**Presenting Author's Name & Research Title**

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Reliance on cooperative mechanisms in the mammalian heart

**Purpose/Background**

Ca\(^{2+}\) binding to troponin C (TnC) and myosin cross-bridge binding to actin act in a synergistic cooperative manner to modulate myocardial contraction and relaxation. The responsiveness of the myocardial thin filament to the activating effects of Ca\(^{2+}\) and myosin cross-bridge binding (i.e., cooperative profile) have been well-characterized in small mammals especially mice. Given the ten-fold difference in resting heart rates and twitch kinetics between small and large mammals, it is unlikely that the cooperative profile is identical in these two instances.

**Materials & Methods**

To test the idea that the cooperative profile is a species-dependent property of mammalian myocardium, we measured the Ca\(^{2+}\)-dependencies of steady-state force and the rate constant of force redevelopment (\(k_{tr}\)) in murine and porcine permeabilized ventricular myocardium.

**Results**

While murine myocardium exhibited a steep activation-dependence of \(k_{tr}\) (i.e., from 3.9 ± 0.7 sec\(^{-1}\) at pCa 6.0 to 29.8 ± 2.1 sec\(^{-1}\) at pCa 4.5), the activation-dependent profile of \(k_{tr}\) was significantly reduced in porcine ventricular myocardium (i.e., from 2.1 ± 0.2 sec\(^{-1}\) at pCa 6.1, to 0.9 ± 0.1 sec\(^{-1}\) at pCa 5.8, and 2.9 ± 0.2 sec\(^{-1}\) at pCa 4.5). Further insight into the cooperative profile was attained by examining force-pCa and \(k_{tr}\)-pCa relationships. In the murine myocardium, the pCa\(_{50}\) for \(k_{tr}\) was right-shifted compared to the pCa\(_{50}\) for force (i.e., △pCa\(_{50}\) = 0.17 ± 0.01, \(P<0.05\)). Thus, a higher [Ca\(^{2+}\)] was required to achieve half-maximal activation of \(k_{tr}\), meaning that increases in steady-state force occurred well before increases in the rate of force redevelopment were observed. In porcine myocardium, we observed a tighter coupling of the force-pCa and \(k_{tr}\)-pCa relationships, as evidenced by near maximal rates of force redevelopment at low levels of Ca\(^{2+}\) activation.

**Discussion/Conclusion**

These results demonstrate that the cooperative profile is a species-dependent dynamic property of the mammalian heart. Such a mechanism suggests a molecular basis for beat-to-beat synchronization of ventricular contractility and circulatory demand across species.