# The Genetics of Brugada Syndrome in Malta - a study using Next-Generation DNA Sequencing

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## Introduction

Brugada syndrome (BrS) is an inherited arrhythmia syndrome associated with increased risk of sudden cardiac death (SCD). Clinical diagnosis is based on defined ECG criteria. Distinction between sporadic and familial BrS is difficult on clinical assessment only. Molecularly, pathogenic variants associated with BrS have been identified in over 16 genes and new genes are emerging.

## Aim

In this study we present the molecular genetic findings in 12 Maltese patients with a clinical diagnosis of BrS using a panel of genes implicated in inherited arrhythmia syndromes.

## Methods

Criteria for inclusion included a definite clinical diagnosis of BrS as per the Shanghai BrS Score System. Molecular genetic analysis was done using a panel of 174 genes (Illumina TruSight Cardio Sequencing Kit) by next-generation sequencing (NGS). Results were filtered for genes specifically implicated in arrhythmias. A total of 76 genes were screened for each patient.

## Results

Analysis of results identified 7 clearly pathogenic mutations in 7 patients, 3 genes for BrS and 4 genes associated with other arrhythmia syndromes. Mutations of uncertain significance were identified in 3 patients. The genetic results will be presented and correlated to the clinical features.

## Conclusion

This is the first study on the genetics of BrS in Malta. Genetic analysis is essential in the correct aetiological diagnosis of patients presenting with clinical features of BrS. NGS using a large gene panel is the appropriate platform. This study highlights the feasibility of NGS testing locally. The genetic result will enable adequate and cost-effective follow-up of familial individuals at risk of SCD.