



GEN92 – Investigating the Genetics of Bicuspid Aortic Valve and Related Aortopathy in Turner Syndrome

OBJECTIVE: Determine if variants in an X chromosome gene interact with previously-identified BAV/TAD-specific mutations, and to determine if there is a parent-of-origin effect in the cause of BAV/TAD in TS.

ORGANIZATION

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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. A potential interaction was identified between gene1, gene2 and a gene on the X chromosome (gene3). Since whole exome sequencing does not capture complete information on X chromosome genes, there is not sufficient information on gene3 to complete the analysis. Hence, we are requesting DNA from the TS cohort to resequence gene3. In addition, we are interested in exploring parent-of-origin effect on the cause of BAV/TAD in TS and request additional DNA on the TS cohort to determine parent of origin of the X chromosome. This data will help us gain a more complete understanding of the genetic underpinnings of BAV/TAD in TS.

DESIGN

Method:

- Gene3 will be sequenced using NextGen sequencing to identify variants within the coding and regulatory regions of those genes. Gene x gene interactions with gene1 and gene2 will be explored.
- Parent of origin will be determined by examining methylation patterns on imprinted genes on the X chromosome of 45,X0 TS subjects, using targeted bisulfide sequencing of that genomic region.

Inclusion criteria:

- Subjects with confirmed Turner diagnosis
- Female

Samples:

- DNA

Data:

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

CONCLUSIONS

Results:

- Pending