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| **eMERGE Network: Manuscript Concept Sheet** |
| **Reference Number** *(to be assigned by CC)* | NT344 |
| **Submission Date** | 05/03/2019 |
| **Project Title** | Pleiotropic Associations Between Predicted JAK Pathway Genes’ Expression and the Clinical Phenome |
| **Tentative Lead Investigator** *(first author)* | Jacklyn N. Hellwege |
| **Tentative Senior Author** *(last author)* | Cecilia P. Chung |
| **All Other Authors**  | C. Michael Stein, QiPing Feng, Nancy Cox, Wei-Qi Wei, Josh Denny, Dan Roden |
| **Sites Participating** | Open to all sitesCurrent participants:Vanderbilt  |
| **Background / Significance** | The JAK pathway is targeted by several medications, including those which treat rheumatoid conditions. Recently there has been concern over adverse medication-related effects of specific JAK inhibitors, including an increased risk of blood clots. Given that the JAK inhibitors tofacitinib (Xeljanz) and baricitinib (Olumiant) are indicated to target different genes in the JAK pathway and may have different adverse effect profiles, we seek to investigate the clinical phenotypes associated with predicted expression of each gene encoding the JAK pathway targets.  |
| **Outline of Project** | We constructed predicted expression scores for JAK-pathway genes derived from GTEx prediction models (Predictdb.org). We will perform PheWAS of predicted JAK-pathway gene expression stratified by race and sex in the eMERGE data omitting the samples used to develop the PRS, adjusted for age, body mass index, and principal components of ancestry. We will also use meta-analysis to calculate estimates of effects and significance across races and sexes. We are also utilizing the MEGA array data at VUMC (currently ~95K).  |
| **Desired Data - Common Variables\*** *(Available from the CC)* | [x] Demographics [ ] ICD9/10 codes[ ] CPT codes[x] Phecodes[x] 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** | [x] 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 [x] No |
| **Planned Statistical Analyses** | PheWAS |
| **Ethical Considerations** | None |
| **Target Journal** | Depends on results |
| **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: 5/2019Conduct statistical analyses: 5-6/2019Write manuscript: 6-8/2019Circulate and submit manuscript: 9-10/2019 |