**Department of Veterans Affairs**
**Genomic Medicine Program Advisory Committee Meeting**
**May 20, 2011**
**Executive Summary**

The 13th meeting of the Department of Veterans Affairs Genomic Medicine Advisory Committee took place on May 20, 2011 in Washington, DC. Chairperson Wayne Grody opened the meeting with a welcome and introductions of the other members and other attendees. The GMPAC members in attendance were Paul Billings, Vence Bonham, Julia Bridge, Bob Wallace, Dan Wattendorf, Kathy Hudson, Cynthia Morton, Michael Watson, and Cathy McCarty.

Ronald Przygodzki, Acting Director of the Biomedical and Laboratory Research and Development, delivered an update on the VA Genomic Medicine Program, including the Million Veteran Program (MVP) and other research projects. John Concato, Director of the Clinical Epidemiology Research Center at the VA Connecticut HealthCare System, and Co-Principal Investigator of MVP updated the committee on MVP progress, including current accrual, some aggregate demographics of enrollees, and plans for roll-out of additional sites across the country. The committee congratulated the program for launch of MVP. They also raised several points for the group's consideration, including outreach efforts to determine how Veterans are hearing about MVP and potential opportunities to promote MVP at science museums across the country. Other issues discussed included enrolling in-patients into MVP, importance of obtaining a truly informed consent, and the addition of solid tissue collection in addition to blood specimens.

Larry Meyer, Director of the VA Clinical Genomic Medicine Service, and ACOS of the Salt Lake City VA talked to the committee about the patient care genomics in the VA. Progress in this area included hiring of genetic counselors and the development of Memoranda of Understanding with all VISNs to enable remote genetic counseling to VA sites. Currently, the Durham VAMC is up and able to receive telehealth services. Dr. Meyer expressed concern about the current electronic health record's ability to incorporate genetic data in its current form. The committee suggested training nurses in the genetic counseling process rather than being solely reliant on the few available genetic counselors. Dr. Meyer responded that training Nurse Practitioners in this role is under consideration, although implementation will differ across VAMCs.

Several invited speakers discussed their experiences with clinical genome sequencing. Wayne Grody, Director of the Molecular Pathology Laboratory at UCLA, presented the likelihood of routine, fast and low-cost whole genome sequencing in the coming years and its potential for identifying molecular causes for polygenic disease. Elaine Mardis, Director of the Genome Institute's Technology Development group at Washington University in St. Louis, presented an assessment of her work with genome sequencing for cancer prognosis and diagnosis. Her group was able to identify specific genetic mutations associated with acute myeloid leukemia relapse. She also discussed the ongoing investigation of many candidate genes that may identify prostate cancer progression. Mike Snyder, professor and director at Stanford University, presented a project of his personal genome sequence and its interpretation. His research attempted to address questions of sequence quality; what can

be learned from genomes of healthy people, how it relates to diseases risk; whether the results are actionable; and whether it is worth the cost. He discussed the process of sequencing his entire genome on two different commercial platforms, the results, and clinical implications.

Eric Green, Director of the National Human Genome Research Institute, charted a course for genomic medicine from a funding agency's perspective. He outlined his five steps between genome sequencing and treatment: 1. Understanding the function of the entire human genome sequence; 2. Assessing human genetic variation; 3. Understanding genetic basis for human disease; 4. Routine whole genome sequencing; 5. Routine analysis of whole genome sequence. Dr. Green outlined the current NHGRI strategic plan for identification and linking the domains of genomic research, which he revealed as research on the structure of genomes, the biology of genomes and disease, advancing the science of medicine and improving the effectiveness of healthcare system.

The committee proposed that the one benefit to using whole genome sequences rather than more targeted genetic tests is that it is hypothesis-free and unbiased. They also discussed issues that will affect genomic sequence's utility in clinical practice. These include the need to improve curation of the genome, identification of false positives, the incidentalome (off-target findings), and return of individual research results. The committee identified bottlenecks in clinical use of genomes as initial analysis and storage requirements of sequence data and medical interpretation of results (which the committee discussed again in detail at the end of the meeting). Additionally, the field needs to remain mindful that it is molecular pathways, not merely genetic sequence, that is important in complex diseases. In the future, metabolites may very well supplant DNA as the analyte interest.

The committee discussed the pervasive issue of healthcare costs. The consensus was that scientific and policy community needs to involve health economists to explain genomic medicine and to educate the policy makers and implementers. Framing the discussion as cost of increasing quality-of-life-years may be beneficial. For example, withholding certain expensive treatments in indolent cancers or in patients that will not respond to expensive drugs based on their genetic make-up will result in cost savings.

The committee also embarked on a discussion about the likelihood of and ethical issues surrounding return of individual research results from genetic sequencing. Currently, the protocol and consent document of the Million Veteran Program will not allow for the release of any individual research results, but committee consensus is that this may change in the future. Releasing genomic data to patients is also going to depend on clinical validity of whole genome sequences, but an ongoing problem is the lack of consensus on the definition of clinical validity within the scientific community. The field may have to wait until FDA weighs in on the issue. The timetable for this will depend on the community becoming comfortable with the type of data generated, and whether the agency decides to focus on certifying machines and technology rather than analysis.

The committee commented on current litigation surrounding gene patents and the potential implications to genomics research, but they did not reach a consensus on what those implications might be.

In conclusion, the committee suggested that implementing genome sequence data into health care decisions will require engaging policy makers, physicians, researchers, students, and behavioral scientists to address the myriad crosscutting issues. They also suggested

the VA engage in ongoing discussions about the increased blurring of the lines between clinical care and research, and its potential implications.

No public comments were made at the meeting.

The committee endorsed the suggestion of constructing an informatics-working group to convene in the fall of 2011. The Minority working group will continue to meet, and the next GMPAC meeting will take place in fall 2011.

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