**Int. Methods**

Isometric skinned fiber analysis: Muscle fibers for skinned fiber studies were prepared using a protocol described by Iyengar and Faulkner, 1998. Single muscle fibers were dissected in rigor buffer at 4°C (20 mM MOPS, 5 mM MgCl₂, 120 mM potassium acetate, 1 mM EGTA, pH 7.0) and attached to a 400A force transducer (Aurora Scientific, Ontario, Canada) with 2-4 µl of 5% solution of methylcellulose in acetone. Fibers were incubated at 20°C in a circulation bath containing oxygenated Krebs solution at 4°C (1 mM NaH2PO4, 5 mM MgCl₂, 2 mM CaCl₂, 1 mM MgSO4, 137 mM NaCl, 11 mM glucose and 1 mM NaHCO3). Muscles were attached with silk thread to the fixed lever arm and force transducer of a BTA strain gauge transducer system (Aurora Scientific, Ontario, Canada) and incubated in Krebs solution at 20°C. After length adjustment, muscles were stimulated via field electrodes with 350 µs trains (5, 10, 20, 30, 50, 80, 100 Hz, 1 ms stimuli) over a 2 minute period. This was repeated every 10 minutes. For compound treatment, muscles were perfused with DMSO (0.1%) or CK-201735 (10 µM) (CK-10.1 µM).

Fatigue assays were performed by pre-incubating Figures 3, 4, and 6 for 10 minutes with 4°C. Pre-incubating temperature was then raised to 30°C and a force frequency relationship established (350 s trains at 5, 10, 20, 30, 50, 80, 100 Hz, 1 ms stimuli). Stimulation frequency was adjusted to achieve a force of 30% of maximal (MaxFSS) and muscles were stimulated at this frequency every 15 seconds for 10 minutes. At the end of each assay, the length and weight of each muscle were recorded, and measured force was normalized to the cross sectional area of the muscle (Nm/cm²).

In situ muscle analysis: In situ studies were performed on experimental procedures described by Brooks et al., 1990. Rats were placed under deep anesthesia using isoflurane and cut off distal end of the extensor digitorum longus (EDL) muscle and its associated tendon were isolated. The knee was immobilized with a clamp and the tendon cut and tied to the arm of a force transducer (BRECK, Aurora Scientific) using silt suture. The muscle was stimulated directly via field electrodes with 350 µs trains at 5, 10, 20, 30, 50, 80, and 100 Hz, 1 ms stimuli. The length and weight of each muscle were recorded, and measured force was normalized to the cross sectional area of the muscle (Nm/cm²).

**References**