Poster Presentation

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An insightful myosin structure reveals how actin triggers force production

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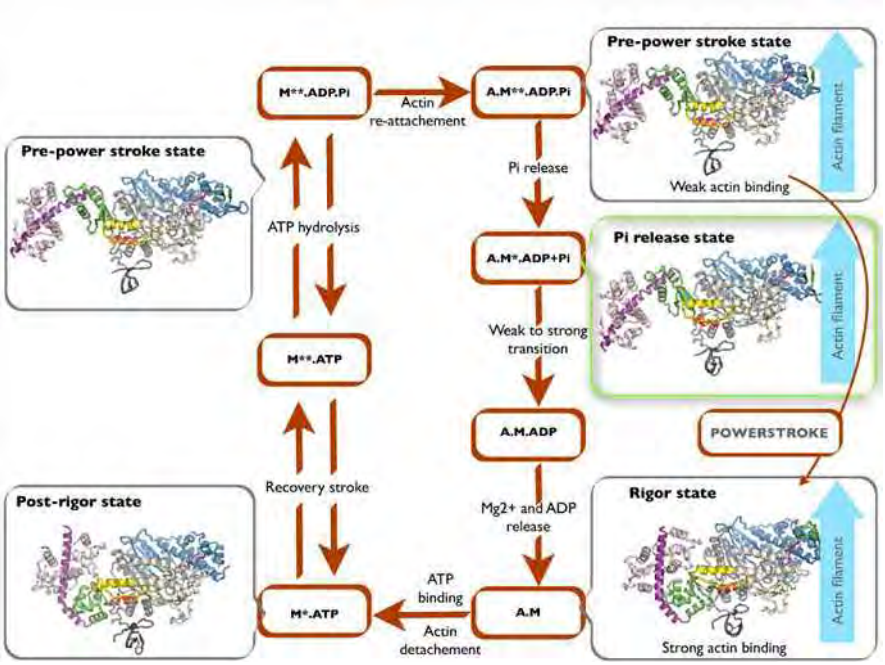
Directed force production is essential for life. Allostery is at the heart of the mechanism that cellular nanomotors use to walk, pull or anchor. Such molecular motors are essential for a cell to migrate, to divide and organise the intra-cellular traffic between its compartments. The actin-based motors, myosins, are critical for many of these movements, for muscle contraction, cytokinesis and sophisticated cellular functions such as hearing. Deficit in these motors can lead to a number of human genetic disorders. Force is produced by these motors by the conversion of chemical energy derived from ATP hydrolysis into mechanical energy via the interaction with their track, the actin filament. Biophysical approaches have provided insights into the chemo-mechanical coupling in the actomyosin system. They show how three allosteric sites communicate via relatively small conformational changes in the motor domain that are coupled and amplified by a lever-arm mechanism that produce a working stroke of several nanometers. While ATP binding and hydrolysis are essential for detachment of the motor from its track and its trapping in the pre-stroke conformation, step-wise rebinding to the track triggers controlled release of hydrolysis products upon the working stroke. A reverse motor, myosin VI has been particularly intriguing and informative regarding the force production mechanism. An unpublished structural state not only reveal how trapping of the hydrolysis products stabilize the primed pre-stroke conformation, it also provides insights for the rearrangements triggered by actin to promote Pi release. This new structural state has all the expected features of the Pi release state populated upon motor re-binding to its track. This allows visualization for the first time of the structural rearrangements triggered by actin binding that are coupled to force generation and product release at the beginning of the powerstroke.

[1] *Sweeney HL and Houdusse A, Myosin VI rewrites the rules for myosin motors, Cell, 141:573-82, 2010.,* ***[2]*** *Ménétrey J*, Isabet T*, Ropars V, et al. ,Processive steps in the reverse direction require uncoupling of the lead head lever arm of myosin VI. Mol Cell. 48,75-86, 2012.,* ***[3]*** *Sweeney HL and Houdusse A, Structural and Functional Insights into the Myosin Motor Mechanism, Annu Rev Biophys. 39, 539-57, 2010.*



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