**WHOLE EXOME SEQUENCE FOR THORACIC AORTIC ANEURYSMS**

B.A. Ziganshin, A.E. Bailey, C. Coons, D. Dykas, P. Charilaou, L.H. Tanriverdi, L. Liu,

M. Tranquilli, A.E. Bale, **J.A. Elefteriades**

Aortic Institute at Yale-New Haven, and Department of Genetics, Yale University School of Medicine, New Haven, CT, USA

*Background*: Hereditary factors play an important etiologic role in thoracic aortic aneurysm and dissection (TAAD), with a number of genes proven to predispose to this condition. We initiated a clinical program for routine genetic testing of individuals for TAAD by whole exome sequencing (WES). Here we present our initial results.

*Methods*: The WES was performed in 102 patients (mean age 56.8 years; range 13 to 83; 70 males [68.6%]) with TAAD. The following 21-gene panel was tested by WES: ACTA2, ADAMTS10, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, ELN, FBLN4, FLNA, FBN1, FBN2, MYH11, MYLK, NOTCH1, PRKG1, SLC2A10, SMAD3, TGFB2, TGFBR1, TGFBR2.

*Results*: Seventy-four patients (72.5%) had no medically important genetic alterations. Four patients (3.9%) had a deleterious mutation identified in the FBN1, COL5A1, MYLK, and FLNA genes. Twenty-two (21.6%) previously unreported suspicious variants of unknown significance were identified in 1 or more of the following genes: FBN1 (n [ 5); MYH11 (n [ 4); ACTA2 (n [ 2);COL1A1 (n [ 2); TGFBR1 (n [ 2); COL3A1 (n [ 1); COL5A1 (n [ 1); COL5A2 (n [ 1); FLNA (n [ 1); NOTCH1 (n [ 1); PRKG1 (n [ 1); and TGFBR3 (n [ 1). Identified mutations had implications for clinical management.

*Conclusions*: Routine genetic screening of patients with TAAD provides information that enables genetically personalized care and permits identification of novel mutations responsible for aortic pathology. Analysis of large data sets of variants of unknown significance that include associated clinical features will help define the mutational spectrum of known genes underlying this phenotype and potential identify new candidate loci.