UNCOVERING GENETIC DRIVERS OF CARDIOVASCULAR DISEASE IN BRAZIL: INSIGHTS FROM NEXT-GENERATION SEQUENCING OF 3,869 CASES IN THE MAPA GENOMA BRASIL PROJECT

Lucas Pires[1], Fernando Giugni[1], Bianca Linnenkamp[1], Bruno Stephan[1], Giovanna Napolitano[1], Eder Moura[1], Atmis Haidar[1], Mariana Carvalho[1], Luciana Sacilotto[1], Emanuelle Marques[1], Rogério Rosa[1], Layara Lipari[1], Vinicius Correa[1], José Krieger[12], Pesquisadores Mapa Genoma Brasil[12]

[1] Instituto do Coração (InCor), São Paulo, Brasil
[2] Beneficência Portuguesa, São Paulo, Brasil

Introduction

Advances in genetic sequencing have transformed cardiovascular medicine by enabling the identification of pathogenic variants that can inform diagnosis, prognosis, treatment, and family screening. In genetically admixed populations like Brazil's, large-scale sequencing initiatives are essential to uncover the underrepresented genetic contributions to cardiovascular diseases.

Objective

To report the findings and implementation experience of a large-scale, multicenter precision medicine initiative in cardiology, the MAPA Genoma Brasil Project.

Methodology

This is an ongoing prospective multicenter study enrolling individuals with clinical diagnoses suggestive of inherited cardiovascular diseases, including cardiomyopathies, channelopathies/arrhythmias, dyslipidemias, thoracic aortic diseases, and congenital heart defects, between January 2021 and June 2025. Genetic testing was performed using whole-exome or whole-genome sequencing on the Illumina platform. Variant calling was conducted using GATK HaplotypeCaller, and annotation and prioritization were done through the Franklin platform by Genoox. Variants were classified according to ACMG guidelines. Secondary findings were disclosed when participants consented. Relatives of probands carrying relevant variants underwent targeted Sanger sequencing and clinical evaluation when indicated. All participants received both pre- and post-test genetic counseling, and cascade testing was offered to at-risk relatives.

Results

A total of 3,869 probands and 1,399 relatives were included. Median age was 50 years [36–60] for probands and 40 years [25–53] for relatives; 45% and 61% were female, respectively. Self-reported race among probands was 50% White, 35% Admixed, and 13% Black. Median age at diagnosis was 43 years [30–54], and 63.9% had a positive family history. Cardiomyopathies accounted for the majority of cases (61%), followed by thoracic aortic diseases (15%), dyslipidemias (9%), arrhythmias (8%), and congenital heart diseases (7%). Among relatives, 45% carried the familial variant.

Conclusions

The MAPA Genoma Brasil Project represents one of the largest precision medicine efforts in cardiovascular genetics in Latin America. The initiative enabled the identification of key disease-associated genes, improved diagnostic yield, and facilitated family-based screening. These findings underscore the feasibility and clinical value of integrating genomic medicine into national healthcare systems, particularly in admixed populations.

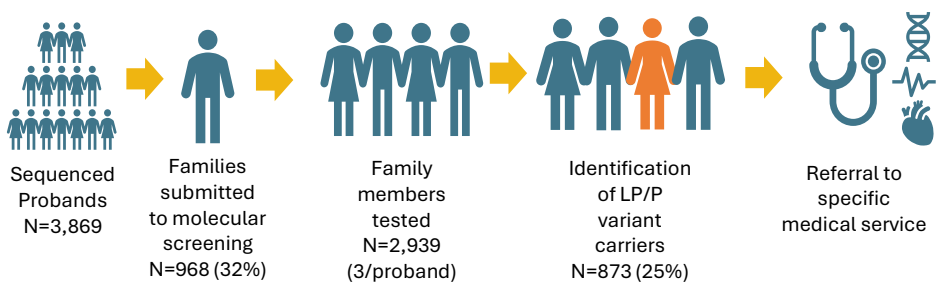

Figure 1. Family molecular/clinical screening workflow

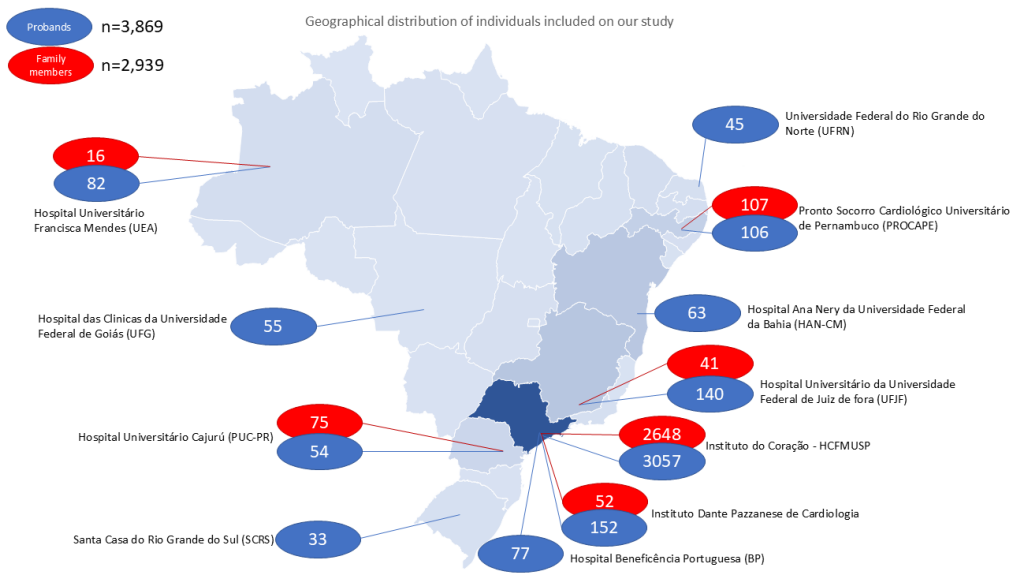

Figure 2. Distribution of individuals tested from each cardiology center

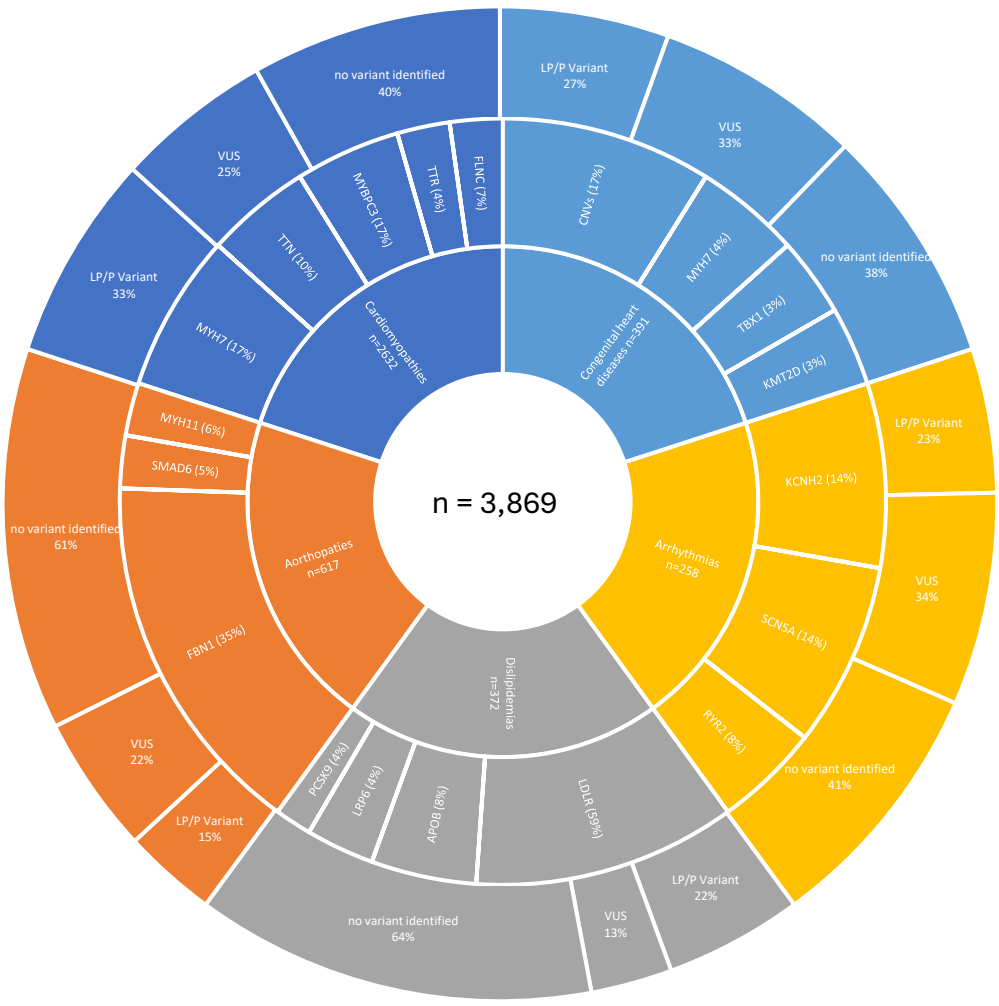

Figure 3. Distribution of individuals tested by main diagnosis, most common genes identified and diagnostic yield.

References

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