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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT377 | |
| **Submission Date** | 2/5/2020 | |
| **Project Title** | Defining the clinical phenome associated with genetic regulation of serum kynurenine levels | |
| **Tentative Lead Investigator** *(first author)* | Minoo Bagheri | |
| **Tentative Senior Author**  *(last author)* | Jonathan Mosley, Jane Ferguson | |
| **All Other Authors** | Mingjian Shi, Ali Manouchehri, Chuan Wang, Katherine Murray, Thomas Wang | |
| **Sites Participating** | Current participants: Vanderbilt  Open to all sites | |
| **Background / Significance** | The kynurenine-tryptophan metabolic pathway has been identified to represent a dominant role in diverse inflammatory-related diseases, including cardiovascular and neuropsychiatric disease. However, uncertainty remains about the specific role of kynurenine as a mediator or biomarker of disease. To address this controversy, we hypothesized that a better understanding of the genetic architecture of plasma kynurenine in humans might shed light on determining its relevance to cardiometabolic and neuropsychiatric disease. | |
| **Outline of Project** | We have constructed a polygenic predictor of plasma kynurenine levels using data from a large meta-analysis of metabolite genome-wide association studies. We will use PheWAS to identify candidate associations between this polygenic predictor as well as the individual SNPs comprising the predictor, and a broad range of phenotype/diseases. | |
| **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** | PLOS Genetics  Science Translational Medicine  AJHG | |
| **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: 3/2020  Write manuscript: 3/2020  Circulate and submit manuscript: 4/2020 | |