Murine models of arrhythmogenic cardiomyopathy benefit from GSK3-beta inhibition

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Arrhythmogenic cardiomyopathy (ACM) is an inherited heart disease that results from mutations in genes that encode components of the cardiac desmosome, which forms the junction between cardiac muscle and the epithelium. Patients with ACM have an increased risk of sudden death due to the breakdown of the muscle wall of the heart with age.

A previous chemical screen in a zebrafish ACM model identified a glycogen synthase kinase 3β (GSK3β) inhibitor (SB2) that reversed disease. In this issue of *JCI Insight*, investigators led by Jeffrey Saffitz of Harvard Medical School and Daniel Judge of John's Hopkins School of Medicine examined the effects of the GSK3β inhibitor SB2 in two murine models of ACM.

SB2 improved cardiac function, reduced fibrosis and inflammation, and improved survival in both ACM models. In cardiac cells from healthy mice, GSK3β was in the cytosol. However, GSK3β localized to intercellular junctions in mice with ACM. The same GSK3β distribution patterns were also present in cardiac cells from healthy individual and patients with ACM.

The results of this study provide further evidence that GSK3β inhibition has potential as a therapeutic strategy for treating ACM.

More information: Stephen P. Chelko et al, Central role for GSK3β

in the pathogenesis of arrhythmogenic cardiomyopathy, *JCI Insight* (2016). DOI: 10.1172/jci.insight.85923