**eMERGE Network Steering Committee Meeting**

January 25th & 26th, 2016 | Nashville, TN

**Attendance**

Baylor College of Medicine Richard Gibbs

Baylor College of Medicine Magalie Leduc

Boston Children’s Hospital Ingrid Holm

CCHMC Armand Antommaria

CCHMC Beth Cobb

CCHMC John Harley

CCHMC Nancy Leslie

CCHMC Todd Lingren

CCHMC John Lynch

CCHMC Keith Marsolo

CCHMC Melanie Myers

CCHMC Bahram Namjou

CCHMC Cindy Prows

CHOP Hakon Hakonarson

CHOP Frank Mentch

Geisinger Lindsay Bailey

Geisinger Yuki Bradford

Geisinger H. Les Kitchner

Geisinger/PSU Sarah Pendergrass

Geisinger Marylyn Ritchie

Geisinger/PSU Shefali Setia

Geisinger Anurag Verma

Geisinger Janet Williams

Geisinger Marc Williams

GHC/UW Deb Bowen

GHC/UW David Carrell

GHC/UW/CC David Crosslin

GHC/UW /CC Adam Gordon

GHC/UW Jane Grafton

GHC/UW Andrea Hartzler

GHC/UW/CC Gail Jarvik

GHC/UW Kathleen Leppig

Harvard Sandy Aronson

Harvard Kurt Christensen

Harvard Robert Green

Harvard Maggie Helm

Harvard Elizabeth Karlson

Harvard Shawn Murphy

Harvard Jordan Smoller

Harvard Scott Weiss

Marshfield Murray Brilliant

Marshfield Scott Hebbring

Mayo Mariza de Andrade

Mayo Adelaide Arruda-Olson

Mayo Suzette Bielinski

Mayo Pedro Caraballo

Mayo Robert Freimuth

Mayo Iftikhar Kullo

Mayo Hongfang Liu

Mayo Jennifer McCormick

Mayo Daniel Schaid

Mayo Richard Sharp

Mayo Erin Winkler

Mt. Sinai Erwin Bottinger

Mt. Sinai Aniwaa Owusu Obeng

Northwestern Rex Chisholm

Northwestern Geoff Hayes

Northwestern Siddhartha Jonnalagadda

Northwestern Luke Rasmussen

Northwestern Laura Rasmussen-Torvik

Northwestern Megan Roy-Puckelwartz

Northwestern Maureen Smith

Northwestern Justin Starren

Northwestern Firas Wehbe

Northwestern Cathy Wicklund

Partners/Broad Tim Desmet

Partners/Broad Birgit Funke

Partners/Broad Maegan Harden  
Partners/Broad Niall Lennon

Partners/Broad Heidi Rehm

Vanderbilt/U of Louisville Kyle Brothers

Vanderbilt Robert Carroll

Vanderbilt Ellen Clayton

Vanderbilt/CC Josh Denny

Vanderbilt Todd Edwards

Vanderbilt Martin Langanke

Vanderbilt/CC Brad Malin

Vanderbilt Tracy McGregor

Vanderbilt Nate Mercaldo

Vanderbilt Kazeem Oshikoya

Vanderbilt Josh Peterson

Vanderbilt Dan Roden

Vanderbilt Jonathan Schildcrout

Vanderbilt Martha Shrubsole

Vanderbilt/CC Sarah Stallings

Vanderbilt Mary Stroud

Vanderbilt Olivia Veatch

Vanderbilt Sara Van Driest

Vanderbilt Digna Velez-Edwards

Vanderbilt Wei-Qi Wei

Vanderbilt Georgia Weisner

Vanderbilt Quinn Wells

CC Melissa Basford

CC Brianne Derveloy

CC Paul Harris

CC Kayla Howell

CC Jacqueline Kirby

CC Brandy Mapes

DNAnexus Darren Ames

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| **eMERGE Network** ***Summary of the eMERGE Steering Committee*** January 25th & 26th, 2016 | Nashville, TN |
| The second Phase III eMERGE Steering Committee Meeting was held on January 25-26th, 2016 in Nashville, TN. In order to ensure that the Network continues on a productive note as we get further into our initial year, please find highlights from the Steering Committee Meeting below.  Presentation slides are [available here](https://emerge.mc.vanderbilt.edu/january-2016-steering-committee-meeting/) (login required). |
| **Day 1: Full-Day Session** |
| Welcome, Opening Remarks, General Updates – *Rongling Li*   * NIH-wide strategic Plan 2016 – 2020: turning Discovery into Health * In the proposed FY 2016 budget, NIH received a substantial increase, much of which will go into the President’s Precision Medicine Initiative. * [Michael Lauer, MD](http://www.nih.gov/about-nih/what-we-do/nih-almanac/michael-lauer-md), a medicine and public health researcher, was named as Deputy Director for Extramural Research at NIH * Meeting Goals:   + Refine the workflow and timelines for genomic sequencing   + Sites – recruiting and sample collection   + Sequencing centers – pipeline for sequencing and data delivery   + CC – Data management and network support   + WGs – genomic discovery and clinical implementation research   Network Overview – *Rex Chisholm*   * Agenda designed to facilitate workgroup cohesion; WG goals and plans should coalesce.   Genomic Data Update- *David Crosslin*   * Legacy Data Management: All legacy data received from Penn State and is being managed by the CC at UW. Analysis sets (eMERGE II Merged and Imputed set, PGx multisample called VCF) and raw data are available to sites through Aspera (can email questions to [e3helpme@uw.edu](mailto:e3helpme@uw.edu) for help). * ***Pre-eMERGE 3 data is due to the CC by Mon, 29 February 2016***. Currently data has been received from 6 sites. * BAMs and multisample VCFs from eMERGE-Seq sequencing data will be harvested, created, and stored by the CC. * The CC is comparing two different imputation methods (Michigan Imputation Server/MInimac3 and IMPUTE 2) and two different reference panels (Haplotype Research Consortium and 1000 Genome) for speed and metrics.   **ACTION ITEM: Sites should submit pre-eMERGE 3 data to** [**David Crosslin**](mailto:davidcr@uw.edu) **by 29 February 2016. (for questions, email e3helpme@uw.edu).**  eMERGE-Seq: Technical and Operational Details for Data Collection and Reporting- *Niall Lennon & Richard Gibbs*   * The eMERGE-Seq panel is 535 Kb: 109 genes and 1552 SNPs (including ancestry and fingerprint SNPs). * CLIA/CAP validation tests for sample preparation and sequencing underway and expected to be complete by 2/16/2016. Reagent performance has been outstanding (102/109 genes have 100% coverage at greater than 20x. 1540/1551 SNPs have coverage greater than 20x). Minor differences are being scrutinized manually.   Overview of Site Recruitment and Return of Results Plans- *Heidi Rehm*   * The CSGs conducted site interviews to determine preferences for return of results and cohort characteristics.   + Most sites samples are CLIA compliant, so will not need new blood draws. Note: CSGs expect to receive only DNA samples from peripheral blood.   + Most sites are ***not*** planning to give the clinical reports directly to patients/providers.   + Most sites are expecting to return ACMG56 genes, their own top 6, some SNPs, and PGx variants. Some intend to return carrier status and other sites’ top 6 genes.   + Most sites want both Pathogenic and Likely Pathogenic variants reported.   + Partners/Broad is discussing the possibility of uploading all variants into GeneInsight so investigators have the ability to search all variants sequenced, whether or not they are returned. * CSGs are working on solutions to provide reports for PGx variants and negative results. In addition, site cohort recruitment and selection processes are expected to increase the number of positive results. * Partners/Broad is working on a way to query GeneInsight based on the inclusion of phenotype at submission. Sites have the ability to upload standardized disease term, a free text field, and disease status. Some available fields (e.g.: Proband, Family #, Date of Death, Germline vs Somatic) are being set to default (e.g.: Proband default to yes; no Family #; No Date of Death; Default to Germline). The group discussed constraining the free text field input to terms from a standard dictionary (ex: HPO, PheWAS, SNOWMED). Sites will upload phenotype data to a portal using a spreadsheet when samples are submitted. Considerations against inclusion of phenotype data on the report itself were discussed, including that use of ICD codes has some amount of error and could lead to possible confusion for providers who may be reading the report in clinical care and the patient does not have the phenotype listed.   **ACTION ITEM: eMERGE members with feedback or questions on GeneInsight query fields should contact** [**Heidi Rehm**](mailto:HREHM@PARTNERS.ORG)**.**  **ACTION ITEM: The Phenotyping WG will discuss standard input for the free text field and CSGs will try to accommodate.**  Content Interpretation Update: Gene Curation and Harmonizing Variant Interpretations– *Birgit Funke*   * Clinical validity (is the gene-disease association backed up by evidence?) differs from clinical actionability (would knowledge of the clinically valid variant affect management and treatment?). There are no universal or mandatory guidelines, so Network discussion is necessary and has begun. ClinGen has developed evidence assessment guidelines. All classification decisions and processes will need to be concordant with global CSG operations. * Gene Curation: 163 gene-disease pairs have been identified in the 53 top 6 genes on the eMERGE-Seq panel. 72 gene-disease pairs have been given a draft ClinGen classification. Next steps are: 1) confirm the draft classification with the experts at eMERGE sites, and 2) define actionable gene-disease pairs. * SNP Curation: This same process will be completed for SNPs. An informatics based triage script was used to categorize SNPs as benign/likely benign (51%) and separate them from other categories that need in-depth assessment to determine whether or not to include them on a report (49%). * CSGs exchanged all previously reported variants and conducted a discrepancy analysis. The two centers are 90% concordant in observed variants called pathogenic / likely pathogenic /VUS only and 67% concordant in calling all variant classification (likely due to Baylor recently adding likely benign and likely pathogenic classifications). Next steps are to compare variant classification rules and establish consensus if possible given difference of opinion.   CERC Survey Results - *Maureen Smith & Ingrid Holm*   * The goals of the survey were to 1) address the [Advanced Notice of Proposed Rule Making (ANPRM) for Revision to Common Rule](http://www.hhs.gov/ohrp/humansubjects/anprm2011page.html), 2) gather data on underrepresented populations’ perspectives on broad consent and data sharing, and 3) gather data on underrepresented populations’ perspectives on enrolling themselves and their children to one of 3 biobank model scenarios (randomly selected). * The group received the final data files on 9/4/15. The overall response rate to the survey was 16% . * Conclusions:   + Methodology: The oversampling strategy and randomization scheme were successful.   + Willingness: 1) Willingness to enroll in a biobank was greatest for the “broad controlled access” biobank model scenario and lowest for the “broad open access” biobank model scenario; 2) Willingness to enroll their child in the biobank was greatest for the broad controlled and lowest for the tiered controlled access scenario; 3) A participant’s willingness to enroll their child was much lower than their willingness to enroll themselves, no matter the biobank model scenario.   + Benefits/concerns/information needs: 1) Did not vary between scenarios; 2) Perceived benefits were lower for child than for respondents. 3) Concerns were higher for children than for respondents.   DNAnexus Tutorial– *Darren Ames*   * The capabilities of the DNANexus product were demonstrated for the Network. DNANexus provides a platform for access data and a variety of tools for working with that data, as well as compute power capable of managing large datasets and complicated analyses. * To facilitate eMERGE work, DNANexus will develop an eMERGE-tailored Dashboard. This will provide a single place for eMERGE members to go to see data, tools, apps, etc.   **ACTION ITEM: The Genomics Workgroup will create an eMERGE analysis pipeline or pipelines as needed - assembled with tools on DNANexus.**  **ACTION ITEM: The Genomics Workgroup will determine and distribute to sites a Best Practice model for DNANexus use.** |
| **Day 2: Half-Day Session** |
| Announcements– *Rex Chisholm*   * Publications Updates: Noted rapid increase in Network publications; Suggested looking at comparative citation rates between network and site-directed papers   Timelines for Recruiting and Sequencing – Rex Chisholm   * The group reviewed a proposal to complete all sequencing by end of Year 3, allowing all of Year 4 for data analysis, discovery, and reporting. The timeline assumed: accuracy in each site’s recruitment rate information, an equitable distribution between sites, that all sequencing would happen on the eMERGE-Seq panel, and used CIDR turn times to project completion dates. A possibility that sites would have the option for exomes in Year 2, if the Network agrees, was discussed. Concerns included: disruption of workflow at the CSGs themselves as some of the clinical annotation pipeline is manual and small batches would necessitate changing workflows frequently; equitable timeline might affect Network productivity since no site would have a dataset of significance until half-way thru sequencing; operations or scientific concerns that impact the sequencing and data return timeline differently at different sites, such as conducting a clinical trial and resourcing of genetic counselors. It was also noted that changing to exomes in the middle alters site strategies and might slow the process overall and increase costs. * Discussion Summary: The CC will create a revised sample flow schedule based upon site accrual rate updates that will still be completed by end of Year 3.   **ACTION ITEM: Sites will send updated accrual rates to the CC in order to restructure the sequencing timeline.**  **ACTION ITEM: The sequencing centers will update the CC with their throughput.**  **ACTION ITEM: The CC will create a second iteration of the eMERGE Sequencing Flow Timeline.**  Outcomes Workgroup Report – *Hakon Hakonarson, Josh Peterson & Marc Williams*   * To clarify the information needed in the Outcomes Map that sites are completing, sites should select and measure outcomes for clinically reported variants only and focus on process outcomes, intermediate or surrogate outcomes. The project timeframe is probably not long enough to include clinical outcomes, but those are of interest and could be pursued with other funding. * Approaches to outcome assessment include case series, cohort (most) and randomized controlled trials. The workgroup reviewed a summary of process outcome data categories that suitable for the Outcomes Map. * A conceptual framework presented with returned variants classified by whether they are accompanied by or presage any existing or subsequently developed phenotype evidence. The classifications are mapped to 1 of 5 expected levels of clinical intervention * The workgroup highlighted two additional tracks of research on outcomes – Pediatric-specific Outcomes and Economic Outcomes. Three tentative projects for the pediatrics track include: asthma, TPMT, and developmental outcomes.   **ACTION ITEM: The CC will help develop a three-tracked agenda and project flow to accommodate the Outcomes Tracks: Clinical Process-related Implementation Outcomes, Pediatrics, and Economics.**  **ACTION ITEM: The Outcomes WG will prioritize phenotype-gene pairs for outcomes data collection.**  **ACTION ITEM: The Outcomes workgroup will design a prototype outcomes evaluation (familial hyperlipidemia, familial colorectal cancer syndromes)**  **ACTION ITEM: The Outcomes WG will consider cascade testing as an approach to expand sample size and power of analyses.**  Return of Results / ELSI Workgroup Report *– Ingrid Holm & Iftikhar Kullo*   * Research projects proposed by this WG: 1) develop and publish standards for ROR for eMERGE, 2) generate a joint publication with the Clinical Annotations workgroup regarding eMERGE process and criteria for actionability of variants for return, 3) provide an overview of approaches to return of results at each site, and4) develop a repository of standard survey and other psychosocial data collection instruments, potentially accessed online via REDCap. * The concept sheet, “Approaches to Returning Clinically Actionable Results from Next Generation Sequencing Panel in a Health Population,” was discussed, and its focus on developing infrastructure for clinically contextualizing variant results for large populations through site developed algorithms and its value as a collaboration between the ROR/ELSI and EHRI workgroups were highlighted. Tracy McGregor, the concept sheet author, will circulate a revised concept sheet to both WGs prior to resubmitting it for approval. * The workgroup reviewed the RoR/ELSI data collection of what is being returned, how results are being returned, which providers will get the results, and which tools will disclose the results. The workgroup clarified that they are incorporating participants’ past medical histories into their data collection. * General process for returning results is: clinical report from CSGs via GeneInsight ⭢ Variant Clinical Contextualization ⭢ disclose results to participants ⭢ disclose negative results to participants ⭢ Assess impact on system, provider and participant. Site differences present opportunity to inform medical community broadly about practice range. * The workgroup noted potential internal collaborations with EHRI (results reporting tools), Clinical Annotation (variant clinical actionability determination) and Outcomes Workgroups (process outcomes from variant information return in the clinic), and external collaborations with CSER and IGNITE Networks, both of which encompass efforts in clinical implementation of clinical sequencing and genomics data.   **ACTION ITEM: RoR/ELSI group to complete RoR survey and determine eMERGE RoR standards**  **ACTION ITEM: Starting with ClinGen recommendations, the RoR/ELSI WG with the Clinical Actionability WG will develop an eMERGE Actionability Assessment protocol.**  **ACTION ITEM: Develop a repository of standardized surveys, potentially accessed online through REDCap.**  **ACTION ITEM: Tracy McGregor will edit concept sheet NT175 and distribute to the RoR/ELSI and EHRI workgroups, who are collaborating on this project.**  **ACTION ITEM:** **RoR/ELSI will attend some CSER workgroup meetings when there is overlap, especially in genetic education and for CSER’s Act-ROR Case presentations.**  A Proposed eMERGE 3 Ancillary Study of Impact of Return of Genomic Results to Health Care Providers*– Ingrid Holm & Iftikhar Kullo*   * Background & Impact: Little is known of healthcare providers’ perspective on the desirability, utility, actionability, and meaning of incorporating genomic sequencing results into clinical care. eMERGE is a good platform to study this due to the size of the Network’s biobank population and resulting large scale return of genomic sequencing results, expertise, and history of success. * Study aims: 1) HCP’s views on clinical genomic sequencing, 2) clinical utility of genomic sequencing results – expected and actual, 3) attitudes towards accessing genomic sequence results in the EHR. * Survey approach: baseline survey offered to HCP with patients enrolled in eMERGE III undergoing sequencing, one-month survey post-receiving results on patient questioning intent of use of information and attitudes regarding accessing genomic sequence results in EHR, and six-month survey post-receiving results on patient to assess actual use of information. * Ingrid and Iftikhar discussed submitting a coordinated administrative supplement proposal to the NHGRI to conduct the study. Partnering with other groups (International Collaboration for Clinical Genomics (ICCG) or the American Medical Association (AMA)) was discussed.   Phenotyping Workgroup Report – *Josh Denny & George Hripcsak*   * Overall workgroup goals: Producing curated phenotypes for genomic analysis, accelerating the process of phenotype curation and discovery, and advancing the science of EHR-based phenomics. * Discussion/decisions: 1.) Adoption of a standard information model to enable broader sharing of more computable phenotype elements 2.) Timeline and prioritization of e1-3 phenotypes. * Data from Common Data Model survey presented and found most inter-site consistency in codes and medication orders with good agreement on terminologies, EHR providers, and Intelligent Medical Objects Encoding use. Options for commonality to facilitate speed and sharing include: common data model; common phenotype definition language applied to local data models; or an hybrid approach. * eMERGE Information Model unfolding from these results. Starting with Core Terminologies and attributes that can be assumed supportable by all sites and incorporating support and transformations to i2b2 and OMOP models. Currently, agreed-on core terminologies are as follows:   + Diagnoses     - Core       * SNOMED-CT       * ICD     - Keep available raw ICD, SNOMED, IMO, text where they are available     - Value sets (PheWAS, OHDSI, SNOMED groupings)   + Meds: RxNorm   + Labs: LOINC * Phenotype Prioritization and Deployment:   + Twelve eMERGE 1 & 2 phenotypes have been prioritized for sites to implement on new and existing data (run 4 phenotypes at a time; target deadlines March, June, and September 2016).   + eMERGE3 phenotypes have been grouped by priority. Sites to complete primary and secondary site validation of the first, highest priority group by end of Summer 2016.   **ACTION ITEM: All sites running 12 existing eMERGE 1 & 2 phenotypes determined to be high priority. First batch of 4 phenotypes due March 2016 (2nd and 3rd due June and September 2016, respectively).**  **ACTION ITEM: CDM group will continue to develop an eMERGE Information model: 1) define expected scope of phenotype data and create a compendium of ontologies for a common model; 2) understand and develop useful table transformations; and 3) write SQL transformation code into tables to support eMERGE definitions on PheKB.**  Genomics Workgroup Report –*Megan Roy-Puckelwartz*   * eMERGE III Data Submission ID Standards: Data must be annotated with both an eMERGE ID (subject) and a unique sample ID as outlined in the New Investigator Manual. * PGx: The full 9000 subject multisample VCF is currently available on Aspera. UW is currently realigning/recalling and re-annotating a dataset that includes an additional 96 participants from CHOP. When complete, it will be available on Aspera and DNAnexus. * Genomic Data: Legacy (array and sequence) data, eMERGE III BAM files, and eMERGE III target multisample data will be stored in Aspera. * Imputation: The group decided to impute pre-eMERGE III array data using Impute 2, 1000 Genome Phase I method, consistent with the way the legacy data is imputed. * WGS data: About 3000 genomes/exomes will be available through dbGAP for eMERGE (not general users). This data is not uniformly processed or called, so basic queries have been sent to understand the cohort. * SPHINX: The tool will be updated (expanded annotation, adding indels). Including phenotype data in the tool is being discussed. The name of the tool will be adjusted to Sequence and Phenotype Integration Exchange.   **ACTION ITEM: The CC will deploy up-to-date reference and calling algorithms for the eMERGE-seq multisample VCFs and make this set available to the Network (timeline: once eMERGE-Seq data are available, expected beginning June or July 2016).**  **ACTION ITEM: Under the direction of the Genomics Workgroup, the CC will impute new pre-e3 data using the identical pipeline as the ~55,000 eMERGE II set (Impute2 to 1000 Genomes Phase 1), merge the data with the existing eMERGE II set and make the data available on DNANexus for analysis as soon as possible.**  **ACTION ITEM: CC will work with Network genomics experts to choose important WGS / WES statistics (platform, read length, depth, quality, etc) and communicate those to PIs and sites as the Network collects shareable WGS and WES data. (Due for presentation at the March PI Meeting in March).**  Efficacy of Whole Genome Sequencing: Impact of Clinically Actionable Genomic Variants Over a Lifetime - *Scott Hebbring & Murray Brilliant*   * Studies leveraging extensive genetic data have provided evidence towards the following conclusions: 1.) nearly all people carry loss of function alleles 2.) Nearly all people carry presumed pathogenic alleles 3.) Nearly all people carry common variants associated with complex phenotypes. * This study investigated the hypothesis that Next-Gen sequencing technologies may make a clinical impact over a lifetime in a general patient population setting. Marshfield is uniquely situated to study this due to its EMR system and population. * The study indicates:   + Nearly all patients studied (93%) carry a clinically relevant pharmacogenetics variant, and 75% of the people studied were given one or more drugs that were potentially contraindicated by their genetic profile over their lifetime.   + 28% of the patients studied carry known pathogenic variants, and 2.5-5% of the population may be effected by disease causing variants.   + Whole genome sequencing will likely have a broad impact on healthcare in a general patient population.   EHRI Workgroup Report – *Sandy Aronson & Casey Overby*   * Focused on 3 primary areas 1) Engineering (process of report/data) flow 2) Science (evaluate effectiveness of innovative approaches) 3) Community (collaborate and engage, disseminating learning/best practices).   + Engineering: Each site shared diagrams of their workflow process. The GeneInsight group is conducting site interviews to define clinical report interface requirements at each site. For other report characteristics, sites requirements are consistent (all want complete files, sFTP preferred, none need realtime interface).   + Science: The workgroup is developing a concept sheet to investigate EHR data access, display, and clinical decision support strategies. The work on barriers begun in eMERGE II will also be further developed.   + Community: The workgroup has reached out to the eMERGE RoR / ELSI group (McGregor/Peterson concept sheet) and the Phenotyping WG (how to code and capture phenotypes).   **ACTION ITEM: GeneInsight staff will work with sites to determine best clinical report data interface format and process by March 2016**  **ACTION ITEM: The EHRI Workgroup will update the Barriers paper published during eMERGE II. Casey Overby will lead the survey information collection with assistance from the Coordinating Center.**  Clinical Annotation Workgroup Report – *Heidi Rehm & Gail Jarvik*   * Goal is agreement across the Network on what is returnable, not a templated report that doesn’t vary between sites. Default reports will include pathogenic and likely pathogenic variants. Reports my vary between sites for reasons including phenotype specific indications, local scientific interest, institution-specific PGx variant choices, and whether returning carrier status (some possible carrier status genes include MUTYH, CFTR, KCNE1, HFE, MCAD, and QTC). * Genes have been preliminarily curated for some sites and sent for feedback/review. The goal is to complete the curation process before test launch. * SNPs have been triaged and more details will be gathered from sites. They will be given a draft classification, and any discordance will be adjudicated within the workgroup. PGx SNPs are being addressed separately. Their return is made more complex by multi-variant PGx alleles and star alleles. Ultimately sites will decide which SNPs the group classifies as returnable are actually returned to their cohort.   **ACTION ITEM: The CSGs will work with sites to develop a common Clinical Report Format. Some site-specific variation, especially around SNP reporting is expected.**  **ACTION ITEM:** **Adam Gordon, Birgit Funke, and Emily Kudalkar will determine via clinical assessment which SNPs are returnable. Sites will be allowed to choose from that list which SNPs they would like on their report.**  **ACTION ITEM: Marylyn Ritchie and Josh Peterson agreed to provide feedback on pharmacogenomics variant reporting options to Adam Gordon, Birgit Funke, and Emily Kudalkar from the PGRN diplotype translation efforts.**  **ACTION ITEM: Sites should provide feedback on the draft classifications of their top 6 genes to** [**Birgit Funke**](mailto:BFUNKE@PARTNERS.ORG)**.** |
| **Summary of Action Items:**   1. Sites should submit pre-eMERGE 3 data to [David Crosslin](mailto:davidcr@uw.edu) by 29 February 2016. (for questions, email [e3helpme@uw.edu](mailto:e3helpme@uw.edu)). 2. eMERGE members with feedback or questions on GeneInsight query fields should contact [Heidi Rehm](mailto:HREHM@PARTNERS.ORG). 3. The Phenotyping WG will discuss standard input for the free text field and CSGs will try to accommodate. 4. The Genomics Workgroup will create an eMERGE analysis pipeline or pipelines as needed - assembled with tools on DNANexus. 5. The Genomics Workgroup will determine and distribute to sites a Best Practice model for DNANexus use. 6. Sites will send updated accrual rates to the CC in order to restructure the sequencing timeline. 7. The sequencing centers will update the CC with their throughput. 8. The CC will create a second iteration of the eMERGE Sequencing Flow Timeline. 9. The CC will help develop a three-tracked agenda and project flow to accommodate the Outcomes Tracks: Clinical Process-related Implementation Outcomes, Pediatrics, and Economics. 10. The Outcomes WG will prioritize phenotype-gene pairs for outcomes data collection. 11. The Outcomes workgroup will design a prototype outcomes evaluation (familial hyperlipidemia, familial colorectal cancer syndromes) 12. The Outcomes WG will consider cascade testing as an approach to expand sample size and power of analyses. 13. RoR/ELSI group to complete RoR survey and determine eMERGE RoR standards 14. Starting with ClinGen recommendations, the RoR/ELSI WG with the Clinical Actionability WG will develop an eMERGE Actionability Assessment protocol. 15. Develop a repository of standardized surveys, potentially accessed online through REDCap. 16. Tracy McGregor will edit concept sheet NT175 and distribute to the RoR/ELSI and EHRI workgroups, who are collaborating on this project. 17. RoR/ELSI will attend some CSER workgroup meetings when there is overlap, especially in genetic education and for CSER’s Act-ROR Case presentations. 18. All sites running 12 existing eMERGE 1 & 2 phenotypes determined to be high priority. First batch of 4 phenotypes due March 2016 (2nd and 3rd due June and September 2016, respectively) 19. CDM group will continue to develop an eMERGE Information model: 1) define expectation scope of phenotype data and create a compendium of ontologies for a common model; 2) understand what develop useful table transformations; and 3) write SQL transformation code into tables to support eMERGE definitions on PheKB. 20. The CC will deploy up-to-date reference and calling algorithms for the eMERGE-seq multisample VCFs and make this set available to the Network (timeline: once eMERGE-Seq data are available, expected beginning June or July 2016). 21. Under the direction of the Genomics Workgroup, the CC will impute new pre-e3 data using the identical pipeline as the ~55,000 eMERGE II set (Impute2 to 1000 Genomes Phase 1), merge the data with the existing eMERGE II set and make the data available on DNANexus for analysis as soon as possible. 22. CC will work with Network genomics experts to choose important WGS / WES statistics (platform, read length, depth, quality, etc) and communicate those to PIs and sites as the Network collects shareable WGS and WES data. (Due for presentation at the March PI Meeting in March) 23. GeneInsight staff will work with sites to determine best clinical report data interface format and process by March 2016 24. The EHRI Workgroup will update the Barriers paper published during eMERGE II. Casey Overby will lead the survey information collection with assistance from the Coordinating Center. 25. The CSGs will work with sites to develop a common Clinical Report Format. Some site-specific variation, especially around SNP reporting is expected. 26. Adam Gordon, Birgit Funke, and Emily Kudalkar will determine via clinical assessment which SNPs are returnable. Sites will be allowed to choose from that list which SNPs they would like on their report. 27. Marylyn Ritchie and Josh Peterson agreed to provide feedback on pharmacogenomics variant reporting options to Adam Gordon, Birgit Funke, and Emily Kudalkar from the PGRN diplotype translation efforts. 28. Sites should provide feedback on the draft classifications of their top 6 genes to [Birgit Funke](mailto:BFUNKE@PARTNERS.ORG) |
| **Next Meeting:** May 5-6, 2016 | Bethesda, MD |
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