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Cardiac hypertrophy and abnormal Ca^{2+} handling in transgenic mice overexpressing junctate

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Junctate is a newly identified integral ER/SR membrane Ca^{2+} binding protein, which is an alternative splicing form of the same gene generating aspartyl □-hydroxylase and junctin. To elucidate the functional role of junctate in heart, transgenic (TG) mice overexpressing mouse cardiac junctate-1 under the control of mouse □ myosin heavy chain promoter were generated. Overexpression of junctate in mouse heart resulted in cardiac hypertrophy, increased fibrosis, bradycardia, arrhythmias and impaired contractility. Overexpression of junctate also led to down-regulation of SERCA2, calsequestrin, calreticulin and RyR, but to up-regulation of NCX and PMCA. The SR Ca^{2+} content decreased and the L-type Ca^{2+} current density and the action potential durations increased in TG cardiomyocytes, which could be the cause for the bradycardia in TG heart. The present work has provided an important example of pathogenesis leading to cardiac hypertrophy and arrhythmia, which was caused by impaired Ca^{2+} handling by overexpression of junctate in heart.