GMPAC Executive Summary
September 18, 2019
Hilton Garden Inn, Washington DC/U.S. Capitol
1225 First Street, NE
Washington, D.C. 20002

The 22nd meeting of the Veterans Affairs (VA) Genomic Medicine Program Advisory Committee (GMPAC) took place on September 18, 2019 in Washington, DC. The following members were in attendance: Dan Roden, MD (chair), Andrea Ferreira-Gonzalez, PhD; Vickie Pratt, PhD (by phone); Kimberly LeBlanc; Adam Berger, PhD, Richard Mooney, MD, along with invited guests and speakers. Jennifer Moser, PhD, Designated Federal Officer, opened the meeting and introduced the new Deputy Chief Research & Development Officer, Dr. Wendy Tenhula. The Chair, Dr. Dan Roden welcomed the committee members, guests, and members of the public. Dr. Tenhula gave a brief update on the strategic priorities of VA Research, which are 1) Increasing access to high quality clinical trials 2) Making VA data work for Veterans and 3) ensuring real world impact of Research. The meeting began with annual ethics training by the Office of General Counsel, followed by scientific presentations and discussions.

Michael Gaziano, MD, co-PI of the Million Veteran Program (MVP), provided an update on the recruitment and enrollment of the MVP. Currently, 780,000 Veterans have enrolled in MVP, and there are 60 VA sites nationwide actively recruiting participants. A new online enrollment portal has been launched in August, and there are plans to do a follow-up survey and a 5-year survey. A saliva kit is being piloted as an alternative to a blood specimen for those MVP participants who live far from a participating MVP site. He also mentioned that over 1.2 M biospecimens have been sent to a backup biorepository in Albuquerque. There are currently over 30 projects using MVP data, and they are accessing the data in secure enclaves within VA and the Department of Energy.

Phil Tsao, PhD, Co-PI of MVP and Saiju Pyarajan, PhD, Director of the MVP Data and Computational Sciences Core (DACS) discussed the current state of the MVP computing environment inside the VA, specifically regarding genotype and whole genome sequence data. There are over 75 analytical tools in the compute environment that researchers can use. The team has also created a new multi-ethnic genotyping chip that contains more genetic markers for African-American and Hispanic populations. Each of these samples will be analyzed on the new chip over the coming years. Dr. Tsao discussed the current status of the Whole genome sequencing analysis, which is done with the help of cloud computing, and the analysis can be done for a few dollars per sequence. The storage and compute bucket of this cloud are controlled access by the VA. One of the main goals for MVP genomics is to have over 100,000 whole genome sequences completed and provisioned to researchers in the next few years. He also discussed data access, and the CAPS team. The overall goal is to develop a secure and efficient cloud-based data commons that can serve the broad research community.

Christopher O'Donnell, MD, MPH, co-PI MVP, discussed the ongoing MVP science projects, which now number over 30. He highlighted the MVP science meeting, which took place in Philadelphia on September 12-13 and featured VA researchers from around the country sharing results from the various ongoing projects on topics ranging from Cardiovascular disease to osteoarthritis to Post Traumatic Stress Disorder (PTSD). Dr. O'Donnell then discussed the planned creation of a resource created from an MVP genome-wide Phenome wide association study (PheWAS) analysis, which will analyze many phenotypes, or characteristics, across all the available genetic variants in MVP participants The summary data from this analysis could be made broadly available to the research community, but decisions remain on where

to place the large amount of resulting data. The National Institutes of Health's database, dbGaP was mentioned as a possible location. Dr. O'Donnell also mentioned potential collaborations with other groups that have large genetic cohorts, including the National Heart, Lung, and Blood Institute's TOPMed (Trans-omics for Precision Medicine) initiative. Finally, he stated that the MVP Executive Committee strongly recommends placement of all summary results from MVP projects into dbGaP to foster a culture of data sharing.

Following these presentations, the committee discussed the progress of MVP and raised questions about the cohort. One question was whether the biospecimens could be used to created cell lines, and the answer was that, no, the samples were not collected in a way that would allow for the creation of immortalized cell lines, but that in the future, participants could be recontacted and resconsented with a new specific collection for this purpose. Dr. Gaziano reiterated that MVP is beginning planning efforts for the collection of the next one million participants, and that all options for biospecimen collection and analysis are being discussed, particularly around the area of CLIA collection and the potential return of results. Another question was about the process of moving novel disease associated genetic variants through a process of validation and then translation. Currently there are no formal mechanisms, and the follow up studies are ad hoc by the individual investigator teams but there are concerted efforts within the Office of Research and Development to support these translational efforts, particularly the validation of drug targets, with more funding opportunities. The committee recommended that the program have a robust outward facing website for scanning summary data and asking questions about the cohort (at a non-individual level). The Committee recommended that MVP continue to prioritize research into Veteran-Specific disease areas and concerns.

Following lunch, Dr. Ben McMahon of the Los Alamos Laboratory within the Department of Energy (DOE) spoke about the DOE-VA scientific collaboration and the three exemplar projects. These projects are jointly between the two departments with scientific expertise from both and are on three areas of importance to Veteran health: cardiovascular disease, cancer, and suicide. Dr. McMahon described the benefits of the collaborative effort to be new cross-cutting methodologies and deep-learning algorithms that can be applied to the electronic health record data, the extensive expertise of VA researchers on the clinical aspects of disease, and the super computing capabilities at the DOE laboratories. The goal outcomes of these collaborative projects will be better predictors of disease and improved clinical decision support for care providers and patients. The three exemplar projects have just gotten underway, and the committee will be apprised of the results at later meetings, but Dr. McMahon shared some preliminary results of a genome wide association study which sugget some genetic variants associated with suicide ideation.

Dr. Deepak Voora of the Durham VAMC and Duke University updated the committee on a new clinical initiative in the VHA that is a partnership with Sanford Health, called PHASeR (Pharmacogenomics Action for Cancer Survivorship). He stated that polypharmacy within the VA is a significant issue and understanding the genetics of drug metabolizing could prevent unwanted side effects and provide more accurate drug choices and dosing for an individual patient. In this project, Sanford Health will provide pharmacogenetic (PGx) testing for about 250,000 Veterans in the VHA system. The test looks at genetic variants for a few common drug metabolizing genes. The initial phase of the project will provide an informational report of these PGx variants to potentially inform prescribing decisions for several drug categories. He mentioned clinician education and buy-in, regulatory issues, and how and where to put the test results into the electronic health record as probable implementation barriers. The goal of the program is to get ultimately have the PGX test results into a clinical decision support tool.

After Dr. Voora's presentation, the committee had several questions regarding the program, especially concerning the FDA regulating PGx testing results informing drug prescribing. The committee also asked whether the Sanford assay can be modified, (it can be), and cautioned that clinicians might need considerable amounts of education about the program and could be sources of resistance. They suggested that buy-in from nurses and pharmacists would be important for PHASeR's success.

Upon conclusion of the presentations, the committee discussed several key areas for the program to focus on 1) Continue to recruit minorities and women and encourage research in these populations 2) encourage follow-up mechanistic and translational studies after initial discoveries from MVP data analysis, especially in issues that are particularly relevant to Veterans, like PTSD , suicide and traumatic brain injury 3) continue engaging Veterans in genomic research and ask them what kinds of research they want to see 4) continue efforts to expand MVP data access to the broader research community, including creation of an outward facing website for the scientific community; 5) continue collaborations with partners, including the Department of Energy; and 6) expand efforts to return results to participants.

There were no public comments.

The meeting was adjourned at 4:00pm.

Jennifer Moser, PhD
DFO, Genomic Medicine Program Advisory Committee

Dan Roden, MD
Chair, Gen Genomic Medicine Program Advisory Committee