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In vitro motility assays and single molecule analyses reveal functional structural transitions in the molecular motor myosin

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The molecular basis of how myosin motors work has been significantly advanced by laser trap and other single molecule studies of myosins V and VI. Myosin V moves processively by stepping arm-over-arm, walking along the 36-nm pseudo-repeat of an actin filament by swinging its long lever arms through an angle of $\sim 70^{\circ}$, and hydrolyzing one ATP per step. Compared to the laser trap, we have improved time resolution to submilliseconds by tracking single gold nanoparticle-myosin V conjugates using darkfield imaging, and have directly observed the behavior of the unbound head as the motor translocates. We have also developed a technique called single-molecule high resolution co-localization (SHREC), which allows simultaneous co-localization of two chromatically differing fluorophores only 10 nm apart. We used SHREC to directly observe myosin V molecules walking hand-over-hand. Myosin VI, a considerably different myosin family member, has been the biggest challenge to the lever arm hypothesis of myosin movement. It has a very short light chain binding domain (the conventional lever arm). Nevertheless, the molecule surprisingly steps processively 36 nm along an actin filament. Furthermore, myosin VI moves in the opposite direction to that of myosin II and myosin V. We now understand how this marvelous molecular motor achieves these feats.