

Genomic Medicine VI: Global Leaders in Genomic Medicine

January 8-9, 2014

National Academy of Sciences Building

Washington, D.C.

Welcome, Introductions, and Expectations – Geoff Ginsburg

Major objectives of Genomic Medicine VI (GMVI) are to: identify areas of active translation and implementation, prioritize common barriers to implementation in healthcare, frame a policy agenda to advance the field, highlight nations with unique capabilities, and discuss opportunities for international collaborations. Key issues for genomic medicine in general include: the development of evidence for value of genomic medicine (GM); ways to engage both institutional leaders and physicians in GM; education of physicians, patients, and the public; effective integration of genomic results into electronic health records (EHRs); and design of financial models that provide cost reductions rather than increase. GMVI welcomes 50 leaders in genomic medicine from 25 countries to tackle these issues. Possible outcomes of GMVI include development of an international steering group and working groups, consideration of international collaborations or pilot projects, and identification of potential funding models for them.

Genomic Medicine and NIH – Francis Collins

Since the mapping of the human genome, several programs have been established to create catalogs of human genetic information and to study the significance of variation, including The Encyclopedia of DNA Elements (ENCODE) Project, the International HapMap Project, The Cancer Genome Atlas (TCGA), and 1000 Genomes. These are now beginning to be applied to clinical cases such as the severely disabled Beery twins, in whom sequencing diagnosed a new genetic disease readily treated by a simple dietary change. Other NIH-supported projects involving genomic medicine include finding Mendelian disease genes and supporting drug discovery and toxin detection.

Effective implementation of scientific progress in genomic technology requires parallel development of appropriate policy and regulation. Such developments include the recent decision by the US Supreme Court invalidating patents on *BRCA1/2* genes and FDA's first regulatory clearance of a high-throughput DNA sequencing device, Illumina MiSeqDx, for authorized clinical use. Other areas of progress in the US include the Genetic Information Nondiscrimination Act (GINA), expanded genomic data sharing policies, and modernizing human subjects rules. International collaborations will need to consider policy and regulatory differences across countries and might promote recognizing or building upon existing policies in other countries as they develop new projects.

NHGRI's Genomic Medicine Research Portfolio – Eric Green

The National Human Genome Research Institute (NHGRI), initially designed to be the NIH arm of the international Human Genome Project (HGP), has grown to become one of the 27 Institutes and Centers of the NIH and has expanded its focus to advancing human health through genomics research. Over time the Institute will place increased emphasis on validation

and implementation of genomics in medical care, while maintaining its long-standing mission of understanding the biology of genomes. Attendees interested in receiving Eric Green's (USA) monthly newsletter *The Genomics Landscape* which monitors genomic medicine events and milestones across the NIH should contact Eric Green (egreen@nhgri.nih.gov) (**action item**).

NHGRI programs in genomic medicine address cancer genomics, pharmacogenomics, genomic medicine pilot projects, newborn genomic analysis, clinical genomics information systems, and ultrarare genetic disease diagnostics. To increase public awareness of the Institute and the state of genomics research today, in June 2013, NHGRI and the Smithsonian National Museum of Natural History unveiled their exhibition "Genome: Unlocking Life's Code," which attendees will visit on day 2 of the meeting.

NHGRI's Genomic Medicine Working Group – Teri Manolio

The NHGRI Genomic Medicine Working Group, a subgroup of the National Advisory Council on Human Genome Research, provides advice on NHGRI programs, guides programs in outlining infrastructural needs for adoption of genomic medicine, and identifies related efforts for future collaborations. One product of the Genomic Medicine IV: *Physician Education in Genomics* meeting was the formation of the Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC). This group seeks to enhance professional societies' efforts to improve genomic literacy among clinical practitioners. ISCC facilitates interactions among medical professional societies and the NIH Institutes & Centers to exchange practices and resources in genomic education and clinical care.

Barriers to implementation of genomic medicine have been identified throughout the series of genomic medicine meetings and are similar across stakeholders; lack of evidence of clinical validity and utility is cited as a major barrier by almost all groups. NHGRI and its GMWG will be exploring the potential for a large evidence generation project in collaboration with military medical services and the Veterans Administration later this year.

Major US Genomic Medicine Programs: NHGRI'S Electronic Medical Records and Genomics (eMERGE) Network – Dan Roden

The Electronic Medical Records and Genomics (eMERGE) Network is demonstrating the utility of DNA collections integrated with EHRs as resources by performing GWAS on phenotypes of interest. Phenotyping algorithms are entered into the Phenotype KnowledgeBase (PheKB) as an online public repository. eMERGE is now implementing actionable variants into EHR using clinical decision support (CDS) tools. In addition, eMERGE has undertaken a large-scale pharmacogenomics sequencing and reporting project in partnership with the Pharmacogenomics Research Network to evaluate the impact on clinical care of pre-prescription identification of several genetic variants predicting poor or adverse drug response.

Discussion – Francis Collins, Eric Green, Teri Manolio, Dan Roden

Successful NIH genomic medicine programs may serve as models for coordination of large, international collaborative efforts. There was agreement that GMVI attendees should review Howard McLeod's Pharmacogenomics for Every Nation Initiative (PGENI) program as a potential model. A collaborative group arising from GMVI should establish vehicles for communication.

A valuable effort would be to develop an evidence base and identify variants important for clinical implementation internationally, perhaps building on efforts such as ClinVar and ClinGen. Ideally, GMVI might create an evidence generation project on a large scale to capture a wide range of genetic variation. The ISCC could provide considerable value to other countries; Teri Manolio (USA) and Paul Lasko (Canada) will discuss the possibility of expansion of the ISCC to involve international societies (**action item**). The group should also engage with the Global Alliance for Genomics and Health (GA4GH) and the International Rare Diseases Research Consortium (IRDIRC). Several participants will be attending a GA4GH meeting in London on March 4, 2014. GMVI attendees will reach out to any GA4GH connections to promote GMVI efforts (**action item**).

CANADA: Genomics and Personalized Health Competition – Pierre Meulien

Genome Canada has partnered with the Canadian Institutes of Health to support the Large-Scale Applied Research Competition in Genomics and Personalized Health. The program is intended to assess whether the technology can deliver real value to patients and whether integrating it within the healthcare system will be cost effective. A total of 17 projects were funded and will include economic analyses for their own addition of value to the healthcare system. Involvement of the private sector is an important and innovative component.

The program includes a component which supports research in the fields of health administration, health technology, and comparative effectiveness. Overall, the program is expected to expand its capacity for clinical and translational research, train healthcare professionals to be proficient users of the technology, improve clinical information systems and harmonize e-patient records, increase the role of patients and advocacy groups in demanding evidence based medicine, and apply robust technology assessments focused on improvement of clinical outcomes and economic benefit analyses.

UNITED KINGDOM: 100,000 Genomes and Genomics England – Tim Hubbard

Improved linking of EHR data to research (“E-Health Research”) and using genomics to improve health are major goals within the U.K. health system. In 2012, the Human Genome Strategy Group announced the 100K Genome Project, to be implemented by a new entity, Genomics England. This project will use whole genome sequencing to map 100,000 patients’ genomes to target variants for rare diseases, cancer, and pathogens. Projected completion date is 2017.

A national effort to sequence clinical grade whole genomes is underway. In its pilot phase, the Genomics England Advisory Board will judge grantees based on the quality of their sequencing methods and annotations. This will generate a “bake-off” competition in research, building a market for sequencing and analysis and also developing ways to share information and methods between projects. Top-ranked projects will be funded by the Advisory Board. Genomics England will create a sample pipeline and biorepository, storing large-scale data usable across NHS Centres. The program is intended to work with the National Health Service (NHS), academics and industry to drive Genomic Medicine into the NHS. It is expected to leave a legacy of next generation sequencing centers, sample pipeline and biorepository, and large-

scale data store that will be usable by the NHS to produce new diagnostics, therapies and opportunities for patients.

BELGIUM: Belgian Medical Genomics Initiative – Gert Matthijs

Belgium has eight government-regulated genetic centers which are linked to private non-profit academic hospitals. Each of the genetic centers has a center for human and medical genetics which is supported by a combination of regional government funding, the national health system, and research grants. There is a push for both whole exome sequencing and also reimbursement for exome sequencing across all centers. The Belgian Medical Genomics Initiative is a network funded by the Belgian Federal Science Policy Office to create an optimal national framework for exome sequencing in a clinical context. Guidelines for next generation sequencing are being developed through EuroGentest2, part of the 7th Framework of the European Community, that is addressing among other things, diagnostic utility, a 'scoring system' for gene panels and exomes, and instructions for incidental findings.

SINGAPORE: Genomic Predictors of Clinical Outcome in Gastric Cancer – Patrick Tan

Multiple research institutes and academic medical centers within Singapore are centers for research on Asian population-specific cancers, particularly stomach cancer. The POLARIS program implements genomic medicine in a city-state health system and aims to prove the clinical utility of genomic testing. In early 2014, POLARIS will launch the *TGFB1* eye test to detect risk of stromal corneal dystrophies. Challenges faced in developing a framework for genomic testing include: complexity of legal and licensing agreements across institutions and ministries; reimbursement for genetic assays that cross medical centers; a lack of genetic counselors; current policies on patient consent, incidental finding, and aggregation of genetic/genomic data.

ESTONIA: The Estonian Approach: Personal Medicine in 2014-2020 – Andres Metspalu

Data in the country's Gene Bank includes medical records, DNA, plasma, and WBCs from 5% of the adult population. Estonian residents over the age 15 are required to carry an electronic ID card which enables secure digital authentication. The ID card is a promising vehicle for storing and sharing genomic information for use in research and clinical care. In December 2013, the Estonian Government Research and Development Council approved the Estonian Program for Personal Medicine comprising a sequencing, pilot, and main phase genotyping projects. Sequencing of 5,000 individuals will be used to develop a 1M SNV "Estonian chip" to be pilot tested in 50K individuals in the Estonian Biobank and linked with primary physicians, eHealth database and decision support software. This chip-based test will then be offered to all 35 to 65 year olds as a disease risk assessment and drug response predictor, producing 500K individuals in the database with EMR, genotypes, samples and prescription data recorded longitudinally. Surveys show that primary care providers agree that the use of genomics in clinical practice will be beneficial and feasible.

KUWAIT: Genome Arabia – Fahd Al-Mulla

Through private funding, the Genatak Center was established in 2013 to diagnose and prevent diseases in Gulf and Middle Eastern states. Genatak is part of a large world-wide network of

laboratories that collectively offer 2,000 highly specialized genetic tests. Arab cohorts are not well represented in the HGP, HapMap, or 1000 Genome Project, and therefore rare variants found only in Arab populations remain undiscovered. In 2012 the Qatar National Research Foundation supported the Genome Arabia working group to conduct whole genome and exome sequencing in 360 -1000 normal Arabs, demonstrating considerably long and more frequent stretches of reduced heterozygosity than in other populations studied to date.

KOREA: Genomic Medicine in Korea: Plan and Infrastructure – Bok-Ghee Han

The Korean Genome and Epidemiology Study (KoGES) is a large-scale population-based prospective cohort study which collects epidemiological data and WGS information. The Korean Genome Analysis Project (KoGAP) has constructed the population-specific Korean Reference Genome. The Korean reference genome and epigenome can be used to identify genetic underpinnings for lifestyle-related diseases that manifest in patients who do not exhibit phenotypes associated with these diseases, i.e. diabetes in patients who are not obese.

THAILAND: Genomic Medicine in Thailand – Wasun Chantratita

Thailand has one of the highest rates of Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS-TEN) in the world, heavily determined by high frequency HLA risk alleles. Risk assessment and prevention of SJS-TEN have been a major component of Thailand's genomic medicine efforts. Ramathibodi Hospital has launched a pharmacogenetics card which carries patients' HLA variant information to assess risk for SJS-TEN. The government is funding this program, and may invest in similar projects if value is proven. Initial cost-effectiveness studies have demonstrated the value of the approach in averting cases. Wasun (Thailand) will share publications on SJS which list potential predisposing factors within specific gene regions with GMVI attendees. A five-year medical genetics project plan includes clinical exome and whole genome sequencing, pre-implantation genetic diagnosis/screening, NGS panels for inherited cancers and other diseases, and viral sequencing for drug resistance assessment.

ISRAEL: Sequencing (Somatic and Germline) as a Clinical Service – Gadi Rennert

Genomic research has shown population stratification between the Ashkenazi and Sephardic/Arabic populations. One million women have been entered into a national database, the National Mammography Screening Program, which collects family history of breast cancer from probands and reports it in the medical records of their first-degree relatives. This program does not reveal the identity of the index cases of the disease.

Centralized databases including *EGFR* and other variants allow researchers to assess somatic mutation frequency in advanced adenocarcinoma of the lung and study their effects on a national scale. Follow-up data clearly show, for example, the lack of treatment effect on outcome in patients without the targeted mutation; this can be helpful in persuading clinicians and patients not to utilize futile but expensive treatments. This investigation demonstrates how both positive and negative results are necessary for changing practices in genomics.

PANEL DISCUSSION: Creating an International Agenda for Implementation of Genomic Medicine

The European Commission (EC) funds research collaborations between European Union (EU) partners and international partners. The EC is looking to support a network of personalized medicine pilot programs during its 2014 funding round. A map of ongoing pilot projects would be helpful in determining best candidate programs for an international demonstration project. A possible host for this could be the EuroBioForum Observatory on Personalized Medicine (<http://www.eurobioforum.eu/2028/observatory/>).

The UK Wellcome Trust, an independent global charity that funds biomedical research, annually spends \$1 billion on grants for national and international efforts. Enhancing data sharing through meta-data sharing and standardizing policy and regulations would be useful for genomics research. Researchers involved in international efforts should create standards for extracting meaning from sequence-level information, including statistical significance of gene association and phenotypes. This will foster agreement on what will be considered as evidence that a variant is actionable.

The creation of reference samples may serve as a cost-saving measure. Once whole-genome sequencing is performed on reference samples, the cost of any further algorithmic analysis is negligible. A network of small pilot projects focused on implementation science would demonstrate cost-effectiveness and should be pursued. GMVI presentations should be circulated widely to increase public awareness of these efforts, and ongoing efforts between groups at this meeting should be documented.

There was discussion of creating an exome database server through which exome information would be linked to a simple phenotype, i.e. “had a myocardial infarction.” The creation of a global exome variant server which just shows variation across 10^6 human genomes may also be useful. Recognizing the diversity of the global population, a good pilot effort for the group may be to establish reference samples for cross-validating and standardizing labs worldwide, since many existing reference samples are US-centric and fail to assess other important variation. Simultaneous development of “push” from policymakers and “pull” from patients and clinicians may aid the adoption of genomic medicine initiatives.

SRI LANKA: Creating the Ecosystem for Taking Genetics from Bench to Bedside in a Developing Country: A Personal Experience from Sri Lanka – Vajira H.W. Dissanayake

Thalassemia is a major focus of Sri Lanka’s translational medicine program. The total thalassemia patient population (3,000) takes up 5% of the annual drug budget of the National Health Service. This expenditure could be prevented by introducing a cost-effective population-based screening program for carrier detection using high-throughput SNP genotyping and counseling.

AUSTRALIA: Genomic Medicine in Australia – Warwick Anderson

Most genetic services in Australia are provided by the public state and territory hospitals. In the 1990s, the national government implemented an EHR system which proved unpopular, leading the government to be wary of renewing such efforts. State governments might be more amenable to support of these programs, especially if EHRs are voluntary. With the

community's consent and involvement, researchers are now able to study diversity in Australia's mostly isolated indigenous population of Australia. Australia's Health and Medical Research Council (NHMRC) has prepared a framework for translating "–omics based" discoveries into clinical care. It includes governing principles in five domains of laboratory research, clinical research, clinical practice and guidelines, data repositories, and ethical/legal/social issues particularly related to return of results. Warwick will share a link to this framework with the GMVI committee attendees.

FRANCE: National and Stratified Development of Genomic Medicine in France – Thierry Frebourg

25 million European citizens and 3.5 million French citizens are involved in the national French Plan for Rare Diseases Program (2011 to 2014) which functions on three levels: competence clinical centers, reference centers, and molecular genetics laboratories. Most of the molecular laboratories are acquiring NGS equipment. They anticipate needing the capability to generate 10K to 50K exomes per year.

The French National Cancer Institute has organized a national network which specializes in inherited forms of cancer for Lynch Syndrome and breast and ovarian cancer.

LUXEMBOURG: Luxembourg Centre for Systems Biomedicine – Rudi Balling

The Luxembourg Centre for System Biomedicine (LCSB) focuses on neurodegenerative disease, specifically Parkinson's Disease (PD). LCSB has, through community effort, created an interactive map charting known genetic and molecular underpinnings of PD which will be integrated with sequence data. The government has funded the National Centre of Excellence on Early Diagnosis and Stratification of PD to move LCSB research into the clinic. Additionally, Luxembourg would like to contribute to an international collaboration their expertise in validation through pathway and network analysis.

JAPAN: New Initiative for Implementation of Genomic Medicine in Japan – Naoko Okamura, Mistuaki Kubo and Satoru Miyano

The goals of the Implementation of Genomic Medicine Project (IGMP) to be achieved by 2015 are: to construct a network of biobanks, both disease-oriented and population-based; to install a Central Genome Center which will perform large-scale genomic research to build a comprehensive genomic variation database; and to establish a Medical Genome Center which will establish optimized treatment through prediction of drug responses and optimized diagnostics. By 2020-2030, the program will conduct studies on the efficacy and cost-effectiveness of its clinical implementation.

In its clinical implementation program, the Institute of Medical Science of the University of Tokyo and its collaborators use WGS to study cancer and blood disorders.

Day 1 Summary Discussion – Wrap Up – Geoffrey Ginsburg, Teri Manolio, Eric Green

The U.K. and Estonia have developed models for databases which provide network-wide access to de-identified EHRs. The UK has shown that a "bake-off" competing grant system can be a

way to share data and build a knowledgebase. Different but effective genomic implementation approaches have been performed in different countries. In Belgium, UK, and France, genotyping for clinical care is performed at specialized genotyping centers, while in Singapore genotyping is deployed across an existing framework. A variety of NGS diagnostic sequencing guidelines are available from nations such as the Netherlands, UK, and US; efforts to harmonize and build upon these may avoid wasteful duplication of effort. Collaborations with the Global Alliance for Genomics and Health (GA4GH), and the International Rare Diseases Research Consortium (IRDiRC), amongst other genomic medicine programs, should continue to be sought. Population-specific research could offer broader insight into global genomic diversity and also potentially lead to a single world-wide “population graph” representation. There was interest in developing a pharmacogenomics card as Thailand has piloted with SJS/TEN variants. Israel voiced the challenges of conducting research on mixed ancestry and stratified populations and demonstrated how FHx data of first degree relatives can be added to EHRs without revealing index cases. Israel also emphasized the importance of collecting both positive and negative results for use in clinical care.

GREECE: The Genomic Medicine Alliance – George Patrinos

The bridging of resources between developing and developed nations is a major goal of the Genomic Medicine Alliance. The Alliance’s current major projects include a pharmacogenomics (PGx) biomarkers project, EuroPGx which genotypes pharmacogenomically relevant variants from samples in developing nations, the pilot NextGenPGx project which analyzes all variants of a select number of whole genomes, a project to create a database of the incidence of genetic disorders of three ethnic groups, nationwide studies of the public and healthcare professionals’ understanding of genomics, and a cost-effectiveness analysis of genetic treatments.

There was agreement that strengthening relationships with other countries will aid the goals of this organization. Interest was expressed in collaborating with the United States.

INDIA: Human Genomic Initiatives and Genetic Epidemiology of Cancer – Sukhdev Sinha and Partha Majumder

The genetic cataloguing of ethnic groups, better pre-natal care, and the examination of cancer genomics are major goals of genomic research in India.

India worked with the WHO to create the Cancer Atlas of India, an epidemiological database which reports heat-maps for all Indian districts for different cancers. Certain regions have characteristically large burdens of certain cancers, including gall bladder in the Ganges and gastric cancer in Nagaland. Sequencing of exomes in blood and tumor DNA in squamous oral cancer cases revealed that certain genes, such as *CASP8*, were mutated. This study determined that several of these genes have novel associations with head and neck cancers. Most of this research was performed in private hospitals which utilize EHRs widely.

NICHD-NHGRI Newborn Sequencing Program – Anastasia Wise

This project examines the role that newborn sequencing may play in future newborn screening efforts. Pilot studies exploring this topic and focused on clinical utility and ethical implications are underway. All grants to this program integrate three components: genomic sequencing; clinical research; and ethical, legal, and social implications of newborn sequencing. It was

agreed that sequence information will likely be useful in the newborn period, but will not replace effective phenotypic tools such as biochemical tests. Additionally, the group discussed the importance of improved communication of these ideas to the press, and noted that press releases on this project in the US were picked up internationally and have implications overseas.

NHGRI's Clinical Sequencing Exploratory Research (CSER) Consortium – Lucia Hindorff

CSER identifies and evaluates the challenges of applying genomic sequence data to patient care in the clinic. Each site includes a clinical study; a pipeline for sequencing, analysis, and informatics; and an examination of relevant ethical, legal, and social issues (ELSI). Nine projects, the NHGRI ClinSeq program, a Coordinating Center, and “R” grants which examine the return of results through the ELSI program are currently funded by CSER. CSER's biggest challenge has been developing sufficient evidence for pathogenicity. CSER is different from TCGA in that CSER examines genomics in the context of clinical workflow and addresses more diseases than cancer, while TCGA addresses discovery and cancer exclusively.

NHGRI's Implementing Genomics in Practice (IGNITE) Consortium – Geoffrey Ginsburg

The goal of IGNITE is to create a consortium of Genomic Medicine Pilot Demonstration projects to expand successful genomics implementation programs into diverse clinical settings. There are currently three IGNITE sites: The Pilot for Hypertension and Kidney Disease in Primary Care is genotyping 900 hypertensive African-Americans at the *APOL1* locus. The Family Health History Evaluation in Diverse Care Settings applies an implementation sciences approach to the collection and evaluation of family history and the development of implementation guidelines. The Personalized Medicine Program (PMP) has a PGx focus. Future aims include the development of best practices for genomic medicine implementation. There was interest expressed in encouraging international pilot projects to join the IGNITE network as affiliate members.

Break-out Group 1: IT/Bioinformatics and CDS Standards – Marc Williams

GMVI attendees identified two main issues that can most feasibly be addressed: 1) definition of key elements to be stored in EHRs, and 2) development of a global resource for actionable clinical variants. Numerous other issues were proposed, including: aggregation of variant/phenotype associations; definition of federated databases for genomic medicine implementation; development of a vocabulary for phenotype ontology, standardized phenotype ontology, and inventory of existing phenotype ontologies; and aggregation of genomic medicine implementation guidelines.

Break-out Group 2: Education and Workforce Building – Bruce Korf

This break-out group (BoG) suggested three potential audiences: the professional genomics workforce, other healthcare professionals, and the public. Priorities for the professional genomics workforce were to increase the number of genomics professionals and to clarify the role of the “genomics professional.” The BoG saw opportunities in comparing different countries' training paradigms, defining best practices in different regions, summarizing existing workforce surveys, extending current capabilities through telemedicine, and potentially

coupling lab certification to the delivery of clinical services. The BoG's proposed next steps for genomics professionals were to collect data concerning different countries' genomic professional workforce, share competencies and training paradigms, and create a "genomics academy" to increase professionals' literacy in modern genomics.

One priority for all other healthcare providers was to develop point-of-care decision support tools. The BoG saw an opportunity in examining curricula to determine where genetics competency training can be incorporated. The BoG's proposed next steps for other healthcare providers were to develop educational materials that are regionally specific, to create common templates for these materials, and to utilize the existing professional workforce structure for education. Next steps for the public were to provide a clearinghouse for information, consider novel educational paradigms, customize materials to the culture of the target audience, and extend DNA Day to the level of a national educational event.

Break-out Group 3: Evidence Generation – Heidi Rehm

The BoG addressed the question of whether evidence generation should be held to a different standard in genomics vs. in other medical specialties. Several steps may be needed prior to initiating large-scale evidence generation projects, including defining evidence needs and criteria, and cataloguing current evidence generation projects. IGNITE may potentially serve in this role. The BoG urged standardization of tests so that results can be more easily compared, and noted that genomics should not be held to higher standards of evidence than other branches of medicine. The BoG also discussed situations in which frameworks for genomic medicine application already exist but are not actively adopted and noted the role of the Inter-Society Coordinating Committee's work in establishing competencies for residency training.

The BoG's suggested next steps included identifying countries and systems willing to allow access to patient data and the creation of systems, such as a network and standard API, to capture these data. In addition, it will also be important to identify areas of overlap with organizations to both prevent wasteful duplication of efforts and to pool efforts.

Break-out Group 4: Pharmacogenomics (PGx) – Howard McLeod

The BoG agreed that two major priorities were a desire for a high-quality evidence base for the implementation of PGx and a focus on low-cost drugs like certain vaccines that have characteristic treatment failure or extreme adverse drug reactions. Additional priorities include the addition of a drug/PGx to induced pluripotential stem cell research initiatives and the development of value derived from cancer NGS, an expensive test that generates use of very expensive drugs. PGx ID cards should continue to be used and developed. The global eradication of Stevens-Johnson Syndrome using a PGx approach, potentially using PGx ID cards, could be a signature initiative of this collaboration.

Break-out Group 5: Policy Agenda – Laura Rodriguez

The Policy BoG framed its discussion by describing genomics as simply another tool, just one element of personalized medicine. The first priority recommendation of this BoG was the engagement of stakeholders: patients, payers, and health decision makers. The second was the

area of privacy, informed consent, and legal issues in data sharing. Other top priorities included regulatory oversight (particularly with the FDA), and the cost-benefit of adding genomics to care systems. Opportunities included the identification of what unique niche this BoG could serve. This BoG should map its proposed activities and pursue gap analyses to identify potential unique contributions. The promotion of a “network-of-networks” structure in areas such as consent and data sharing groups would also have value. The BoG noted that, to demonstrate positive cost/benefit results for GM, GMVI attendees should look to the historical examples of past tools that were adopted with and without evidence. Examples include PET scans and PSA levels. The BoG proposed several ways to improve economic analysis, such as incorporating economists into research teams. The engagement of payers would be facilitated by working within a healthcare system that has a small number of centralized payers.

Day 2 Summary Discussion – Next Steps – Teri Manolio

The group agreed that the areas addressed by these five break-out groups will carry forward as working groups (WGs). The leadership of these groups should be multinational, and volunteers will be solicited to determine leadership or potentially co-leadership. Both an International Steering Group to promote leadership and a Communications WG to promote synergy within the WGs and facilitate interactions with other organizations working in related areas will be created. The top ideas of the five BoGs were:

IT: 1) Define key elements to be stored in EHR, 2) Global resource for actionable variants;

Education: 1) Define workforce needs, and 2) Develop existing/new educational tools that can be widely shared;

Evidence: 1) Develop systems to capture evidence, such as a federated network and standardized APIs, and 2) Identify poolable/extendable projects;

PGx: 1) Global eradication of SJS/TEN, and 2) PGx Card; and

Policy: 1) Improve capacity for economic analysis, and 2) Pursue cost assessment

Summary of Action Items

- 1) Teri Manolio (USA) and Paul Lasko (Canada) will discuss the possibility of expansion of NHGRI's Inter-Society Coordinating Committee (ISCC) to involve international agencies.
- 2) GMVI attendees will reach out to their connections with Global Alliance for Genomic Health to promote GMVI efforts.
- 3) Wasun Chantratita (Thailand) will share publications on SJS which list potential predisposing factors within specific gene regions with GMVI attendees.
- 4) Warwick Anderson (Australia) will share a link to a framework for translating “-omics based” discoveries into clinical care.
- 5) GMVI attendees should identify important groups or individuals who were unable to attend this meeting but may be interested in Genomic Medicine to participate in future meetings through an email to Geoff Ginsburg. The Communications WG will play a key role in reaching out to such individuals.
- 6) Potentially, the GMVI break-out groups may write reports for a special issue of *Pers Med* in collaboration with George Patrinos and the Genomic Alliance.
- 7) NHGRI will post the video recording of this presentation on its website and distribute a meeting summary and an executive summary. Attendees who presented and breakout

leaders will be authors on a white paper of this meeting. BoG leaders who decide to write journal articles of their BoG's meetings are encouraged to move forward with this process.

- 8) Any attendee who would like to volunteer for WG leadership or membership will email Geoff and Teri. The Steering Group and WGs will be convened once members have been identified.
- 9) The full committee will consider a follow-up meeting.
- 10) GMVI attendees will contact Paul Lasko (Canada) if interested in attending an upcoming Canadian meeting on genomic medicine in April.
- 11) The full committee decided that in order to establish more formal relationships with European organizations that address personalized medicine, group members should send relevant information to Geoff and Teri.
- 12) Attendees interested in receiving Eric Green's (USA) monthly newsletter *The Genomics Landscape* which monitors genomic medicine events and milestones across the NIH will contact Eric Green (egreen@nhgri.nih.gov).