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Molecular analysis of inherited cardiomyopathy using next generation semiconductor sequencing technologies.

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Abstract

BACKGROUND: Cardiomyopathies are the most common clinical and genetic heterogeneity cardiac diseases, and genetic contribution in particular plays a major role in patients with primary cardiomyopathies. The aim of this study is to investigate cases of inherited cardiomyopathy (IC) for potential disease-causing mutations in 64 genes reported to be associated with IC.

METHODS: A total of 110 independent cases or families diagnosed with various primary cardiomyopathies, including hypertrophic cardiomyopathy, dilated cardiomyopathy, restrictive cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, left ventricular non-compaction, and undefined cardiomyopathy, were collected after informed consent. A custom designed panel, including 64 genes, was screened using next generation sequencing on the Ion Torrent PGM platform. The best candidate disease-causing variants were verified by Sanger sequencing.

RESULTS: A total of 78 variants in 73 patients were identified. After excluding the variants predicted to be benign and VUS, 26 pathogenic or likely pathogenic variants were verified in 26 probands (23.6%), including a homozygous variant in the SLC25A4 gene. Of these variants, 15 have been reported in the Human Gene Mutation Database or ClinVar database, while 11 are novel. The majority of variants were observed in the MYH7 (8/26) and MYBPC3 (6/26) gene. Titin (TTN) truncating mutations account for 13% in our dilated cardiomyopathy cases (3/23).

CONCLUSIONS: This study provides an overview of the genetic aberrations in this cohort of Chinese IC patients and demonstrates the power of next generation sequencing in IC. Genetic results can provide precise clinical diagnosis and guidance regarding medical care for some individuals.

KEYWORDS: Inherited cardiomyopathy; Mutation; Next generation sequencing; TTN

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