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Molecular and Functional Characterization of Mouse Cardiac Junctate

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Junctate is a newly identified integral endo(sarco)plasmic reticulum membrane calcium binding protein, which is an alternative splicing form of the same gene generating aspartyl -hydroxylase and junctin. Screening a mouse heart cDNA library using canine junctin cDNA as a probe yielded 3 complete mouse heart cDNAs. The three mouse junctate proteins are composed of 270, 259 and 215 amino acids (We named them junctate-1, -2 and -3). The apparent molecular masses of the mouse junctates in SDS-PAGE were in the range between 40 and 53 kDa. To elucidate the functional role of junctate in heart, transgenic (TG) mice overexpressing junctate-1 under the control of mouse α-myosin heavy chain promoter were generated. Overexpression of the junctin in mouse heart was associated with heart enlargements, bradycardia, and atrial fibrillation. Ultrastructural alterations such as frustrated sarcoplasmic reticulum and myelin like structure were observed in TG heart. According to echocardiography, TG mice showed enlarged both ventricles and atria, and impaired left ventricular systolic function. Overexpression of junctate led to down-regulation of ryanodine receptor. This study provides an important example of pathogenesis leading to substantial cardiac remodeling and atrial fibrillation, which was caused by overexpression of junctate in heart.