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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT424 | |
| **Submission Date** | 05/28/2021 | |
| **Project Title** | Association Between Calcium Sensor Receptor Variants and the Clinical Phenome | |
| **Tentative Lead Investigator** *(first author)* | Heather Beasley | |
| **Tentative Senior Author**  *(last author)* | Amos M. Sakwe | |
| **All Other Authors** | Jacklyn Hellwege, Ky’Era Actkins, Lea Davis | |
| **Sites Participating** | Open to all sites  Current participants:  Vanderbilt | |
| **Background / Significance** | The calcium-sensing receptor (CaSR) lies at the center of calcium homeostasis, which is tightly regulated by circulating levels of calcitonin, parathyroid hormone (PTH) and vitamin D. Missense polymorphisms, such as rs1801725 (A986S), can reduce the sensitivity of CaSR to serum calcium and lead to various chronic diseases as a result. The effects of other inactivating variants, like rs1801726 (Q1011E), are less well established, which may be, in part, due to the fact that A986S is common among subjects of European ancestry while Q1011E is common variant among subjects of African descent. In this replication analysis, we aim to understand the phenotypic associations of these SNPs in an independent dataset and further elucidate the role of ancestry in their health outcome differences. | |
| **Outline of Project** | We will examine the clinical associations of two CaSR variants, A986S and Q1011E, through a phenome-wide association study (PheWAS). We will perform PheWAS of these SNPs in the full trans-ethnic population, adjusting for sex, age, and principal components of ancestry. Additional analyses will include stratifying by ancestry and sex. | |
| **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 the results. Targets may include a genetics journal such as Physiological Genomics, a general journal such as eLife, or an endocrinology journal. | |
| **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: 5/2021  Conduct statistical analyses: 6-7/2021  Write manuscript: 7-8/2021  Circulate and submit manuscript: 8-9/2021 | |