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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT371 | |
| **Submission Date** | 1/10/2020 | |
| **Project Title** | Placental Predicted Gene Expression Phenome-Wide Analysis | |
| **Tentative Lead Investigator** *(first author)* | Todd Edwards and Jacklyn Hellwege | |
| **Tentative Senior Author**  *(last author)* | Digna Velez Edwards | |
| **All Other Authors** | David Aronoff, Jacob Keaton, Jacqueline Piekos, Jacklyn Hellwege, Elizabeth Jasper | |
| **Sites Participating** | Open to all sites  Current participants:  Vanderbilt | |
| **Background / Significance** | This project’s premise is rooted in knowledge that mother-to-child transmission of risk for adult disease is multifactorial and begins with conception *in utero* and in the idea that the “developmental origins of health and disease” (DOHaD), shapes the future health during childhood and later adult life. The placenta is an important biological conduit to mediate the non-genomic transmission of risk for noncommunicable diseases. We propose using eMERGE genome-wide association study (GWAS) and phecode data to validate associations from a phenome-wide association study (PheWAS) of placental predicted gene expression conducted within pediatric and adult subjects within BioVU at Vanderbilt University Medical Center. The idea underlying this approach is that we can predict the gene expression of placental tissue from an adult individual with GWAS data using with an appropriate eQTL-tissue atlas because their germline DNA is unvarying and their eQTLs can predict expression. | |
| **Outline of Project** | Discovery PheWAS analyses are being conducted within BioVU, race-stratified, where we are evaluating the association between placental predicted gene expression and multiple phenotypes using summary statistics from phecode-based GWAS and other published GWAS. MetaXcan is being used for predicted gene expression analyses. We are scanning across all genes that are expressed in the placenta. Significant findings will be validated within eMERGE and results will be meta-analyzed across discovery and validation. | |
| **Desired Data - Common Variables\***  *(Available from the CC)* | Demographics  ICD9/10 codes  CPT codes  Phecodes  BMI | Common Variable Labs  Common Variable Meds  Other: Case/Control status on Phase I and Phase II phenotypes |
| **Other Desired Data *(Available from participating sites)*** |  | |
| **Desired Genetic Data** | eMERGE I-III Merged set (HRC imputed, GWAS)  eMERGE PGx/PGRNseq data set  eMERGEseq data set (Phase III)  eMERGE Whole Genome sequencing data set  eMERGE Exome chip data set  eMERGE Whole Exome sequencing data set  Other (not listed above): | |
| **Does project pertain to an existing eMERGE Phenotype?** | Yes, if so please list  No | |
| **Planned Statistical Analyses** | PheWAS | |
| **Ethical Considerations** | None | |
| **Target Journal** | Depends on results, likely a genetics journal such as Human Molecular Genetics or a general journal such as elife, Nature Communications, or Scientific Reports | |
| **Milestones**  *(This section should include the key dates for completion of project, including approval, project duration, draft completion, and submission.)* | Gather data from coordinating center: 2/2020  Conduct statistical analyses: 2-6/2020  Write manuscript: 6-8/2020  Circulate and submit manuscript: 9/2020 | |