Normal and abnormal functions of stretch-activated channels in the heart

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Stretch-activated non-specific cation channels (SAC_{NSC}) have been identified electrophysiologically in skeletal and cardiac muscle though their functional roles are unclear. Recently Maroto *et al.* (2005) determined that SAC_{NSC} were encoded by canonical transient receptor potential gene type 1 (TRPC1). SAC_{NSC} are blocked by streptomycin, Gd^{3+} and the spider venom toxin GsMTx-4. We have shown that the slow component of the increase of force following a stretch to ventricular myocardium is inhibited by the three pharmacological blockers of SAC_{NSC}. The slow component of force increase is accompanied by a gradual increase in the amplitude of the Ca^{2+} transients, or in the resting $[Ca^{2+}]_i$ for quiescent muscle, which are also blocked by streptomycin. Furthermore ventricular myocardium expresses TRPC1 by Western blotting. These results suggest that the slow component of the response to stretch is partly caused by increased Ca^{2+} entry through SAC_{NSC}. We have also shown that in the hearts of 9 month old mdx mice, which display a dilated cardiomyopathy, that resting $[Ca^{2+}]_i$ is elevated and can be returned to normal by streptomycin and GsMTx-4. The elevated resting $[Ca^{2+}]_i$ is not present before the myopathy develops at 2 months and the TRPC1 expression increases by 5 fold between 2 and 10 months in the ventricular myocardium of the mdx, but not the wild type, mouse. These results suggest, as previously proposed in skeletal muscle (Yeung *et al.*, 2005), that increased Ca^{2+} entry through a TRPC1 encoded SAC_{NSC} could contribute to the muscle damage, which results in dilated cardiomyopathy.

Maroto R, Raso A, Wood TG, Kurosky A, Martinac B & Hamill OP. (2005) Nature Cell Biology, **7**: 179-185.
Yeung EW, Whitehead NP, Suchyna TM, Gottlieb PA, Sachs F & Allen DG. (2005) Journal of Physiology, **562**: 367-380.