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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT364 | |
| **Submission Date** | 11/1/2019 | |
| **Project Title** | Associations between *HMGCR* genetic variations and non-cardiovascular effects | |
| **Tentative Lead Investigator** *(first author)* | Ge Liu | |
| **Tentative Senior Author**  *(last author)* | QiPing Feng | |
| **All Other Authors** | C Michael Stein, Vivian Kawai, Wei-Qi Wei | |
| **Sites Participating** | Current participants: Vanderbilt  Open to all sites | |
| **Background / Significance** | Statins have been widely used to lower circulating low-density lipoprotein (LDL) cholesterol levels and reduce cardiovascular (CVD) risk. Evidence from both clinical trials and retrospective cohorts support the CVD benefits of statin treatment. Yet, statin treatment may also have non-cardiovascular effects. For example, meta-analysis of large clinical trials suggested that statin treatment increased the risk of newly-onset type 2 diabetes. Furthermore, because cholesterol is critical component of neurons, lipid lowering treatment may also affect the risk of neuro-degenerative diseases such as Alzheimer’s disease and Parkinsons’ disease. | |
| **Outline of Project** | We will use the mendelian randomization principle to investigate potential pleiotropic effects of statins. We will construct genetic risk score (GRS) using single nucleotide polymorphisms (SNPs) in the *HMGCR* gene region which associated with LDL cholesterol levels in previous large genome-wide association studies (GWAS). We will test the associations between the HMGCR GRS and clinical phenotypes defined by ICD codes that available from electronic medical recodes (EHRs). We will conduct the discovery analysis in BioVU, followed by replication within eMERGE. | |
| **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 | |
| **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: 11/2019  Conduct statistical analyses: 12/2019-2/2020  Write manuscript: 2-5/2020  Circulate and submit manuscript: 5-6/2020 | |