



POSTER

Cell-cell junctions and arrhythmogenic right ventricular cardiomyopathy (ARVC)

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Abstract

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a hereditary disorder of the cardiac muscle characterised by ventricular arrhythmias, cardiac failure and sudden cardiac death. Desmosomes - the intercellular junctions of both epithelial and cardiovascular tissues that connect intermediate filaments of adjacent cells, generating a large and mechanically resilient network - are disordered in ARVC. Here, we exploit new insights into desmoplakin (DP), a critical component of desmosome structures. Indeed, both patient skin and keratinocytes expressing DP mutant construct showed large intercellular aggregates and a decrease in the amount of junctional proteins at areas of cell-cell contact. Moreover, experiments with DP knockout mice indicated that mislocalization of another junctional protein, connexin 43 was ameliorated by b-blocker (beta-blocker), or b-adrenergic receptor blocker - known to interfere with the binding to the receptor of epinephrine and other stress hormones to weaken the effects of stress hormones. Thus, these novel findings fortify the genetic and cellular mechanisms behind the marked heterogeneity of the disease and provide new therapeutic interventions that target intercellular junctions.

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Keywords

ARVC, desmoplakin, intercellular junctions, cell-cell contact

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