.

miRNA expression was screened and examined for correlation with cancer diagnosis. It was found that there is differential expression of miRNA between metastatic and nonmetastatic patient groups. The researchers found a 20 miRNA signature that is both predictive and associated with patient outcome (i.e., risk for metastasis and recurrence). Substratification by stage can be achieved. A functional followup study found that certain miRNAs were associated with poor survival and affect tumor cell proliferation, colony formation, migration, invasion of cells, and wound recovery. miRNAs could be an effective target for the disease.

HCC heterogeneity also was studied in the same group of patients. HCC is a heterogeneous disease, and this heterogeneity is hypothesized to arise as a result of lineage-specific tumor subtypes that have prognostic impact. In fact, different gene expression profiles that relate to survival and outcome have been found in different HCC subtypes. Using bioinformatics, a stem-like subtype of HCC was identified. Follow-up studies with phenotypic and quantitative polymerase chain reaction (qPCR) experiments both *in vitro* and *in vivo* confirmed the stem-like properties of cells within this subgroup. Similarly, array and functional studies showed that certain miRNAs were significantly altered in stem-like, aggressive HCC.

A final study example involves gender and miRNAs in liver carcinomas. Liver carcinoma is more common and aggressive in men than women. There are miRNAs that are dysregulated between men and women; one specifically is miRNA26, which is an abundant metabolite. This miRNA is associated with outcome, and patients with low levels have poor survival. Low miRNA26 levels are associated with inflammatory networks. This knowledge can assist in predicting patient response to interferon therapy.

Integrating genomic information is important. High-throughput studies have begun that examine genomic gains (oncogene regions) and losses (tumor suppressor regions) in cancer patient cells. Measuring mRNA levels in the same cohort of patients has revealed that there is a shift away from a normal random distribution. Genetic clusters develop that predict poor patient prognosis.

Metabolic products have an effect on cancer properties; therefore, a study was designed to integrate metabolomics with mRNA signatures (transcriptomics). Tumor and nontumor cells were analyzed in cohorts of patients that expressed different gene subtypes. With transcriptomics being performed in parallel, metabolites and their gene surrogates were found to be related to aggressive HCC with poor outcome. The integration of these 'omics' data supply a discrete pathway that can be targeted clinically.

Discussion

Dr. Budhu's research highlights some of what is occurring in cancer cells and the microenvironment; however, at any given moment or location near or in the tumor cells, the genetic and phenotypic occurrences can vary.

The cohorts in the discussed studies were patients from China with hepatitis B infections; patients from the United States will be examined in upcoming studies. In developing gene signatures, multivariate analyses were performed to ensure that the signatures were independent of clinical parameters.

Differential gene expression can indicate what is occurring in the cell; however, it is important to input all of the genetic information into pathway information. The key is not to determine if a certain gene is altered, but to be able to determine what pathway is being altered in some fashion.

Epigenetic modification currently is being studied. The bioinformatics therein are complicated, but correlative analyses are being done. These modifications, as well as mutations, gene expression, protein expression, and so forth all culminate in the presence or absence of biochemicals (metabolomics). Whether certain biochemicals are present or absent determines whether or not a tumor cell will proliferate. These alterations culminate to determine the risk of HCC development and the prognosis of HCC patients.

WRAP-UP, NEXT STEPS, ADJOURNMENT
Dr. Sanabria and Dr. Agodoa

As part of the NMRI 10th Anniversary celebration, Dr. Agodoa acknowledged those NMRI members who have served in leadership positions for the NMRI since 2003.

Chairs of the NMRI Annual Workshop
Jackie Tanaka, Dale Abel, Ricardo Aziz, Carlos Isales, Eddie Greene, Sylvia Rosas, Bessie Young, and Juan Sanabria

Chairs of the NMRI Regional Workshops
Carlos Isales, Jesus Lopez-Guisa, Shirley Blanchard, Mark Lawson, Francisco Villarreal, Eddie Greene, Omaima Sabek, and Yvonne Romero

Chairs of the NMRI Oversight Committee
Shirley Blanchard, Virginia Sarapura, Daisey DeLeon, Carlos Isales, and Charmaine Stewart

Dr. Agodoa presented an award statue and certificate to Dr. Sanabria for chairing the NMRI 2012 Annual Workshop Planning Committee. Dr. Sanabria accepted the certificate and thanked everyone who helped him make the workshop successful.

Dr. Agodoa presented an award statue and certificate to Dr. Blanchard for chairing the NMRI 2011 Midwest Regional Workshop. Dr. Blanchard thanked the members of her planning committee who worked to make the workshop well organized and successful. The Planning Committee members included Mario Ascoli, Joyce Balls-Berry, Luis Cubano, Trudy Gaillard, Eddie Greene, Neali Hendrix Lucas, Judith McElhiney, Charmaine Stewart, Monique Williams, and *ad hoc members* Ira Combs and Bennie Upchurch.

Dr. Agodoa announced that the Chair-elect of the NMRI Planning Committee for the 2013 NMRI Annual Workshop is Dr. Carmen Castaneda-Sceppa.

Dr. Agodoa announced that, because of recent budget cuts, there will not be a Regional Workshop in 2012. He said he is hopeful that the NMRI will be able to resume the regional meeting in 2013.

Dr. Agodoa asked participants to stand and announce any promotions, honors, and successful grant applications they had had since the 2011 workshop. The following NMRI members announced their successes:

Greg Florant—Distinguished Professor Award
Lincoln Edwards—An R15 award and promoted to Assistant Professor
Shirley Blanchard—The RFK Award at Creighton University
Bridgett Rahim-Williams—K22 Award from NIMHD
Joyce Balls-Berry—Promoted to Assistant Professor
Manu Platt—Innovator Award
Mark Lawson—R01 renewal and started a T36 mentoring program
Marion Sewer—Two R01 Awards and another grant
Healani Chang—30-year Faculty Award
Bob Ferry—Promoted to Chief/Program Director
Marina Ramirez-Alvarado—Grant renewal and promoted to Associate Professor
Rhonda Bentley-Lewis—Promoted to Assistant Professor
Charmaine Stewart—Elected Chair of the Women Faculty Cabinet
Detrice Barry—Received an Undergraduate Award for Public Service

Adjournment

Dr. Sanabria thanked participants for attending and for making this workshop successful. He encouraged attendees to plan on coming again next year.

Dr. Agodoa said he is excited about the number of successes he hears about each year at the workshop. He thanked Dr. Sanabria for organizing a very exciting agenda and for his hard work in planning the workshop. He thanked Ms. Martinez for her organizing efforts on the NIDDK side, and thanked the contractors, especially John Hare (The Scientific Consulting Group), for their support.

Dr. Agodoa concluded by saying that he was troubled by the statements from one of the junior investigators who has not been able to find a mentor. He reiterated that the mentoring program is critical to the success of the NMRI, and stressed that everyone should make an effort to find a mentee or mentor.

Dr. Agodoa thanked everyone again and announced that the tentative dates for the 2013 NMRI Annual Workshop will be April 18-19, 2013. He asked that attendees complete the evaluation form before leaving. Hearing no more comments or questions, Dr. Agodoa adjourned the workshop.