SickKids
Industry Partnerships & Commercialization

TECHNOLOGY BRIEF

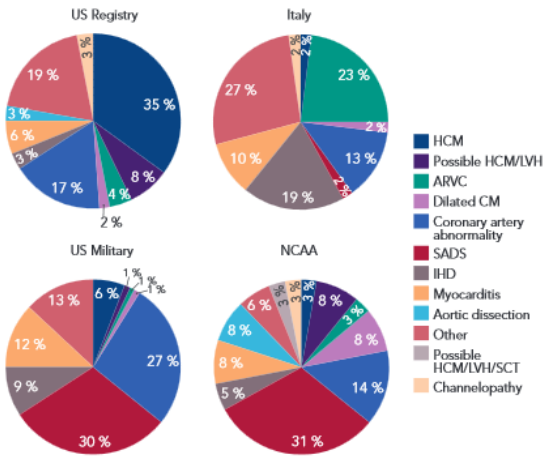
DIAGNOSTICS & RESEARCH TOOLS
Highly sensitive diagnostic tests for the prevention of sudden cardiac death

BACKGROUND

Sudden cardiac arrest (SCA) is the abrupt loss of heart function, breathing, and consciousness. SCA is usually caused by an electrical disturbance in the heart, which disrupts heart pumping and consequently the blood flow. In the case of a defect in electrical impulses or in the sinus node, SCA can lead to abnormal heart rhythm or arrhythmia. If not treated immediately, SCA can lead to Sudden Cardiac Death (SCD), which is the second largest cause of life-years lost in the US. Some SCD disorders are difficult to diagnose, including Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) and Brugada Syndrome (BrS).

ARVC is an inherited disease of the desmosomal proteins that hold together cardiomyocytes, and can result in sudden cardiac death. The prevalence of ARVC is as high as 1 in 1000 individuals, accounting for 11% of SCD in adults, 22% in athletes, and 25% in children. Currently, ARVC is diagnosed using a combination of imaging and electrocardiography in addition to genetic screening. However, 2/3 of ARVC patients are gene-elusive and go undiagnosed. Disease management includes exercise restriction and an implantable defibrillator for high risk cases.

BrS is a heritable disorder associated with an increased risk of SCD from ventricular arrhythmias and is characterized by a unique ECG pattern of coved "ST" segment elevation (>2mm) followed by a negative T wave in anterior chest leads (called the Type 1 Brugada Syndrome pattern). BrS causes 4-12% of SCD, where 20% of the patient hearts are structurally normal. The world prevalence is 1 in 2,000 persons, but it is much higher in those of southeast Asian descent. Once diagnosed, patient management includes alcohol avoidance and implantation of a defibrillator for high-risk cases.



ARVC = arrhythmogenic cardiomyopathy; CM = cardiomyopathy; HCM = hypertrophic cardiomyopathy; IHD = ischaemic heart disease; LVH = left ventricular hypertrophy; NCAA = National Collegiate Athletic Association; SADS = sudden arrhythmic death syndrome; SCT = sickle cell trait. Reproduced with permission from Harmon et al.[13] with data taken from Corrado et al.[7]

Fig 1: Comparison of causes of Sudden Cardiac Death

KEYWORDS
Arrhythmogenic right ventricular cardiomyopathy, sudden cardiac death, Brugada Syndrome, biomarker, autoantibody, diagnostic

DESCRIPTION OF THE INVENTIONS

ARVC: The Hamilton lab has discovered an anti-desmosome autoantibody that is present in the blood of subjects with ARVC but is absent in healthy individuals. Levels of antibody track with arrhythmia burden and specific epitopes targeted by the antibody have been identified. As an alternative to current diagnostic methods, a clinical ELISA has been developed as a simple, cost-effective test to identify the presence and severity of the ARVC condition, allowing for sensitive and specific diagnosis to inform treatment and prevent SCD.

BrS: The Hamilton lab has discovered a biomarker profile of autoantibodies against 4 cardiac proteins-alpha-cardiac actin, alpha-skeletal actin, keratin and connexin-43. These autoantibodies can be identified from sera of BrS patients, using a novel method that is highly sensitive, specific, and independent of the genetic cause of BrS.

COMMERCIAL APPLICATIONS & ADVANTAGES

ARVC: Currently, ARVC diagnosis involves genetic testing and clinical testing. These existing methods are unsatisfactory: genetic testing is only 33-50% sensitive, while clinical testing costs $1,000/year and provides only 70% sensitivity with false positives. The ARVC biomarker discovered by our researchers **identifies 98% of ARVC cases** with the following commercial opportunities:

- Development as a prognostic biomarker
- Poses as a potential companion biomarker
- Predictive testing of disease progression, which is in development

BrS: Genetic testing for SCN5A mutations is only performed in patients with a likelihood of developing BrS. However, mutations in SCN5A is only found in 11-28% of BrS patients. Clinical diagnosis is costly and is based on identification of the typical ECG pattern, which is often transient. Our researchers' profile of biomarkers **identifies 100% of probable cases that develop into BrS**, with possible commercial applications of:

- Development as a prognostic biomarker
- Predictive testing of disease progression, which is in development

DEVELOPMENT STAGE

In vitro diagnostic assays have been developed, and researchers are currently collaborating with all Canadian Inherited Arrhythmia Clinics and major US and European centres.

PATENT STATUS

ARVC - Patent applications filed in Canada, US, and Europe.

BrS - PCT/CA2020/050578 filed May 1, 2020.

IP&C is seeking an industry partner complete development, validate and commercialize these clinical diagnostic tests.

LEAD INVENTORS:
Dr. Robert Hamilton, MD, Staff Physician, The Hospital for Sick Children

LICENSING CONTACT:
Konrad Powell-Jones, Director Business Development, Tel: 416.813.7654 ext. 309572, konrad.powell-jones@sickkids.ca
IP&C Ref. | RDLP 1138 and RDLP 1238