



## GEN33 - Burden of rare exomic variants in patients with thoracic aortic dissections

**OBJECTIVE:** To identify rare exomic variants in patients with sporadic TAD.

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### ORGANIZATION

*Lead Investigator:* Diana Milewicz MD, PhD

*Co-Investigators:* John Belmont MD, PhD, Siddharth Kumar Prakash MD, Dongchuan Guo PhD, Suzanne M. Leal PhD, Scott LeMaire MD

*Funding Source:* GenTAC and NHLBI SCCOR

*Samples:*

- Genetic material

*Data:*

- Demographic data

### BACKGROUND AND RATIONALE

Research project GEN01 identified a major locus for sporadic thoracic aortic aneurysms and dissections (TAAD). However, the previous SNP array was unable to detect rare genomic variants. These rare genomic variants are hypothesized to have a larger effect in terms of disease risk than common genetic variants. We propose to use the most updated technology of Illumina exome rare variant array to test if rare exomic variants are enriched in genes in patients of European descent with sporadic thoracic aortic dissections (TAD; both type A and B dissections). The results of this study could potentially identify genes that increase the risk for TAD and provide insight into the molecular pathogenesis of the disorder.

### DESIGN

*Inclusion criteria:*

- Study participants of European descent with sporadic thoracic aortic dissections

*Exclusion criteria:*

- Study participants with the following: mutations in known TAAD genes, known syndrome, or family history of TAAD

### CONCLUSIONS

*Results:*

- Identification of a gain-of-function mutation in PRKG1 as a cause of thoracic aortic disease provides further evidence that proper SMC contractile function is critical for maintaining the integrity of the thoracic aorta throughout a lifetime

<http://www.ncbi.nlm.nih.gov/pubmed/23910461>

