

Complete Citation: Marrett, Garth and Laws, Nicola and Watson, Michael and Hoey, Andrew (2006). Altered contractile, electrophysiological and Ca^{2+} release from left atria and isolated ventricular myocytes from MDX mice. In Denis Crane and Greg Monteith (Eds.), *COMBIO 2006, Australian Society for Biochemistry and Molecular Biology Inc*, 109.

(Combined ASBMB, ASPs, AuPS, ANZSCDB, NZSBMB, NZSPP, 24 - 28 Sep 2006, Brisbane, Australia.)

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ALTERED CONTRACTILE, ELECTROPHYSIOLOGICAL AND Ca^{2+} RELEASE FROM LEFT ATRIA AND ISOLATED VENTRICULAR MYOCYTES FROM MDX MICE

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Cardiomyopathies reduce the average life expectancy of boys with Duchenne Muscular Dystrophy (DMD). The absence of dystrophin in cardiac myocytes is associated with calcium overload and is a major contributor to heart failure, muscle necrosis and fibrosis in DMD. The present study used hearts from *mdx* mice, an animal model for DMD to investigate the underlying mechanisms responsible for the development of cardiac myopathies in DMD. Mice (13-17 months) were anaesthetised with sodium pentobarbitone (70 mg/kg, ip) prior to euthanasia by excision of the heart. In left atrial (LA) contractility studies, *mdx* mice had a significant reduction in; basal contractility ($P < 0.05$); time to peak force ($P < 0.05$) and time to 50% and 90% relaxation ($P < 0.05$). Microelectrode studies in the LA revealed that *mdx* mice had a significantly longer action potential duration (APD) at 50% repolarisation ($P < 0.05$) but a shorter APD at 90% repolarisation (APD_{90}). Action potential recordings from isolated *mdx* ventricular myocytes in current clamp confirmed a shorter APD_{90} as observed in the LA studies. Ventricular myocytes from *mdx* mice had significantly impaired force-frequency responses at all stimulation frequencies from 0.25 to 3 Hz ($P < 0.05$). Measurements of intracellular Ca^{2+} using FURA 2 revealed that *mdx* ventricular myocytes had significantly increased Ca^{2+} release following field stimulation (0.25 through to 2 Hz; $P < 0.05$). In conclusion, both the atria and ventricles of *mdx* mice show altered electrophysiological, contractile and Ca^{2+} release properties all of which may contribute to the Ca^{2+} overload and impaired cardiac function.