Application number/Title: **44578** - Phenotypic characterization of genetic variants associated with sex steroid differences

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Keywords provided by the Applicant PI to describe the research project: sex steroids, asthma, gender, phewas, polymorphisms, prostate cancer

**Application Lay Summary:**

Sex steroids are hormones that have a variety of functions in the body. Research demonstrates that alteration in levels of sex steroids play an important role in disease. The phenotypes associated with genetic variants linked to differences in sex steroid hormones are not fully known. Therefore, this study investigates the phenotypes associated with variants linked to differences in sex steroids in two common diseases: asthma and prostate cancer.

A variant associated with resistance to advanced prostate cancer has been identified. Whether possessing this variant is linked to other disease or abnormalities is currently poorly understood. Knowing this relationship is important because it will enable clinicians to be on the lookout for these disease in patients harboring the variant, thus allowing them to better treat the disease and counsel the patient about what to expect. Thus, the first part of this study will investigate the association between harboring the variant and having certain diseases or abnormal laboratory values, imaging, or physical measurement findings.

Levels of sex steroid hormone vary in men and women. Notably, differences in the frequency and severity in asthma have also been found by gender. These differences may be linked to genetic polymorphisms; genetic studies have identified multiple variants associated with severe asthma. Knowing whether these variants affect asthma severity by gender would allow clinicians to provide more optimal asthma therapy. Thus, the second part of this study will determine the effect of asthma risk genetic variants on severe asthma differentially by gender.
After implementing rigorous quality control on the data, we will use various methods, including logistic and linear regression, genome wide interaction study, and candidate gene analysis, to address to answer our research questions.