Control of Myosin-I Motility and Force Sensing

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Abstract

Myosins are actin-based motors that are mechanically and kinetically tuned to function in a range of cellular processes. The myosin-I family members myosin-IB (Myo1b) and myosin-IC (Myo1c) have similar structures and unloaded kinetics, however under working conditions, they display very different behaviors. Myo1c can generate power over a range of loads, enabling it to act as a transporter, while Myo1b is extraordinarily force-sensitive, allowing it to act as a tension-sensing anchor. We recently determined the high-resolution structure of the motor domain and first IQ-motif of Myo1b and found the N-terminal region (NTR) to be in a unique conformation that has not been seen in other myosins. The NTR sequence is highly variable within the myosin-I family, and may play a role in tuning the mechanochemical properties of the myosin motors. We generated recombinant constructs of Myo1b and Myo1c in which their NTRs were deleted and swapped, and we characterized their kinetic and mechanochemical properties using stopped-flow techniques, single molecule optical trapping techniques, and in vitro motility assays. Our results show that the NTR plays a role in tuning the mechanochemical properties of Myo1b and Myo1c. Moreover, our results demonstrate differences in how the NTR tunes Myo1b and Myo1c, suggesting that sequence diversity and alternative splicing has a role in functional tuning of the motor.