We evaluated the mechanical properties of *Drosophila* indirect flight muscle (IFM) fibers expressing a myosin converter domain R759E mutation. The interaction of R759 with relay loop residue I508 is thought to be critical for relay-converter inter domain communication. By changing the charge on residue 759, we are testing if this inter domain interaction is important for the mechanical performance of muscle fibers. Electron microscopic examination of muscle fibers from young adult R759E flies indicates normal myofibril assembly. Using the work loop analysis technique we found that the maximum power (P_{max}) generated by the mutant R759E fibers from two day old flies was significantly reduced by 50% compared to control fibers while the frequency at which maximum power is generated (f_{max}) was reduced to 67%. Maximum power occurred at peak-to-peak strain amplitude of 2% resting muscle fiber length. Varying ATP concentration at 15°C revealed no significant difference in K_m for P_{max} or f_{max} between control and mutant R759E fibers, suggesting that the mutation does not affect ATP affinity. Small amplitude sinusoidal analysis revealed a significant reduction in complex stiffness by 48% compared to control fibers, with elastic modulus, E_e, reduced by 31% and viscous modulus, E_v, reduced by 45%. This reduction in power and mechanical performance of the flight muscle fibers led to a decrease in wing beat frequency from 140 ± 2 Hz for control flies to 127 ± 2 Hz. The reduction in wing beat frequency contributed to a decrease in flight index from 2.31 ± 0.1 for control flies to 1.25 ± 0.1 at 15°C. Thus, this study suggests that the interaction between relay loop I508 and converter domain R759 is critical for myosin inter domain communication, muscle fiber power generation and *Drosophila* flight performance.

1100-Plat
Single Skeletal Muscle Fiber Performance is Altered in Heart Failure Patients
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A decrease in whole skeletal muscle performance is common in heart failure patients. We examined the viscoelastic properties of individual human skeletal muscle fibers using small amplitude sinusoidal analysis to test the hypothesis that heart failure affects skeletal muscle mechanics and kinetics at the single fiber level. We obtained *vastus lateralis* (quadriceps) muscle from needle biopsies of 7 heart failure patients and 4 sedentary controls. At low [Ca^{2+}] (pCa 8, 25°C), Type I (slow contraction velocity) and Type IIA (fast contraction velocity) muscle fibers from heart failure patients had lower isometric tensions as well as lower elastic and viscous moduli. Notably, Type I and IIA fibers produce positive oscillatory work and power at pCa 8. Type I fibers from heart failure patients at low [Ca^{2+}] produced less oscillatory work and had a higher frequency of maximum work, indicating an increase in myosin kinetics, compared to controls. At high [Ca^{2+}] (pCa 4.5, 25°C), Type I and IIA fibers from heart failure patients showed similar isometric tensions and myosin kinetics parameters as controls. In contrast to low [Ca^{2+}], at high [Ca^{2+}] Type I and IIA fibers from heart failure patients had a larger elastic modulus at low oscillation frequencies and consistently produced greater oscillatory work and power than control fibers. Together, these results indicate that heart failure modifies single skeletal muscle fiber performance at the level of the myosin-actin cross-bridge, although the effect differs between low and high [Ca^{2+}]. The relevance of these differences to reduced whole muscle function in heart failure patients awaits further studies.

1101-Plat
Skeletal Muscle Lacking the Extreme C-Terminal SH3 Domain of Nebulin Exhibits Heightened Vulnerability to Eccentric Contraction-Induced Injury
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Nemaline myopathy is a congenital myopathy afflicting roughly 1 in 50,000 children. Nemaline myopathy is a disease of the thin filament, and mutations in the giant thin filament template nebulin contribute to its etiology. A clinical case report has demonstrated that loss of the extreme C-terminal Src homology 3 (SH3) domain of nebulin can cause nemaline myopathy. The nebulin SH3 domain is believed to anchor the thin filament to the Z-disk through its interaction with myopalladin. To further elucidate the physiological roles of the nebulin SH3 domain, the skeletal muscle phenotype of wild-type (*nebulin*$^{+/+}$) mice was compared to that of mice homozygous for the I6611X mutation in the nebulin gene (*nebulin*$^{I6611X/I6611X}$). The I6611X mutation introduces a premature truncation of the nebulin transcript and eliminates the SH3 domain from the nebulin protein. Contractile measurements revealed that baseline isometric stress production was identical in *nebulin*$^{I6611X/I6611X}$ and *nebulin*$^{+/+}$ muscle (247 ± 6 kPa vs. 253 ± 6 kPa, respectively; P=0.50). However, *nebulin*$^{I6611X/I6611X}$ muscle exhibited a greater vulnerability to eccentric contraction-induced injury compared to *nebulin*$^{+/+}$ muscle, where "injury" was defined as a decline in isometric stress production across a series of 10 eccentric contractions (39.3 ± 0.8% vs. 29.1 ± 1.6%, respectively; P<0.01). The corresponding decline in passive stiffness was identical in *nebulin*$^{I6611X/I6611X}$ and *nebulin*$^{+/+}$ muscle (13.5 ± 2.4% vs. 14.4 ± 2.1%, respectively; P=0.79). Muscle fiber type distributions and cross-sectional areas were also identical in *nebulin*$^{I6611X/I6611X}$ and *nebulin*$^{+/+}$ muscle. These data indicate that the nebulin SH3 domain is dispensable for isometric stress production in skeletal muscle but necessary for protecting muscle from injurious eccentric contractions. It is conceivable that heightened vulnerability to eccentric contraction-induced muscle injury, or to other types of biomechanical challenges, explains the pathology observed in children with nemaline myopathy.

1102-Plat
Extremely Low Maximal Force-Generating Ability in Hummingbird Flight Muscle Fibers
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Hummingbird flight muscle has the highest mass-specific mechanical power output among all vertebrates. The wingbeat kinematics and aerodynamics of hummingbird flight have been studied in multiple species, but little is known about fundamental contractile properties of these remarkable muscles. The objective of this study was to measure the maximal force-generating ability (maximal force per unit of fiber cross-sectional area, P_o/CSA) of single muscle fibers from the pectoralis muscle, which powers the wing downstroke, in adult hummingbirds and in another similarly-sized species, zebra finch, which does not hover but also has a very high wingbeat frequency during routine flight. Single, skinned pectoralis fibers were maximally calcium-activated and P_o/CSA was measured across a range of temperatures. P_o/CSA in hummingbird pectoralis fibers was 1.1 ± 0.4 (mean ± SEM), 5.2 ± 1.6, and 10.8 ± 2.4 kN/m^2, at 10, 15, and 20°C, respectively. P_o/CSA in zebra finch pectoralis fibers was 2.0 ± 0.4 (mean ± SEM), 10.4 ± 1.6, and 21.6 ± 3.2 kN/m^2, at 10, 15, and 20°C, respectively. For comparison, P_o/CSA in adult mammalian limb muscle fibers at 15°C is typically 100-120 kN/m^2. The mean P_o/CSA in hummingbird leg muscles fibers, which are used for perching, was 73.4 ± 11.6 kN/m^2 at 10°C. These results indicate that hummingbird pectoralis fibers have an extremely low force-generating ability, compared to mammalian limb muscle fibers and hummingbird leg muscle fibers, even when maximally activated, and have an unusually high temperature-dependence of force generation. The unusually low force-generating ability of hummingbird and zebra finch pectoralis fibers may reflect a constraint imposed by a need for extremely high contraction frequencies, especially during hovering flight in hummingbirds. Supported by the National Science Foundation.

Symposium 9: Sensing the Membrane

1103-Symp
Mechanisms of Signaling and Regulation of Membrane Properties by a Bacterial thermosensor
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The ability of bacteria to control the biophysical properties of their membrane phospholipids allows them to thrive in a wide range of physical environments. When bacteria are exposed to temperatures below those of their normal conditions, the lipids of their membrane become rigidified, leading to a suboptimal functioning of cellular activities. These organisms can acclimate to such new conditions by an increase in the desaturation of the acyl chain of membrane phospholipids. Phospholipids containing unsaturated fatty acids have a much lower transition temperature than those lipids made of saturated fatty acids. As a result, the physical properties (fluidity) of the membrane lipids return to their original state, or close to it, with restoration of normal cell activity at the lower temperature. We discovered that in the model Gram-positive bacterium *Bacillus subtilis* the transcription of the *des* gene, coding for an acyl lipid desaturase, is controlled by a two component system that senses changes in the membrane properties due to abrupt temperature change. The membrane component, named DesK, of this transcriptionally regulatory system is a thermosensor with histidin kinase and phosphatase activities that senses membrane biophysical properties and transmits this signal to the transcriptional