APPLYING GENOMICS TO BIOMEDICINE
DIAGNOSIS OF ARRHYTHMOMEGIC RIGHT VENTRICULAR DYSPLASIA
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INTRODUCTION
The arrhythmogenic right ventricular dysplasia/cardiomypathy (ARVD/C) is an inherited heart disease. It is characterized by death of myocytes in the right ventricle and their replacement by fibro-fatty tissue. Major genetic defects are found in desmosomes whose function is cell adhesion. Sudden cardiac death (SCD) is the main problem of ARVD; around of 20% of SCD are involved by ARVD (table 1). 50% of cases have familial distribution with at least one affected patient. The pattern of inheritance is AD and the prevalence range is 1:2500, but varies between populations.

The main objective is to discuss the possibility of applying genomics to biomedicine as a genetic test for a long-term disease, for example in ARVD; extrapolating this use in many diseases such as cancer and cardiomyopathies. In particular, presentation of all features of ARVD: clinical characteristics, genetic causes, genetic testing and genetic counseling. Also, introducing a real case to explain improvement of applying genomic testing.

OBJECTIVES
The real case

To introduce genetic testing in ARVD, here it is presented a familial with two affected females (figure 2). They were diagnosed when they were 30-35 years old. Any genetic test hasn’t been done and any mutation hasn’t been found. Also, sons and daughters are too young to present any clinical symptoms. The possible genetic diagnostic is explained in this work.

GENETIC CAUSES
PKP2: is the most prevalent gene affected in ARVD. There are more than 150 pathogenic mutations identified only in PKP2 that represent 35-40% of total ARVD cases. A lot of types of mutations have been detected (CNV, splicing, missense, nonsense and frameshift).

DSC2, DSG2, DSP and JUP are genes that encodes desmosomes, too (table 2 and figure 3). More than 200 mutations have been found in this four genes. Majority of variations are punctual changes as missense mutations. All types of mutations may be detect.

Non-desmosomal genes: recent genes have been discovered, these could relate with cases of misdiagnosis and are important in genetic test; their prevalence is low (10%). These genes are: DES, TGFβ3, TMEM43. LAMA, TTN and PLN (table 2). They encode, mainly, intermediate filaments or regulatory elements.

In ARVD/C Genetic Variants Database, it is possible to find all variants in this 12 genes with all important information. For that is a good tool for genetic diagnostic.

CONCLUSIONS
• ARVD is a polygenic disease and can evolve to a SCD (20%) or other malignant symptoms.
• Applying genomics to biomedicine may help as a good tool in some complicated diseases as cardiomyopathies or cancer.
• Whole-genome testing will be important in research and diagnostic to these diseases.
• Genetic causes and diagnostic of ARVD have been explained to solve real cases of affected families and the manner to help to improve their life.

REFERENCES