

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 3 \$\beta\$](#) (GSK3 β) inhibitor (SB2) that reversed disease. In this issue of *JCI Insight*, investigators led by Jeffrey Saffitz of Harvard Medical School and Daniel Judge of Johns Hopkins School of Medicine examined the effects of the GSK3 β 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, GSK3 β was in the cytosol. However, GSK3 β localized to intercellular junctions in mice with ACM. The same GSK3 β distribution patterns were also present in cardiac cells from healthy individual and patients with ACM.

The results of this study provide further evidence that GSK3 β inhibition has potential as a therapeutic strategy for treating ACM.

More information: Stephen P. Chelko et al, Central role for GSK3 β

in the pathogenesis of arrhythmogenic cardiomyopathy, *JCI Insight*
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