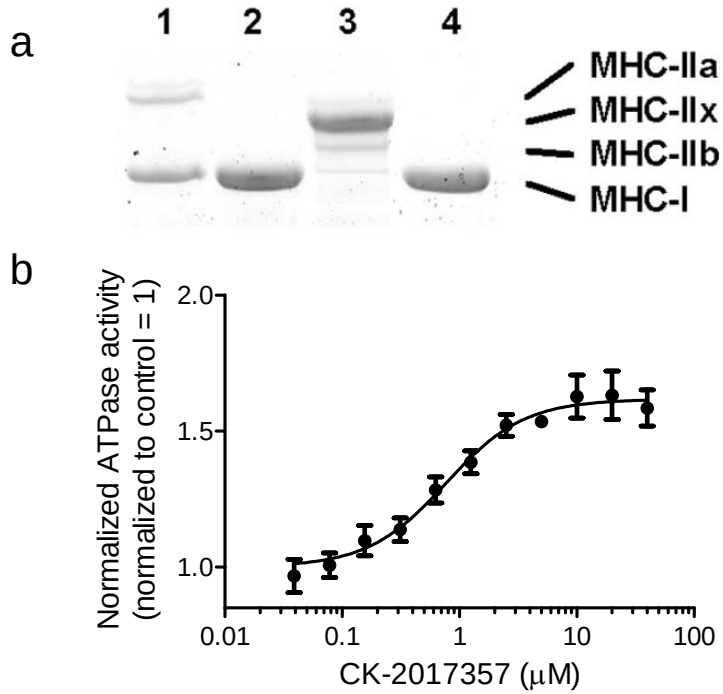
Activation of fast skeletal muscle troponin as a potential therapeutic approach for treating neuromuscular diseases

Alan J Russell[1], James J Hartman[1], Aaron C Hinken[1], Alexander R Muci[1], Raja Kawas[1], Lena Driscoll[1], Guillermo Godinez[1], Kenneth H Lee[1], David Marquez[1], William F Browne IV[1], Michael M Chen[2], David Clarke[1], Scott E Collibee[1], Marc Garard[1], Richard Hansen[1], Zhiheng Jia[1], Pu-Ping Lu[1], Hector Rodriguez[1], Khalil G Saikali[2], Julia Schaletzky[1], Vipin Vijayakumar[1], Daniel L Albertus[3], Dennis R Claflin[3], David J Morgans[1], Bradley P Morgan[1], Fady I Malik[1*]

Affiliations:
[1] Preclinical Research and Development and [2] Biometrics, Cytokinetics, Inc., South San Francisco, CA, 94080, USA. [3] Department of Surgery, Section of Plastic Surgery and the Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, 48109 USA.

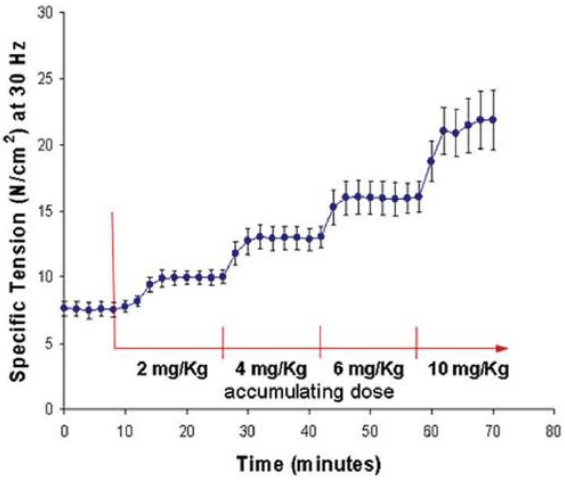
***To whom correspondence should be addressed:**
E-mail: fmalik@cytokinetics.com

Supplementary Fig. 1



Characterization of myofibrils. (**a**) Glycerol SDS-PAGE analysis of myosin isoforms present in myofibrils prepared from different muscles. Lane 1-4: rat diaphragm muscle (myosin isoform loading control), bovine slow skeletal muscle, rabbit fast skeletal muscle, and bovine cardiac muscle. (**b**) Calcium-dependent ATPase activity (mean ± SD) with CK-2017357 in bovine fast skeletal muscle myofibrils at fixed pCa (~25% of full activation, pCa_{25}).

Supplementary Fig. 2



Time course of force response following CK-2017357 administration. Force changes in rat EDL muscle *in situ* after four sequential intra-aortic infusions of CK-2017357 (mean ± SEM, *n* = 5).