Arrhythmias and Device Therapy – Arrhythmias, General, Pathophysiology and Mechanisms, Cellular Mechanisms of Arrhythmias

Persistent proteomic alterations after recovery from pvc-induced dilated cardiomyopathy reveal potential biomarkers of disease recurrence

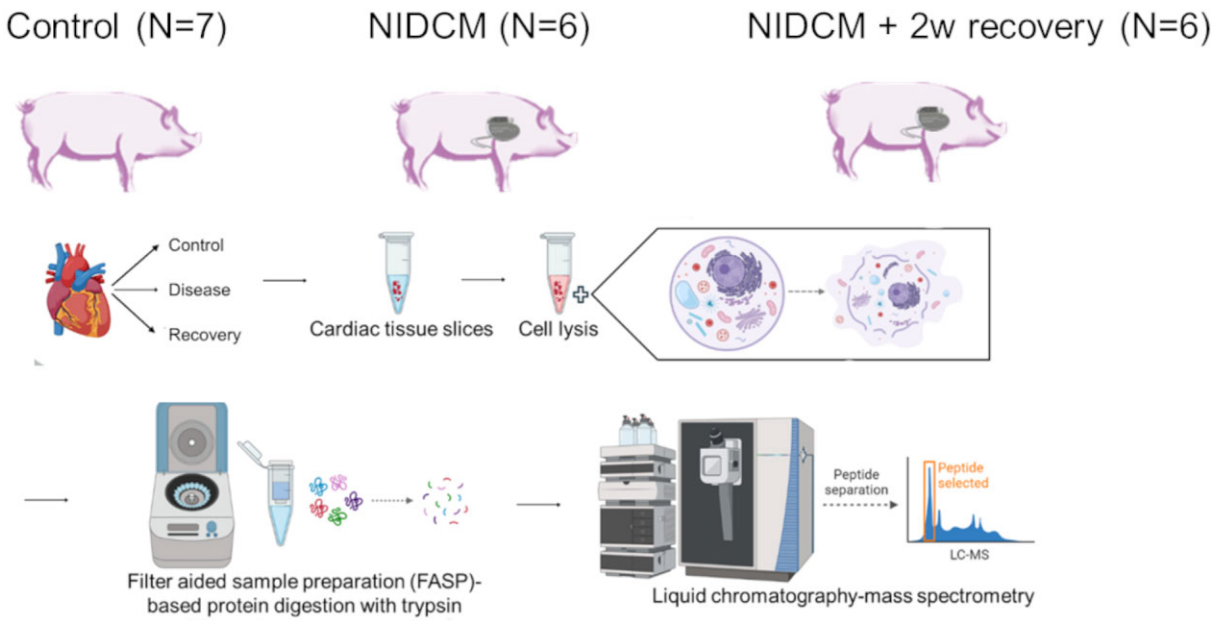
G. Amoros-Figueras[1]; C. Ayala-Carrasco[1]; S. Casabella-Ramon[2]; M. Soriano-Amores[1]; Z. Moreno-Weidmann[1]; C. Li[1]; V. Llorente-Cortes[1]; M. Carrascal[3]; J. Guerra[1]

[1]Hospital de la Santa Creu i Sant Pau, Institut de Recerca Sant Pau (IR SANT PAU), CIBERCV, Barcelona, Spain
[2]Departament de Biologia Cel·lular, Fisiologia i Immunologia, Universitat Autonoma de Barcelona, Barcelona, Spain
[3]Biological and Environmental Proteomics Group, Institute of Biomedical Research of Barcelona, Spanish National Research Council (IIBB-CSIC/IDIBAPS), Barcelona, Spain

Funding Acknowledgements: Type of funding sources: Public grant(s) – National budget only. Main funding source(s): This study has been funded by Instituto de Salud Carlos III (ISCIII) through the project “PI20/01702”
and cofunded by the European Union and by grant SECARIT-FOR-NAC 24 from Sociedad Espanola de Cardiología.

Background/introduction: Tachycardia-induced cardiomyopathy (TIC) is a reversible form of dilated cardiomyopathy (DCM) characterized by left ventricular (LV) dilatation and systolic dysfunction secondary to sustained arrhythmias. Although functional recovery is commom after rhythm control, the molecular mechanisms underlying incomplete or recurrent ventricular remodelling remain poorly understood. Proteomic profiling may uncover persistent alterations that signal residual vulnerability.
Purpose: To characterize proteomic changes in LV and right ventricular (RV) tissue from a porcine model of TIC and identify molecular signatures that persist after recovery.
Methods: Nineteen pigs were studied: controls (n=7), TIC induced by 4 weeks of RV tachypacing at 180 bpm (disease group, n=6), and TIC followed by 2 weeks of recovery (n=6). LV and RV samples were analyzed using label-free shotgun proteomics (LC-MS/MS) (Figure 1). Differential expression was assessed using standard thresholds (adjusted $p \leq 0.05$; fold change ≥ 1.5).
Results: After pacing, disease animals showed LV dilatation, reduced LV ejection fraction (LVEF), and QRS widening. Across all samples, 3,615 proteins were quantified. In the diseased group 71 proteins were upregulated in RV and 49 in LV (Fold change RV vs. LV: 2.7±2.0 vs 2.3 ±2.3) (Figure 2). Notably, despite normalized cardiac function after recovery, 6 proteins remained overexpressed in RV and 17 in LV (Fold change RV vs. LV: 5.3±8.2 vs 2.7±2.0).
Conclusions: Persistent proteomic alterations were detected after functional recovery, suggesting subclinical myocardial injury. These sustained molecular signatures may serve as biomarkers of recurrence and potential therapeutic targets to prevent progression to dilated cardiomyopathy and relapses.

Fig 1. Study methodology



Arrhythmias and Device Therapy – Arrhythmias, General, Pathophysiology and Mechanisms, Cellular Mechanisms of Arrhythmias

Fig 2. $\log_2$ fold-change vs. $-\log_{10}$ p-val