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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)* | [x] Demographics [x] ICD9/10 codes[ ] CPT codes[x] 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** | [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** | PLOS GeneticsScience Translational MedicineAJHG  |
| **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: 2/2020Conduct statistical analyses: 3/2020Write manuscript: 3/2020Circulate and submit manuscript: 4/2020 |