UNIVERSITÀ DEGLI STUDI DI PADOVA

SELEZIONE PUBBLICA N. 2022N51, PER ESAMI, PER L'ASSUNZIONE A TEMPO INDETERMINATO DI N. 1 PERSONA DI CATEGORIA D, POSIZIONE ECONOMICA D1, AREA SOCIO-SANITARIA, A TEMPO PIENO, PRESSO L'UNIVERSITÀ DEGLI STUDI DI PADOVA. TECNICO DI LABORATORIO BIOMEDICO - PROFILO CONVENZIONATO CON IL S.S.N.

QUESITI COLLOQUIO

1. Banche dati e linee guida per la nomenclatura e classificazione delle varianti genetiche per le patologie cardiovascolari.
2. Secondo le correnti linee guida cosa deve contenere il pannello genico per la cardiomipatia aritmogena e quali tools vengono utilizzati per la prioritizzazione genica e la classificazione delle varianti genetiche. Se l'analisi bioinformatica identifica la variante c.6517G>A nel gene della *FBN1-classe3*, tale variante dovrebbe essere riportata nel report e perché?
3. Cos'è la VEQ?
4. Femmina di 60 anni, riferita dall'ambulatorio di scompenso di Treviso per una possibile cardiomiopatia eredo-familiare, si sottopone al test genico.
   a. Secondo le correnti linee guida quali sono i geni di maggior rilievo contenuti nel pannello genico?
   b. Se l'analisi bioinformatica evidenzia la variante c. 2549delA sul gene *APOB- classe 5*, tale variante dovrebbe essere riportata nel report e perché?
5. A cosa serve l'ISO 15189?
6. Cosa prevedono le linee guida per il sequenziamento di nuova generazione?

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Article

Next-Generation Sequencing Gene Panels in Inheritable Cardiomyopathies and Channelopathies: Prevalence of Pathogenic Variants and Variants of Unknown Significance in Uncommon Genes

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Citation: Mazzaccara, C.; Lombardi, R.; Mirra, B.; Barretta, F.; Esposito, M.V.; Uomo, F.; Caiazza, M.; Monda, E.; Losi, M.A.; Limongelli, G.; et al. Next-Generation Sequencing Gene Panels in Inheritable Cardiomyopathies and Channelopathies: Prevalence of Pathogenic Variants and Variants of Unknown Significance in Uncommon Genes. *Biomolecules* **2022**, *12*, 1417. https://doi.org/10.3390/biom12101417

Academic Editors: Elena Sommariva, Milena Bellin and Chiara Di Resta

Received: 27 July 2022
Accepted: 30 September 2022
Published: 3 October 2022

Abstract: The diffusion of next-generation sequencing (NGS)-based approaches allows for the identification of pathogenic mutations of cardiomyopathies and channelopathies in more than 200 different genes. Since genes considered uncommon for a clinical phenotype are also now included in molecular testing, the detection rate of disease-causing variants has increased. Here, we report the prevalence of genetic variants detected by using a NGS custom panel in a cohort of 133 patients with inherited cardiomyopathies (n = 77) or channelopathies (n = 56). We identified 82 variants, of which 50 (61%) were identified in genes without a strong or definitive evidence of disease association according to the NIH-funded Clinical Genome Resource (ClinGen; "uncommon genes"). Among these, 35 (70%) were variants of unknown significance (VUSs), 13 (26%) were pathogenic (P) or likely pathogenic (LP) mutations, and 2 (4%) benign (B) or likely benign (LB) variants according to American College of Medical Genetics (ACMG) classifications. These data reinforce the need for the screening of uncommon genes in order to increase the diagnostic sensitivity of the genetic testing of inherited cardiomyopathies and channelopathies by allowing for the identification of mutations in genes that are not usually explored due to a currently poor association with the clinical phenotype.

Keywords: cardiomyopathies; channelopathies; next-generation sequencing; genetic testing; uncommon genes; diagnostic sensitivity; genes panel analysis; inherited diseases

1. Introduction

Inheritable cardiomyopathies and channelopathies are disorders with phenotypic and genetic heterogeneous features caused by the presence of structural or electrical heart abnormalities [1]. Variable penetrance and incomplete expression are also common and may be due to the interaction of the causal mutation with modifier genes, epigenetic changes, environmental factors, or individual factors such as age, gender, ethnicity, or physical activity [2]. According to their functional and morphological features, cardiomyopathies are commonly classified as hypertrophic cardiomyopathy (HCM), arrhythmogenic cardiomyopathy (ACM), dilated cardiomyopathy (DCM), or restrictive cardiomyopathy (RCM) [3].