

Genomic Medicine 4, January 28/29, 2013, Dallas, Texas.

Welcome and Overview-Marc Williams and Teri Manolio

After welcome and introductions, Chairpersons Marc Williams and Teri Manolio noted that health professional education, particularly physician education, is becoming increasingly important with the maturation of genomic science. A portrait of current efforts in physician education in genomics is planned by means of eleven presentations to be followed by more general discussion of whether collaboration among various stakeholders may lead to a more effective and efficient transfer of knowledge and competencies from bench and translational researchers to physicians and patients in the clinic and at the bedside.

Remarks by NHGRI Director-Eric Green

Eric Green noted that the Genomic Medicine meetings grew out of discussions at the National Advisory Council of the Human Genome Research Institute. These meetings have identified and discussed a number of important problems and opportunities. Genomic Medicine 4 is designed to address an equally important matter, physician genomic education. While much NHGRI support is focused on basic and technical research in genomics, the 4th and 5th domains in its strategic plan address the use of genomics to advance the science of medicine and improve the effectiveness of healthcare of populations.

Dr. Green provided an update of NHGRI activities including the October 1, 2012 NHGRI reorganization that now includes 7 separate Divisions: 4 engaged in Extramural Research Programs, a Division of Intramural Research, a Division of Management and a Division of Policy, Communication and Education. Subjects discussed at Genomic Medicine meetings transcend Division boundaries.

NHGRI currently supports a variety of genomic education efforts including the Genetic/Genomic Competency Center for education (G2C2-an education clearinghouse for genetic counselors, nurses, physician assistants and soon pharmacists), a talking glossary, Global Genetic and Genomic Community (G3C- case scenarios), a series of genomic reviews published in the NEJM (2010-2012) and a joint NHGRI/Suburban Hospital/Johns Hopkins Medicine lecture series for practicing physicians. All of these efforts can be found at www.genome.gov.

Other news since the GM3 include the expansion of the NIH Undiagnosed Diseases Program funded by the NIH Common Fund in the amount of \$145 million over 7 years with the addition of a coordinating center, 5-7 new clinical sites, funding for basic research on the mechanism of genomic variants found and funds for training new investigators.

A new NIH initiative has grown out of a working group report on big data submitted to Dr. Collins in June 2012. A problem in particle physics and astronomy is now an issue in biomedicine. Examples include genomics, other 'omics, imaging, phenotypes and exposure data. Implementation has begun with a search for an Associate Director for Data Science (Dr. Green will serve as an Acting Director in the interim), creation of a Scientific Data Council, and a Big Data to Knowledge (BD2K) effort.

The year 2013 is the 60th anniversary of the seminal Watson and Crick publication of DNA structure and the 10th anniversary of the publication of the Human Genome. There will be a series of lectures at NIH over the next several months, an all day symposium held at NIH on April 25th and a joint effort of NHGRI and the Smithsonian Institution in the design of a celebration of genomics entitled Genome-Unlocking Life's Code- in Hall 23 of the National Museum of Natural History beginning in June.

Mira Irons-Training in Genomics

Dr. Irons noted that physicians learn by doing. She believes that it is important to focus physician education on how to function at the point of care, to learn to apply genomics in their scope of practice and this involves a focus on competencies. Some physicians believe that expertise in genetics/genomics is only useful in pediatrics and obstetrics, a misapprehension that is being erased. She related successful experiments of embedding a geneticist in cardiology, orthopedic and otolaryngology clinics.

Dr. Irons noted that medical students are often attracted to genetics in their first year but the interest wanes. There are problems with resident and fellow education in genomics as it must compete with other established subject areas. Only one-half of residency slots in genetics are filled. A barrier that could be addressed is the lack of opportunity to do subspecialty genomics. For example, an oncologist might choose to specialize in cancer genetics and genomics rather than qualify in genetics in general, particularly given its current heavy emphasis in genetics on dysmorphology and complex pediatric syndromes. However this change would entail developing a program and a certifying test.

Dr. Irons noted that ordering genomic tests is often not done correctly and believes that the short term solution to this is to credential physicians, as physicians are credentialed to do procedures. It was noted that there are experiments in credentialing already being done at some institutions. Developing and keeping track of the criteria for competence and training prior to credentialing is important.

ACGME and ACCME –Dr. Nasca and Dr. Kopelow

Dr. Nasca began with an exponential curve displaying the number of scientific papers published each year to make the point that it is impossible today to cover the whole of medicine and that information technology at the point of care is becoming increasingly important. He noted that part of the problem in GME is that the educator often does not know and therefore will not teach genomics. He observed that a multipronged approach on the part of professional societies in both graduate medical education and continuing education is important. There must be pressure on review committees and on Boards to incorporate genomics into initial and maintenance of certification and licensing.

Dr. Kopelow added somewhat facetiously that in the past the “ballistic model” of physician education provided for a massive overshoot of knowledge at the end of formal training followed by progressive decay, with the hope that retirement might occur just before the level of knowledge dropped below an acceptable level. Such an approach is clearly not supportable in an era of rapid evolution of medical knowledge. He pointed out three levels of knowledge- what a physician knew, vs. what was known, on entering practice; what was not known on practice entry and what the physician knew that is clearly wrong. These are all knowledge gaps. He advised that there is a systematic way to approach CME and it begins with identifying a practice gap and proposing a variety of ways to address it.

He noted that ten years ago physicians knew that there was a gap in physician knowledge of how to use opiates in patients complaining of pain. This has recently become a public health issue. Dr. Kopelow believes that the medical profession needs to take steps now to prevent errors in the use of genomics from becoming a similar issue in the future. Were medical schools to fully educate students in genomics, the matter would be solved in 2025, if done in GME, in 2018. Sooner is preferable.

American College of Genetics and Genomics (ACMG) - Clinical Medicine and Genomics

Bruce Korf

Dr. Korf began by noting that inadequate education of health care professionals will limit the integration of genomics into clinical care and thus will deny patients’ access to useful and perhaps disruptive technology. There is room for optimism since medicine has adapted to new diagnostic and therapeutic innovations such as imaging, antibiotics and others that are now incorporated into practice, and add value to health care. He believes that genomics will follow a similar evolutionary pattern.

He presented a family history of MEN1 and analyzed the steps taken by an endocrinologist to determine the risk of 18 month old child of a mother with MEN1. The example demonstrates the importance of both competencies and knowledge in the choices made and the dilemma of

a variant of unknown significance. The error in the lesson is not to have studied the mother first.

He reviewed the competencies required including: test indications; testing the affected family member first; shared decision making with consent after discussion of the risks, benefits, alternatives, cost; selection of the lab; interpretation of the test, recognizing test limitations, referral to a specialist if needed; and discussion with the family. There are parallels in competencies to those required prior to the performance of invasive diagnostic procedures. In genomics one size does not fit all; one clinical situation may be quite straightforward while the next, very deceptive in its complexity.

He noted that there is much to learn before an accurate, fully- annotated genome is available, and that point-of-care decision support will be an important aid to practitioners. He added that mature, sophisticated decision support technology such as GPS sometimes lead us astray. It is unlikely that any computer-based support will prevent all error.

Application of genomics in the clinic will always be a team endeavor as it is impossible for anyone to be fully knowledgeable in this area of medicine. Pharmacogenomics will be embedded in the electronic medical record, and will likely reduce harm caused by medication. He agrees that the creation of subspecialty geneticists, for example, oncologists who are expert in cancer genetics, but not forced to learn the rest, is a useful model that will require a good deal of effort to bring to fruition. He noted that direct-to-consumer testing is a potentially disruptive technology as well and it is hard to predict its ultimate place in patient and family care.

College of American Pathologists (CAP) – Debra Leonard

Dr. Leonard reviewed a 5-year (2008-2013) systematic and successful effort to incorporate genetics and genomics into the daily practice of pathologists. A CAP survey of 1028 pathologists in 2010 revealed that 61% stated that they were familiar with whole genome sequencing and analysis, 74% were familiar with gene panel tests and 79% with single gene tests. With some initial resistance to change, CAP defined a strategy for transformation (2009-2012) to assist pathologists to embed new genomics and informatics in their work. The College has now implemented a multi-year transformation initiative (2013+) to further this work.

Dr. Leonard summarized the transition to next generation sequencing (NGS) in molecular pathology and reviewed the pace of early adoption at various institutions as this new technology became available. CAP is an accrediting body as well and has issued NGS inspection checklists and a proficiency testing program utilizing characterized genomes. The College has also authored resource guides for genomic analyses, defining needed competencies. There have been substantial increases in the educational opportunities at the annual CAP meetings

that last year featured 37 genomic courses. The College has also formulated a very popular webinar series that attracted 4500 CAP members even without the added incentive of CME credits. The College also publishes a variety of other educational materials including guidelines issued in collaboration with various other societies such as ASCO and ASH.

The College has gathered data on utilization of these educational offerings but it is unclear how many of the estimated 17,000 pathologists practicing in the US are aware of, and use, these materials. CAP has not tried to systematically measure substantive change in pathology practice as a result of these educational offerings, but is now assessing proficiency with characterized genomes.

CAP has successfully developed a rather large body of educational materials that begins with the education of residents and extends to practicing pathologists. This program could serve as a best practice model for other professional societies.

American Academy of Pediatrics (AAP)-Robert Saul

The AAP has established the Genetics in Primary Care Institute (GPCI) in collaboration with Health Resources & Services Administration (HRSA) Maternal and Child Health Bureau (MCHB) to improve primary care provider (PCP) knowledge and provision of genetic medicine. Goals include the utilization of a quality improvement innovation network of 300 practices to measure improvement in the provision of genetic related services, to establish a technical assistance center and by these means to embed genetic medicine into the future PCP workforce.

In February 2012 a survey including 43 items was sent to the 300 practices, and 88 (29%) responded. Results included the findings that 100% thought that taking a family health history (FHH) was important but only 32% noted that they gather a 3 generation FHH. Further responses include that the most common approach to FHH was to ask is there any disease in the family (82%). Eighty-six percent reported that they had ordered genetic blood tests, but the average was less than 3 times annually. The 88 responders reported that on average 4.8 patients were referred to a geneticist each year. A reassuring 89% have access to genetics professionals and 75% were within 30 miles. One-half agree strongly or agree that they are fully competent in providing genetic medicine. Dr. Saul noted that this convenience sample is likely biased as it is drawn from 300 highly motivated practices.

In an attempt to further understand barriers to incorporation of genetics in primary care, in-depth interviews were carried out with 7 expert stakeholders. These revealed substantial opportunities for improvement in competencies such as which test to order, what to do with positive or negative tests, when to seek specialist input, and the ability to communicate with families and to manage complex care.

A Genetic Literacy in Primary Care Colloquium was held on October 2nd and 3rd, 2012 that focused on FHH, genomics, genetic literacy, epigenetics, and primary care and genetics. Consensus statements included a definition of how PCPs should incorporate genetics and genomics in practice, a definition of tools needed, integration of genomics into primary care training, and development of an evidence base for integrating genomics into primary care.

The GPCI produced 10 half-hour educational webinars in 2012 (available at www.medicalhomeinfo.org/gpci.aspx#webinars), a soon to be released new AAP manual on medical genetics in primary practice and a variety of policy statements on ethics of testing, and approaches to specific problems such as Down's, Fragile X, and Prader-Willi syndromes.

It was emphasized during discussion that incorporating genomics into practice is an evolutionary and not a revolutionary process. Multiple societies have found that downplaying the "genomic revolution" message eases the reluctance of physicians to engage in educational efforts. Several societies have noted some frustration with the delay and difficulty of winning approval for CME credits, particularly the requirement to survey the literature and prove that the proposed educational effort fills a gap. Dr. Irons noted that new knowledge is by definition a gap and might make CME approval less difficult.

American College of Physicians (ACP)-Michael Murray

Dr. Murray noted that the pace of sequencing has increased substantially in recent years. In September, 2009 only seven fully sequenced genomes had been completed. The number at the end of 2012 was estimated at 73,000 and it is estimated the number will reach one million by the end of 2014. He organized yearly courses on genomics for primary care physicians in Boston from 2005-2010 and had difficulty filling the course which was discontinued in 2011. There is a new NHGRI-supported educational effort at the Brigham and Women's Hospital that plans to study the effect of case study on competencies involving 20 internists, 10 in general internal medicine and 10 cardiologists.

The ACP employs a variety of educational efforts including its annual spring meeting, the MKSAP, the Physician Information and Education Resource (PIER) and the ACP online. Other opportunities include ethics case studies, the ACP review for ABIM exams, and the ACP Scientific Chapter meetings. ACP clinical recommendations come in three flavors: Clinical Practice Guidelines, Guidance Statements and Best Practice Advice; the latter may be a useful format for genomics as it seeks to provide information on benefit, harm and cost.

Drs. Tooker, Weisman and Murray undertook a survey, in preparation for this meeting, seeking to learn what internists know about genomics. The survey took place in November and December 2012. The survey was sent to 806 ACP members who were based in the U.S., actively working in medicine and spending some or all of their time in direct patient care. A total of 486

responded with 20% being residents and fellows, 18% age less than 40, 35% 40-55, and 27% over 55. Most (46%) are in private practice, 25% work in hospitals, 23% in academic medical centers and the remaining 11% are in other settings. They rated their basic knowledge as adequate (60%) but in specific competencies (ordering, interpreting, explaining results) only 10-25% graded themselves as confident in their abilities. Other self-rated skills in successfully using genomics in practice were in the teens. A majority would devote 1-2 hours to improve their knowledge and skills in genomics; they favor print, online, and lectures in format, and 81% said the CME credits would provide a welcome incentive.

There was much discussion following Dr. Murray's presentation. The use of "evolution" to describe the integration of genomics into practice rather than "revolution" was suggested. Best Practice Advice seemed the most useful ACP means as clinical trials are not easily employed in genomics and small sample sizes are the rule. Evaluation of genomics needs to be embedded in the disease process. The use of pharmacogenomics was not questioned in the ACP survey and perhaps should be in the upcoming survey.

It was noted that guidelines are often issued without conclusive clinical trial evidence. An analysis (JAMA 2009;301(8):831-841) of 16 current AHA/ACC guidelines reporting levels of evidence revealed that 1246 of 2711(48%) recommendations were level C (based upon expert opinion, case studies or standards of care) and only 314 of 2711 (11%) were level A (evidence from multiple randomized trials or meta-analysis). It was observed that technical advances often lead to liability issues and perhaps this should be considered as discussion of educational efforts proceeds.

American Society of Clinical Oncology (ASCO)-Sandra Swain and William Pao

Dr. Swain noted that 5-10% of cancers are due to mutations inherited from biological parents and the rest are caused by somatic mutations. An early example of a somatic mutation driven cancer is the Philadelphia chromosome, a translocation across chromosomes 9 and 22 that creates the *BCR-ABL* fusion cancer gene. Described in 1960 and associated with chronic myelogenous leukemia, an effective treatment in the form of imatinib was approved by the FDA in May 2001 and celebrated by Time magazine as a magic bullet. This paradigm is now driving research in many cancers offering the possibility of specific therapy and providing incentives for many oncologists to learn to use cancer genomics in both diagnosis and therapy. A major challenge is to differentiate driver mutations from passenger mutations in cancers. The pace of discovery is rapid as is the surrounding hype, amplified by the gravity of a diagnosis of cancer. This is further complicated by the fact that 85% of cancers are treated in the community setting by community based oncologists who will need assistance in understanding and using this exciting innovation in diagnosis and treatment.

ACGME issued proposed oncology training requirements in 02/05/11 that became effective in 07/01/12. These require that trainees must demonstrate knowledge of genomics and developmental biology; and in physiology and pathophysiology of oncogenes. ASCO has developed a number of self-learning programs including flash cards, online questions, and chapters on molecular biology treatment. The 2013 ASCO annual meeting will feature a 1.5 day seminar on genetics and genomics for practicing physicians. There will also be several 75 minute education sessions dedicated to genomics in the diagnosis and treatment of various cancers. ASCO has published 23 practice guidelines and has a formal consensus development process. It has collaborated with CAP on breast cancer guidelines and these collaborations may serve as a model for wider collaboration in genomics. ASCO is also planning a rapid learning system, as a means to gather baseline descriptors and outcomes in patients drawn from a large number of oncologists to permit data aggregation and evaluation of outcomes.

Dr. Pao presented an innovative IT system developed at Vanderbilt to simplify reporting of cancer somatic mutations in melanoma and aid in decisions about therapy based on these data. It can also display trials that are open locally, nationally and internationally. Discussion about data aggregation and privacy revolved around the notion of trusted brokers and safe harbors. Dr. Swain noted that cancer patients very much want data aggregation, and seem less concerned about privacy, as they see data aggregation as a means to improve therapy for them and patients with similar cancers.

American Heart Association (AHA) - Donna Arnett

There has been substantial progress in the scientific understanding of genomics in the etiology and pathophysiology of cardiovascular disease and stroke. GWAS studies have identified a large number of variants that each add risk in small amounts that in aggregate increase risk by perhaps 70%. Some of these variants are located near rare variants that, for example, are associated with hypertrophic cardiomyopathy. The science is very exciting but for common, complex diseases falls short of evidence needed for action. There are also dangers in findings of older studies that seem related to disease but on further consideration and study are not. This is also a problem in direct-to-consumer (DTC) services that may be providing false positives and false negatives leading to false worry and false reassurance. There are a number of pharmacogenomic variants that the FDA has placed in black boxes, such as those involved in the metabolism of clopidogrel and warfarin, that are under active clinical trial testing that should clarify whether action is required if these variants are detected.

The AHA has published a summary of science, Genetics and Genomics in the Prevention and Treatment of Cardiovascular Diseases, that is being updated now. The second, the Use of Genetics and Genomics in Cardiovascular Disease and Stroke Patient Care is also being prepared. The AHA is also preparing the Massively Open Online Course (MOOC) that will

provide an educational background for health care professionals from undergraduates to providers and include nursing, pharmacy and others as the intended audience.

There was discussion of the use of observational science in the absence of clinical trial evidence in developing guidance for providers. It was observed that it is not uncommon for variants that were thought important to subsequently be judged benign. It was noted that modifying drug dose based upon renal function seems similar to some pharmacogenomic interventions and thus an evolution rather than a revolution in practice.

American College of Cardiology (ACC)-William Zoghbi and Robert Roberts

Dr. Zoghbi noted that genomics is quite important in cardiovascular Mendelian disorders such as hypertrophic cardiomyopathy (HCM), long QT syndromes, Marfan's disease, dilated cardiomyopathy and others. These diseases, however, constitute a very small portion of the work of the ACC membership of 43,000 cardiovascular health providers. Perhaps 95% of their time is devoted to caring for common, complex diseases such as coronary heart disease, hypertension and atrial fibrillation. Pharmacogenomics is closer to the clinical horizon and clinical trials are testing the hypothesis that use of genomics offers better outcomes.

Dr. Zoghbi presented results of an ACC survey of 150 members carried out in October 2010 that revealed that interest in personalized medicine was modest among cardiologists and their patients. However, a future role of genomics was thought to be quite promising by over 90% of those surveyed. The members noted that there are many challenges and distractions faced by cardiologists today with substantial change in structure of practice including the fact that over 70% are now employed by hospitals or academic medicine. He noted that the ACC has a modest number of educational offerings in genomics and believes that education must be offered in the context of the disease. He noted that with maturation of genomic understanding of complex disease there would likely be more demand for these educational offerings.

Dr. Roberts reviewed the inherited causes of sudden cardiac death and believes that genomics should be used in defining risk, particularly in young athletes, HCM is the most common cause of cardiac death in those under 36 years and observational data from Italy reveal a reduction in the rate of death in those not exposed to exertion after being diagnosed with HCM. He noted that recommending that a gifted athlete should not continue his career because of the risk of sudden death is very difficult. There are observational data supporting the use of beta blockers in some forms of long QT syndromes while others require a different medication regimen, an important reason to use genomics in this population. Dr. Roberts noted that with respect to complex diseases it is estimated that the traditional risk factors explain about half the variance in incidence and he suspects that the rest is the result of genes with modest effects. He is particularly interested in the effect of chromosome 9p21 variants and noted that the addition

of genomic risk factors to may ultimately drive the thresholds for the use of medication to lower levels as in the treatment of elevated cholesterol. The ACC believes that a focus on competencies and basic education is important.

American Congress of Obstetrics and Gynecology (ACOG) – Nancy Rose

Dr. Rose noted that ACOG includes over 55,000 members and that the goal of ACOG is to provide the membership with basic tools for patient management. The membership relies on ACOG statements, is concerned about litigation in practice, and faces heavy marketing from companies engaged in genetic evaluation. As busy surgical-specialty physicians, some view genomics as a nuisance, with family health history recorded often inaccurately and clinical findings noted during pregnancy often not engaged after pregnancy is complete (examples include hypercholesterolemia and BRCA syndromes). The ACOG Committee on Genetics is a formal affair with multiple liaisons and multiple internal and external collaborators. A barrier to and an opportunity for collaboration is that at present guidance from multiple societies can take conflicting positions leading to confusion (spinal muscular atrophy [SMA] screening- ACMG supports and ACOG does not).

ACOG has issued many useful guidance documents over the past several years. Dr. Rose believes that the process is often delayed by extended review periods. She reviewed the activities of Boards in the design of exams. She noted the upcoming challenges of meaningful use of IT systems, the problem of family health history in meaningful use and the promise and difficulties of telemedicine.

During discussion efforts to reduce the delay in issuing guidance documents was identified as an opportunity for joint professional society work and a concern that some guidelines in cancer and other disorders are issued with very little if any outcome data.

NHGRI Clinically Relevant Variant Resource Initiative -Erin Ramos

Dr. Ramos presented the background (multiple workshops and subsequent discussions) leading to the issuance of RFA-HG-12-016 to identify and fund a resource for curation and dissemination of published information regarding genomic variants that may require clinical action. This resource will be helpful to professional societies in their educational and guidance activities. The resource will begin activities in the summer of 2013 and would welcome professional society collaboration.

Current status –Professional Societies

The CAP has developed a systematic approach used by a subset of their membership and this was made possible by the recognition on the part of pathologists that they needed to build the

competencies and the knowledge quickly to respond to the dramatic changes in oncology diagnostic and therapeutic strategies. There is also a financial incentive. It is unclear how far this attractive plan has penetrated to community practice. This appears to be a best practice.

The AAP has recognized that primary care pediatricians, in contrast to those in academic settings, have substantial gaps in competencies as well. In a small survey of a highly motivated group of practicing pediatricians only about half agreed that they were fully competent to provide genetic medicine. AAP has a plan to address this gap with standard educational techniques, the success of which depends upon interest generated and applicability of genomics to their members practice.

The ACP developed survey data that reveal the paradox of belief on the part of members that genomics will be important to practice in the future coupled with self-ratings on competencies in the teens. Additional evidence includes lack of success of attracting academic and practicing internists to an outstanding 2 day educational session in Boston. The “spinach metaphor” was used-- that some participated because they thought it would be good for them but most chose something else.

ASCO is now struggling to keep up with the scientific revolution begun with imatinib. Oncologists in academic settings are exploring and consolidating the new paradigm, but busy practicing oncologists are struggling with a substantial gap in genomic competencies and knowledge.

The AHA has attempted a number of genomic educational activities in a variety of settings and found that the spinach metaphor is operative-- the members choose other offerings. This is likely due to the small proportion of daily practice that is devoted to Mendelian disorders and the belief that genomic science is of little use clinically in patients with common, complex diseases such as coronary heart disease, hypertension, hypercholesterolemia, myocardial infarction and stroke. The AHA publishes excellent scientific summaries and believes that advances in cardiovascular science will be needed before large numbers of cardiologists will elect to study genomic competencies and knowledge.

The ACC surveyed 150 members in October 2012 and found confirmation of AHA experience. Members believe that genomics will be important to future practice but only 6% believe that the time is now. Dr. Roberts made a strong case for the use of genomics in Mendelian disorders that presage sudden cardiac death and this area might be a prototype for educational efforts among cardiologists.

Inter-Society Collaborations-Existing and Potential-Marc Williams

Dr. Williams led a wide ranging discussion of potential next steps that might lead to a more effective and efficient transfer of knowledge and competencies from bench and translational researchers to physicians and their patients in the clinic and at the bedside.

There seemed to be some enthusiasm for joint publication of the discussions at this meeting.

It was noted that CAP, AAP, ACP and ACC had reported on surveys of convenience samples of their memberships totaling 1750 members. Common data collection on genomics that societies might want to add to planned larger surveys to assess interest and knowledge/competency gaps would be useful.

A repeated refrain was the need to correctly balance educational efforts between competencies and knowledge of genomic science and an agreement that an initial focus on competencies seems warranted.

It is clear that many physicians across different specialties lack the basics of when and how to order genomic tests and what to do with the results. This set of gaps is paradoxically coupled with an appreciation that genomics will be important for patient care in the future and for some physicians soon.

The possibility of establishing an Inter-Society Coordinating Committee for Genomics Physician Education was discussed at length and elements of this discussion included the following:

Goals

1. Gather best practices in genomic education and clinical care.
2. Recognize genomic science about to enter the clinical arena.
3. Identify pitfalls in current practice
4. Seek optimal educational balance between competencies and basic knowledge.
5. Assist societies in jointly and separately publishing papers of common interest.

It was agreed that there was a need to add detail to this idea and that it should be discussed by means of a conference call in a month's time. Additional ideas should be sent to Gene in the interim.

Payers Meeting Recap - Derek Scholes

Derek Scholes provided a brief summary of a workshop that grew out of discussions at GM3 regarding coverage of promising genomic tests and the willingness of payers to fund research to permit gathering further data. A number of examples of this type of potential funding were discussed and a summary is being prepared.

Summary of NHGRI Genomic Medicine activities. –Teri Manolio

Dr. Manolio presented a summary of recent activities of the Genomic Medicine Working Group including NHGRI's working definition of genomic medicine, recent publications and ongoing efforts.

Periodontal Microbiome WG Update – Murray Brilliant

Dr. Brilliant provided an update including goals and accomplishments. The overall goal is to establish an oral/systemic cohort across multiple institutions. Phase I has been completed at Marshfield and Phase II is about to begin with standardized entrance criteria and data collection. Initial clinical results were presented.

MD Anderson genomic medicine integration efforts - Andrew Futreal

Dr. Futreal presented a "Moon Shot" in patients with leukemia from patient presentation, planned to be comprehensive, collaborative and innovative. It will involve research genomics, big data analytics and adaptive learning in 1000 leukemia patients by the fall of 2013. It will focus on the newly diagnosed patient, with samples at diagnosis and thereafter, with exome sequencing. It will examine the progression from myelodysplastic syndrome (MDS) to leukemia, risk of death during induction, and subclonality and risk of relapse or progression.

Cincinnati Children's Hospital genomic medicine integration efforts-John Harley

Dr. Harley reviewed Cincinnati Children's Hospital statistics that include 822 faculty, 512 beds, 13,000 employees, \$173 M in research funding. The hospital cares for 1.1 million patients yearly with 70,000 new patients, 27,000 outpatient and 6300 inpatient surgeries that include 550 liver and 24 heart transplants. The hospital has extensive capacity in genomics and the service is expanding rapidly. He reviewed outstanding pharmacogenomics and diagnostic services.

eMERGE-PGx project implementation and possible collaborations – Josh Denny

Dr. Denny reviewed the Vanderbilt experience with preemptive genotyping with a focus on clopidogrel, simvastatin, warfarin and thiopurine. The program was designed around preemptive testing because side effects show up early in the use of medications. He reviewed interim results with choice of medication and dose.

GM5 – International efforts and possible collaborations – Geoff Ginsburg

Dr. Ginsburg noted that genomics is not limited by national boundaries. There are extensive efforts in Europe, China, India, Japan, Korea, Israel, Australia, Canada and the U.S. It would seem useful to explore opportunities for collaboration and sharing of results and plans. Plans to

develop an international meeting for the fall with emphasis on coordinating US efforts at the GM5 meeting in May are under discussion.

Preliminary Action Items – Marc Williams

1. Convene society representatives by conference call in roughly one month as a nascent Coordinating Committee and invite other relevant societies and disease-specific Institutes to collaborate.
2. Send to Gene Passamani (from societies): Links for available physician education materials for posting in G2C2; individual societies' areas of interest; societies' process for developing guidelines and pseudo-guidelines; current approaches and best practices in genomic medicine.
3. Work with societies to produce a white paper from this meeting, potentially including the surveys, or encourage the societies to publish surveys separately.
4. Consider developing a working group to address liability issues presented by genomic medicine implementation and convening societies' guideline producers to outline process and evidence needs (GM VII?).
5. If focus of GM V in May will be on coordinating federal/domestic efforts in genomic medicine, Include Health Resources and Services Administration (HRSA), Veterans Affairs (VA), possibly Office of Civil Rights (OCR) as related to HIPAA, possibly Office of Human Subjects Research Protections (OHSRP).
6. Consider setting aside 60-90 minutes in May to follow-up on payers' meeting.