eMERGE Network Steering Committee & ESP Meeting
October 7-8, 2013
Bethesda, MD

Attendance

Network Members in Attendance

CCHMC/BCH	Armand Antommaria
CCHMC/BCH	Beth Cobb
CCHMC/BCH	John Harley
CCHMC/BCH	Todd Hoffert
CCHMC/BCH	Ingrid Holm
CCHMC/BCH	Zak Kohane
CCHMC/BCH	Todd Lingren
CCHMC/BCH	Melanie Myers
CCHMC/BCH	Bahram Namjou
CCHMC/BCH	Cassandra Perry
CCHMC/BCH	Cindy Prows
CCHMC/BCH	Guergana Savova
CCHMC/BCH	Imre Solti
CHOP	Berta Castillo
CHOP	John Connolly
CHOP	Hakon Hakonarson
CHOP	Michael Holmes
CHOP	Brendan Keating
CHOP	Frank Mentch
CHOP	Patrick Sleiman
CHOP	Lyam Vazquez
Geisinger	David Carey
Geisinger	Andy Faucett
Geisinger	Helena Kuivaniemi
Geisinger	David Ledbetter
Geisinger	Gerard Tromp
Geisinger/U. Maryland	Casey Overby
Geisinger	Marc Williams
GH/U WA	David Carrell
GH/UWA	Andrea Civan
GH/U WA	David Crosslin
GH/UWA	Andrea Hartzler
GH/U WA	Gail Jarvik
GH/U WA	Eric Larson
Marsh/Essentia/PSU	Gretta Armstrong
Marsh/Essentia/PSU	Molly Hall
Marsh/Essentia/PSU	Simon Lin
Marsh/Essentia/PSU	Cathy McCarty
Marsh/Essentia/PSU	Peggy Peissig
Marsh/Essentia/PSU-CC	Marylyn Ritchie
Marsh/Essentia/PSU	Shefali Verma
Mayo	Sue Bielinski
Mayo	Chris Chute
Mayo	Mariza de Andrade
Mayo	Hayan Jouni
Mayo	Iftikhar Kullo
Mayo	Jen McCormick
Mayo	Adelaide Olson
Mayo	Jyoti Pathak
Mayo	Caer Rohrer Vitek
Mt. Sinai/Columbia	Erwin Bottinger
Mt. Sinai/Columbia	Steve Ellis
Mt. Sinai/Columbia	Eimear Kenny
Mt. Sinai/Columbia	Saskia Sanderson
Northwestern	Sharon Aufox
Northwestern	Rex Chisholm
Northwestern	Geoff Hayes
Northwestern	Abel Kho
Northwestern	Laura Rasmussen-Torvik
Northwestern	Luke Rasmussen
Northwestern	Justin Starren
Vanderbilt-CC	Kyle Brothers
Vanderbilt	Will Bush
Vanderbilt	Ellen Clayton
Vanderbilt	Dana Crawford
Vanderbilt-CC	Josh Denny
Vanderbilt	Nanibaa' Garrison
Vanderbilt	Raymond Heatherly
Vanderbilt	Tracy McGregor
Vanderbilt	Jonathan Mosley
Vanderbilt	Josh Peterson
Vanderbilt	Dan Roden
Vanderbilt-CC	Jonathan Schildcrout
Vanderbilt -CC	Sarah Stallings
Vanderbilt	Sara Van Driest
CC	Melissa Basford
CC	Jonathan Haines
CC	Lauren Melancon

Affiliate Members

Air Force	Ruth Brenner
Air Force	Ronald Miller
Air Force	David Watson
Air Force	Catherine Witkop

Network Invitees and Guests

CIDR	Kim Doheny
CIDR	Jane Romm
Moffitt Cancer Center	Gillian Bell
Moffitt Cancer Center	Howard McLeod
Moffitt Cancer Center	Dana Rollison

Monday, October 7th

Full Session

Announcements, Opening Remarks –Rex Chisholm
Rex noted that although NHGRI could not be present and the External Scientific Panel (ESP) meeting could not be held, the meeting would continue as planned with only slight changes to the agenda. Les Biesecker's talk would also be cancelled, as an NIH employee he could not attend.

eMERGE PGx Workgroup Session (Plenary)
Laura began by outlining the similarities and differences between the different sites for various aspects of the eMERGE PGx project including:

- Drug/Gene pair implementation
- Sites performing PGRNSeq sequencing
- Sites returning results directly from PGRNSeq
- Recruitment

Sites were reminded that the CC is tracking all aspects of the eMERGE PGx project through editable documents on Google drive. In addition to the grids, progress is being tracked for specific areas of the project such as enrollment. A private workgroup page and a public eMERGE PGx page are located on the eMERGE website. Each contains additional information about the project and progress made by the sites.

Two sites, Mayo and Mount Sinai, are pursuing the validation of their CLIA-run PGRNSeq platform for returning results directly without orthogonal genotyping validation. Both sites are following New York State regulations for this validation. Mayo will have 10-20 alleles whose clinical testing is valid in the NGS platform.

Process Outcomes have been organized into 7 domains:

- Recruitment (Lead: Vanderbilt & BCH)
- PGRN-Seq Sequencing (Lead: Geisinger & CHOP)
- Genotype Validation (Lead: Penn State & CHOP)
- Return of Results (Lead: CCHMC & Mount Sinai)
- Clinician Education (Lead: Mayo & CCHMC)
- Patient Education (Lead: BCH & Northwestern)
- EMR Integration & CDS (Lead: Northwestern & Vanderbilt)

Each domain site will collect descriptive meta-data (algorithm for selecting patients to genotype), quality controls and track metrics, and process outcomes (prescription change). Clinical outcome measures will be collected at the sites' discretion and capacity. Each process outcome has been defined by its lead sites. In addition to the seven process outcomes defined above, a list of optional outcomes has also been defined and sites are encouraged to participate in as many of these optional outcomes as possible.
It was noted that the Network will need to decide how to address clinical validation results that do not match PGRNSeq results. Proposed options include: select a variant call to be used by the Network with the variant repository and for future studies or discard data.

The group discussed that the eMERGE Network could have a large impact in education assessment. Quality measures for pharmacogenomics education could drive adoption. The ease of access to education, particularly at the point of care, may be important. The optimal placement of genomic results within the EMR, i.e., within a lab report, as an entry in the problem list, is unknown. CSER has made placement of genomic information in the record a cross-network comparative deliverable.

Provider response to genetic-based guided therapy is a critical variable. It could be interesting to collate information on how CDS is delivered (passive vs. active) and responded to at each site. A record of why

decisions about placement and delivery methods were made could prove valuable as implementation guides for varying environments. Each site could collect issues as they arise.

SPHINX, the repository for eMERGE PGx data, has been created. The SPHINX public side is a variant repository which will contain minimal summary phenotypic data. Variants will be searchable by gene symbols, drugs, or pathways. A password-protected private side will be a phenotypic data repository allowing eMERGE Network members access to view populations with similar phenotypes and will pull variant data on those populations from the public variant repository. Private side search criteria can include demographic data, ICD-9 and CPT codes, and medications mapped to RxNorm Qualifiers. The private site will also have the capability to put search results into charts showing demographic breakdown for subjects. Searches may also be saved.

Sites should submit all requested information to the CC for input by November 30th.

Network members were reminded that the use to the SPHINX resource, like all other resources created by and for the network, will follow the established eMERGE data sharing mechanism detailed in the Data Sharing Agreements signed by all sites and the Publication Policy.

Josh discussed potential eMERGE PGx phenotypes. These phenotypes would include drug outcome use cases and/or phenotypes for rare variants in the six ACMG priority genes overlapping PGRNSeq. A possible discovery analysis plan was also presented involving continued development of SPHINX version 1 and the eMERGE-CC (PSU) performing preliminary association analysis on common variants and burden analysis on binned rare variants.

Cross-Site PGRN-Seq Concordance
Marylyn walked the group through the differences between RAW and reduced BAMs. Reduced BAMs are approximately 10-15x faster than RAW BAMs and the extra step required seems to be worth it. Reducing the BAMs is quite variable in the amount of resources it takes ranging from 2-12GB of memory and 1-4 hours of CPU time. To date, CIDR, Mount Sinai, and UW concordance has been evaluated on the Coriell HapMap Trio samples run on the PGRNSeq platform at each institution. In summary:

- Among calling sites, there's roughly a 99% concordance after filtering with < 0.5% discordance
- Other ~0.5% is disagreement including missingness
- The CIDR pipeline is calling the most variants after filtering
- It requires much more work when the reference choice isn't the same, but the choice of reference doesn't significantly impact the results

CIDR – eMERGE PGx Update
Kim from CIDR briefly outlined data analysis information relevant to the PGx project. Samples have been received from most sites and CIDR will release the data for five of the participating sites (nearly 1300 samples) by November 1st. Quality metrics for UW, Mayo and Mount Sinai were presented and the platform is performing well.

Data Analysis Projects
The SC discussed possible data analysis projects including a descriptive analysis and a possible discovery project. Different projects were discussed including a PheWAS project around lipids and a PheWAS using ICD 9 codes (it was suggested that codes could be further grouped for rare diseases). The PGx Workgroup was charged with further defining a project and circulating to the PI group.

Genetic Variants Influencing Cardiorespitory Fitness: an EMERGE Network Project –Hayan Jouni
Hayan began by providing the group with a broad definition of cardiorespiratory fitness. CRF is studied due to its association with overall health and aging. CV outcomes underscore the public health relevance of this quantitative trait. Prior studies have shown that ~ 50% of CRF is heritable, and this algorithm will aid identification of genetic variants influencing CRF and may provide new insights into insulin

resistance, metabolic syndrome, cardiopulmonary physiology, human athletic performance and endurance. The gold standard for CRF is the maximal oxygen consumption. Due to the maximal symptom-limited exercise requires continuous ECG and physiologic monitoring by MD making this phenotype not feasible in non-EMR based cohorts. The phenotype for CRF has been defined and validated both at Mayo and at Geisinger. Six of the nine eMERGE sites have patients with CRF data. Statistical analysis has been completed and early analysis results were presented and are encouraging. Next steps include adding additional patients from eMERGE sites.

Scalable Phenotyping: Use Case of Autism –Todd Lingren and Guergana Savova

Portable phenotyping is described as a phenotype that is able to generate flexible, stable algorithms for inter-institutional discovery of phenotype cases. Factors such as EMR, clinical workflow, free-text notes, and expert resources are taken into consideration. Scalable phenotyping is the ability to process big data in a reasonable time. CCHMC/BCH proposed the following approach to generate portable scalable phenotypes, which differs from the current rule-based approach used in eMERGE, to the group:

- Apply exclusion and inclusion criteria based on ICD9 code filtering
- Acquire EMR data for the filtered patients
- Process clinical notes using Apache cTAKES to discover SNOMED-CT and RxNORM concepts and frequencies and generate feature vectors
- Apply machine learning (ML) prediction on feature vectors based on training from expert-provided labels
- Communicate ML model to other sites to run on their data

CCHMC/BCH believes there are many advantages to this proposed approach and outlined their reasoning for this through autism and extreme childhood obesity use cases. In addition to the autism and childhood obesity phenotypes, the process for machine vs. rule-based learning along with results generated from each were outlined. The group's next steps are to improve PPV, validate these phenotypes at other eMERGE sites, apply this workflow to other phenotypes, and create the framework for general portable and scalable phenotyping.

Genetic Variation associated with the Susceptibility to Herpes Zoster in the eMERGE Network — David Crosslin

Zoster (or shingles) is caused by a virus called varicella zoster virus. The patient is initially infected with the virus that causes chickenpox and the virus continues to remain latent in the body – how the virus remains latent is not well understood. David outlined the algorithm and criteria for cases and controls. Each site's basic demographics were presented and genetically determined ancestry was plotted. Including genetically defined ancestry helps to deal with unknowns in the gender data. Manhattan Plots of each ancestry were displayed and it was discussed how Mayo's data appears to be skewing the larger data set. The group is looking at associations especially as they relate to latency. David will continue to work with the data to determine what is causing this affect. Network members suggested that the diversity found within the Hispanic population may be causing this problem. It was also noted that controls are much younger than cases though it may be difficult to collect matched controls.

Replication of Gene-Gene Interaction Models Associated with Cataracts in the eMERGE Network – Molly Hall

As of October 2013, the NHGRI GWA Catalog contains 11,680 SNPs. From these SNPs, the number of associations is very small. In order to perform an epistasis analysis in the GWAS data, Molly used prior biological knowledge to evaluate specific combinations – "Candidate Epistasis". The process for doing this was outlined and two major tools were utilized: Biofilter and PLATO (PLatform for Analysis, Translation, and Organization of large-scale data). Domain data was collected from public human genetic data sources such as the Library of Knowledge Integration (LOKI). The process followed included:

- Create SNPs list
- Biofilter
- Map SNPs to genes
- Build gene-gene models
- Build SNP-SNP models

The Marshfield discovery set was compared to the replicated set, including Vanderbilt, Mayo and GroupHealth, to look for consistent direction of effect. From this analysis, Molly was able to identify the top 10 replicating SNP-SNP models, and these results demonstrate a potential biological mechanism by which gene-gene interactions may be at play in such complex disorders as cataracts. Biofilter was successfully utilized in a genome-wide interaction analysis to identify replicating/confirmatory gene-gene models related to developing cataracts. Moving forward the group will investigate the role of retinol in the development of cataracts, assess other environmental variables and their involvement in cataract status, and examine gene-environment interactions at play in cataract development.

Null (Loss of Function) Variants Project –Dana Crawford & Gerard Tromp

Null variants are any genetic variation leading to the loss of gene function. Two approaches for identifying null variants were proposed: nomination of each site's favorite null variants or brute -force annotation where "all" null variants would be pulled from the existing eMERGE data set. Some genes have been nominated. Using the eMERGE genotyping data, brute-force annotation will be performed by a few different platforms to confirm results, including SNPEff, ANNOVAR, and VAAST. A brute-force analysis approach using the PheWAS method is an exciting option that only eMERGE will be able to use because of the Network's unique data availability. It was noted that annotation and implied function is not obvious. Challenges the group will need to overcome include:

- Power – counts of heterozygotes are likely to be low, sample size, and standard analyses may not be possible;
- Phenotype definitions: nominated variants and well defined phenotypes, annotated variants and "PheWAS" approach.

The group presented possible avenues for moving forward, including beginning with the variants that were nominated and lipids. Reviewing CNVs would be of interest, but would not be feasible in a short time frame. A few potential projects and publications were also outlined: "Demonstration Project", spectrum of null variants in clinical population, genotyped vs. imputed, and a genotype-phenotype study.

Tuesday, October 8th

eMERGE Network Overview: Priorities and Goals, Review of Progress Prior to ESP Recommendations & Best Practices Topics -Rex Chisholm

Rex reviewed the Network's response to the ESP's April 2013 recommendations. In total, 273 eMERGE projects, including 103 Network studies, have either been completed or are in process. The number of eMERGE projects published by year and citation analysis for published works were reviewed. The October 2013 Genetics in Medicine special issue, led by Marc Williams and Joseph Kannry, features nine articles specific to EMR implementation and integration experiences of the Network. A genomics-specific Frontiers in Genetics special issue, led by Marylyn Ritchie, is currently in process. eMERGE science and products are disseminated by way of GWAS.org, PheKB.org, and the eMERGE RecordCounter. Myresults.org and the SPHINX repository are developing platforms for further connecting eMERGE with the larger scientific and public communities. Rex also inventoried Network-related tools specific to the following areas of eMERGE science: phenotyping, genotyping, privacy, consent, clinical decision support, natural processing languages, and clinical integration. The Network has also worked to refine the eMERGE PGx project goals and develop a plan for realistically measuring PGx implementation process outcomes and clinical outcomes across the sites. Lastly, the Network has addressed the recommendation to use common instruments among the sites' Genomic Medicine projects - using existing methods and creating new common resources, the Network is collaborating to develop an Infobutton platform, provider education, and patient/provider assessments.

Site Specific Genomic Medicine Implementation Projects

Mayo Clinic –Iftikhar Kullo
Iftikhar provided an update for the Myocardial Infarction Genes Study, also known as MI-GENES. 966 biobank participants with intermediate coronary heart disease risk were screened for 28 CHD-associated SNPs. Of the 996, 400 participants with the highest genetic risk scores were invited to participate in the randomized control trial. 231 were interested, 129 did not respond, and 40 were not interested in participating. An allocation ratio of 2:1 was used to randomly group participants so that 100 will receive Framingham and Genetic Risk Scores and 50 will receive only Framingham Risk Scores. Results will be returned via a genetic counselor and clinician. The study also includes an initial blood draw, a three and six month follow-up visit and a patient survey. The primary endpoint is LDL cholesterol and secondary endpoints comprise fat intake, activity and weight. Iftikhar briefly overviewed the screening genotyping results and the model used to integrate results into the EHR. Patient and physician focus groups were used to determine how to best communicate genomic risk. The team is interested in learning how physicians respond to genomic risk scores and also how patients comprehend risk, respond to the information and plan lifestyle changes accordingly.

Children's Hospital of Philadelphia –Hakon Hakonarson
Hakon summarized preliminary results from CHOP's Return of Results from Genomic Discoveries project. Recent discoveries and validation of disease-causing variants in rare diseases were overviewed as well as the site's process for transporting these results from CLIA validation through to the patient medical record. All results that emerge from rare disease discoveries are Sanger validated and then confirmed in a CLIA lab. Families are informed that results will be returned to them via a CAG genetic counselor if a discovery is made, findings are placed in the EMR. Hakon also briefly overviewed the return of Autism-specific CNV results. CNVs are called on the Illumina OMNI-Express and subsequently validated. Families have the choice to receive these results and if they choose to, the results are returned via a CAG genetic counselor and imported into the EMR. The study has been approved for 1,000 patients and has been completed for160 subjects so far. Feedback from families has been positive. Families are also invited to participate in more in-depth Phenotyping via CHOP's Autism center. The team is in the process of obtaining a new informed consent for the entire recruitment process to include patient/family choice for receiving "actionable" results. All existing samples will be handled based on institutional policy, which dictates that specific actionable variants of medical value/interest are returned.

Workgroup Updates

CERC Survey –Ingrid Holm
The project will assess the perceived impact of the ANPRM proposal to require consent for research on de-identified human data and specimens in biobank research on participants and patients in the eMERGE Network. Ingrid reviewed the project proposal, aims, and funding details. According to the project timeline, survey development will begin in October –November 2013, the survey will be deployed beginning April –May 2014, and survey results will be disseminated beginning June-July 2015. To accomplish tasks in a timely fashion, the full Workgroup will hold teleconferences twice a month. Subcommittees have also been assigned to accomplish tasks and these smaller groups will meet on a weekly basis. Ingrid described her and Maureen Smith's duties as co-chairs as well as Coordinating Center support, and the responsibilities of each subcommittee, which include: IRB Protocol, Literature Survey, Survey Development, Cognitive Interviews, Sampling Strategies, Data Management, and Survey Analysis.

Genomics –Dana Crawford & David Crosslin
The co-chairs presented a preliminary analysis of GroupHealth/UW's PGx sequencing project thus far. David Crosslin briefly reviewed the site's PGx algorithm; 600 samples have already been sequenced at UW and 300 at CIDR. The GATK pipeline metadata and SnpEff metadata were briefly described and preliminary analysis of the site's sequencing data was reviewed. Potential genes of interest include:

- ABCB1 –multidrug resistance
- CACNA1S & RyR1 –malignant hyperthermia

- SCN5A –transport statins associated with muscle toxicity

Carbamazepine genes of interest include: HLA-B*1502, FLOT1, SCN1A, and SCN2A. The Integrative Genomics Viewer will be used to explore the integrated datasets.

Phenotyping –Josh Denny & Peggy Peissig

The co-chairs gave a status update for current Network phenotype progress. Since June 2013, CRF (Mayo), Extreme Obesity (Geisinger), and Asthma (CHOP) have been completed. 11 Phase II phenotypes are complete and 22 are either in process or awaiting Network execution. Progress has been slowed due to limited site resources and the eMERGE PGx effort. To streamline the Phenotyping process, primary sites will now begin coordinating with other sites earlier in the process to determine if there are enough subjects available to execute a planned phenotype across the Network. Sites can then determine if they want to participate in the phenotype and if they can contribute usefully. The group could explore setting minimum thresholds for participation. The Workgroup also presented the advantages of using a portable NLP graphical user interface. As David Carrell presented, using a GUI will facilitate task-specific NLP processing with minimal or reduced deployment effort and expertise. To further streamline, the workgroup, led by Luke Rasmussen, is in the process of further developing PheKB as not only a data repository, but a validation tool for parsing data dictionary submissions for errors and formatting inconsistencies. The Workgroup is also in the process of contributing to the development of the SPHINX repository for PGx by having all sites submit demographics, diagnoses, procedures, and medication data for inclusion.

Pediatrics –Hakon Hakonarson & John Harley

Kyle Brothers discussed progress in pediatric research consent development. There is model language for biobank consent on the NHGRI website, but this group is providing specific advice for pediatric populations. They collected pediatric consent forms and abstracted them for pediatric-specific decision points. The group is currently writing a manuscript and may follow that with a more detailed white paper for policy. Vanderbilt is excluded from this project as they employ an opt-out model.

The Workgroup is exploring patient surveys and provided an overview of CHOP's intake questionnaire, comparing this data collection method to data extraction via EPIC. The intake survey is completed by the family and the recruiter and survey data are added to EMR data (Epic) and associated with the blood or saliva sample. CHOP has analyzed correlation across some measures between the survey and Epic data for validation. The intake survey typically allows for more complete data collection in terms of patient demographics, medications, and health background.

The co-chairs also reviewed standard pediatric measures, both pediatric-specific and across all age groups including adults. Sanger sequencing is currently underway at CHOP to evaluate the existence of TPMT variants within their participant population; imputation has already revealed the presence of these variants within their cohort.

Lastly, the co-chairs made recommendations to the other sites for more closely aligning pediatric and adult research efforts across the Network, which include:

- Querying EMR for existing data across all subjects
- Prospective collection of survey data for new samples
- Compiling survey information from all sites
- GWAS analysis (meta-analysis across sites) for developmental traits/milestones and pediatric/adults disease traits such as asthma or obesity.
- CNV analysis (meta-analysis across sites)

Return of Results –Gail Jarvik & Iftikhar Kullo

The co-chairs briefly reviewed site–specific RoR plans for the Genomic Medicine Pilots and PGx. Site-specific Genomic Medicine Pilots range in scope including genetic risk scores, SNPs, whole genome sequencing, and pharmacogenomics results. Current plans for returning incidental findings for PGx range across the Network from not returning these findings at all to returning based on patient choice, but plans

are still evolving at many of the sites. The co-chairs also provided status updates for Workgroup-related Network projects and described internal and external collaboration efforts.
The Workgroup, in collaboration with CERC, plans to assess patient and provider responses to return of results for PGx by identifying or developing survey instruments for use across many of the Network sites. Plans are in place to hold joint calls with CERC to discuss overlapping projects on a bi-monthly basis. Other workgroup-related efforts include:

- Hemochromatosis Penetrance Project– Identifying penetrance for relevant phenotypes in the adult, eMERGE cohort. Chart abstractions are underway at many of the sites.
- PGRN-Seq Incidental Findings –PGRN-Seq includes five incidental findings recommended for return by ACMG –CACNA1S, KCNH2, LDLR, RYR1, RYR2, and SCN5A. Most of the adult sites are interested in return of pathogenic variants.
- Chromosomal Abnormalities –Identifying phenotypic correlates of autosomal chromosome abnormalities in an attempt to standardize nomenclature. Many sites are participating in this Network project.

In close, the co-chairs reviewed the Workgroup's planned discussion topics for the joint eMERGE/CSER Return of Results Workgroup breakout session, scheduled for later in the evening.

EHR Integration –Justin Starren & Marc Williams
The Workgroup's Genetics in Medicine Special Issue was released as Volume 15, Issue 10 at the beginning of October 2013. The co-chairs briefly reviewed site-specific timelines for the following categories: EHR genomic clinical decision support, EHR integration, recruitment and sample design, and educational materials development. The co-chairs also discussed the outcomes of the joint October EHRI/CERC breakout session, which focused on developing and adapting content for genomic medicine. The EHRI Workgroup has designed an Infobutton study to standardize content and evaluate it with healthcare providers across the sites. CERC volunteers will assist with content development, IRB language, and adapting the content evaluation survey for patients. The Workgroup will invite CERC members to attend the latter half of each EHRI call to discuss project action items and progress. The co-chairs also reviewed the Infobutton project in detail, including the aims, participating sites, implementation plan, sources of content and a live demo. The co-chairs completed the update by reviewing Infobutton accomplishments thus far and future plans.

Consent, Education, Regulation, and Consultation –Ingrid Holm
Ingrid briefly overviewed the status of several ongoing projects including MyResults.org, which is a patient education website led by John Connolly. John provided a brief demonstration of the site and several of its features. Content is currently focused on PGx, but is expected to expand. Data has been collected for the Pediatric Biobanking Model Consent Language project, led by Kyle Brothers, and a manuscript is in process. A process manuscript for PGx Consent, led by Maureen Smith, is also in process. Malia Fullerton is leading the effort to address the similarities and differences in implementation strategies for joint projects taking place across diverse healthcare settings though the project is on hold for now. Ingrid briefly reviewed the timeline for the CERC Survey supplement and discussed collaborations with other eMERGE workgroups. CERC is collaborating with EHRI to contribute educational content for the Infobutton project. The Workgroup is also working with the Pediatrics Workgroup to assess consent and return of results in pediatric settings. Finally, the Workgroup is in the process of establishing joint calls with the Return of Results Workgroup to discuss common issues and overlapping projects every other month in lieu of the regularly scheduled individual calls. The two workgroups are planning a potential joint project to explore return of results issues related to the ACMG recommendations. Externally, the Workgroup is holding discussions with CSER by way of the joint eMERGE/CSER Consent, Community Engagement and Governance meeting and via the newly formed CSER Genetic Counseling Workgroup, of which Maureen Smith is an active member.

Action Items:

1. The PGx Workgroup will create a data analysis proposal with a year-end deliverable and circulate to the PI Workgroup.
2. Sites will report all eMERGE IDs from the eMERGE PGx project to Marylyn Ritchie.
3. Questions regarding specific eMERGE PGx outcomes should be directed to the lead of that particular outcome measure.
4. The Network will work to harmonize race and ethnicity among sites to ensure that this data is represented consistently in SPHINX.
5. Ellen Clayton will draft a response to NIH's Genomic Data Sharing Policy published in the Federal Register 78:57860 and circulate to the CERC group for review.
6. The Genomics Workgroup, with the guidance of the PIs, will formulate a streamlined system for putting eMERGE PGx variants into ClinVar.
7. The JAMIA special issue led by Abel Kho, Josh Denny, and Jyoti Pathak will be added to the eMERGE ESP response slides.
8. To ensure that all sites are participating in the CERC survey project, the topic of site participation in the project will be added to the next PI call.
9. The CC will coordinate with the ESP members to schedule a meeting with the PIs during the November PI call.