Abstract ID: - 52

Abstract Topic: - Complex traits and polygenic disorders

Abstract Title: - Identification of deleterious mutations in genes associated with cardiomyopathy in the pathogenesis of atrial fibrillation

Presenting author name: - Aarthi Manoharan

Presenting author institute: - Aarupadai Veedu Medical College

Co-authors name: - Manoranjani M, Ravikumar S, Anand Sekar

Co-authors institute: - Aarupadai Veedu Medical College, Aarupadai Veedu Medical College, Aarupadai Veedu Medical College

Aims: - Atrial fibrillation (AF) is the most common cardiac arrhythmia. Atrial remodeling of both heart structure (increased fibrosis and atrial dilatation) and ion channel function play an important role in both triggering and maintaining AF. Persistent AF can lead to arrhythmia-induced cardiomyopathy. Prevalence of AF in cardiomyopathy patients is up to six-fold higher compared to general population. The aim of the study is to identify pathogenic variants in genes associated with cardiomyopathy in AF patients.

Methods: - We performed targeted sequencing of 200 genes involved in cardiomyopathy in 17 patients diagnosed with atrial fibrillation and dilated cardiomyopathy on Illumina sequencing platform.

Results: - This study identified mutations in genes encoding sarcomeric proteins MYH7 (p.Gly1928Asp), TTN (p.Pro581Ser), myocardial desmosomal structures DSG2 (p.Pro528Ala), calcium release channel on the sarcomeric reticulum RyR2 (p.Glu2959Ala), lamins the nuclear filament proteins LMNA (p.Arg644Cys), cardiac myosin-binding protein MYBPC3 (p.Ser25Cys), splicing factor that targets multiple pivotal cardiac genes RBM20 (p.Arg726Ter) and PSEN2 (p.Tyr427His) that regulates the systolic function of heart by modulating Ca2+ signaling via interactions with RyR2.

Conclusions: - This study highlights the role of pathogenic mutations in cardiomyopathy associated genes in triggering AF as sarcomeric structural changes and ion function changes may induce atrial electric abnormalities leading to AF.

Keywords: - This study identified mutations in genes encoding sarcomeric proteins MYH7 (p.Gly1928Asp), TTN (p.Pro581Ser), myocardial desmosomal structures DSG2 (p.Pro528Ala), calcium release channel on the sarcomeric reticulum RyR2 (p.Glu2959Ala), lamins the nuclear filament proteins LMNA (p.Arg644Cys), cardiac myosin-binding protein MYBPC3 (p.Ser25Cys), splicing factor that targets multiple pivotal cardiac genes RBM20 (p.Arg726Ter) and PSEN2 (p.Tyr427His) that regulates the systolic function of heart by modulating Ca2+ signaling via interactions with RyR2.