



GEN91 – Investigating New Genes for Bicuspid Aortic Valve and Related Aortopathy

OBJECTIVE: Determine if mutations in two previously-identified genes are associated with BAV and TAD in the euploid population.

ORGANIZATION

Lead Investigator: Cheryl L. Maslen PhD
Co-Investigators: G. Michael Silberbach MD
Funding Source: OHSU Knight Cardiovascular Institute

BACKGROUND AND RATIONALE

A recent study investigating the role of rare genetic variants (mutations) in the cause of BAV/TAD in Turner syndrome (TS) of individuals with BAV/TAD (cases) to those with normal cardiovascular systems (controls) revealed mutations in two genes to be specifically associated with BAV and TAD. The identities of the genes are currently under embargo as they explore the protection of intellectual property, so here will be referred to as gene1 and gene2. Mutations in gene1 were associated with BAV with genome-wide significance. Additionally, mutations in gene2 were associated with increased ascending aorta dimensions as a proxy for TAD, also with genome-wide significance.

The mutations are predicted to be deleterious to gene expression and protein function, and are therefore likely to be pathogenic. The implication of these genes in the etiology of BAV/TAD resulted in the hypothesis that mutations in these genes may be involved in the cause of BAV in the euploid population. We will investigate this hypothesis by targeted resequencing of gene1 and gene2 in a cohort of euploid BAV subjects from the GenTAC registry. Targeted resequencing provides the best coverage of the genes of interest and is therefore the preferred method for this type of study.

DESIGN

Method:

- All variants in gene1 and gene2 will be analyzed for association with BAV and aortic dimensions using a bioinformatic approach to predict which variants are deleterious.
- The data will be stratified by race/ethnic background, but all available samples will be analyzed. We will also stratify by gender, as males are at an increased risk for having a BAV.

Inclusion criteria:

- Subjects with confirmed BAV diagnosis

Samples:

- DNA

Data:

- Surgical
- Organ System Review
- Genetic
- Image
- Medication Use
- Family History
- Demographics

CONCLUSIONS

Results:

- Pending