Biochemistry IN PERSPECTIVE

Myosin: A Molecular Machine

How does the motor protein myosin cause muscle contraction? The myosins are a family of motor proteins that transduce ATP bond energy into unidirectional movement along actin filaments. Found in all eukaryotic cells, the myosins are involved in a wide variety of cellular movements. The role of myosin in movement is best understood in skeletal muscle contraction. Skeletal muscle myosin, referred to as myosin II, consists of two heavy chains and two light chains (Figure 5A). The N-terminal globular head domain (Figure 5B) of the heavy chain possesses separate binding sites for ATP and actin. A long α-helix extending from the head domain forms the flexible neck region and the C-terminal tail. The actin-binding cleft and ATP-binding site are on opposite sides of the myosin head domain. These sites are connected by so-called switch helices. As a result, the ATP-hydrolyzing activity of the ATP-binding site is activated when the myosin head binds to actin. In the *swinging neck–lever model* of the actin-myosin crossbridge cycle, ATP-induced changes in myosin conformation cause a leverlike swinging motion in the neck relative to the catalytic domain. The relative motion of thick (myosin filaments) and thin filaments (actin polymers complexed with several other proteins) in the muscle sarcomere (the functional unit of skeletal muscle) is caused by the swinging stroke of the myosin neck domain (Figure 5C).

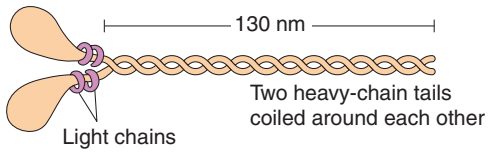

FIGURE 5A

Myosin II Structure

A myosin II molecule is composed of two heavy chains, each of which contains a globular head, a hinge region and a long rodlike tail, as well as four light chains. Two small light chains are wrapped around each myosin head.

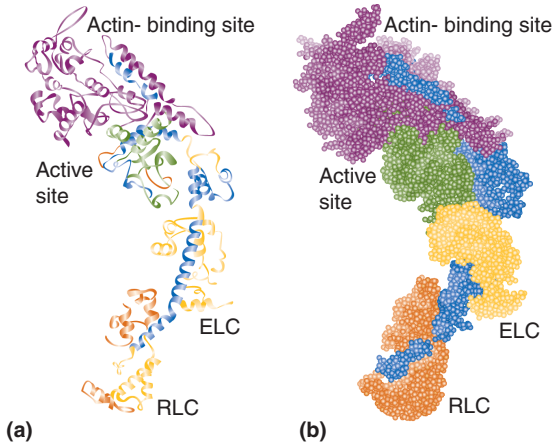

FIGURE 5B

Myosin II Head Domain Structure

(a) Ribbon model and (b) space-filling model: green, heavy-chain residues 4–204; red, heavy-chain residues 216–626; purple, heavy-chain residues 647–843; yellow, essential light chain (ELC); orange, regulatory light chain (RLC). The light chains encircle and stabilize the long α-helix formed by the heavy chain.

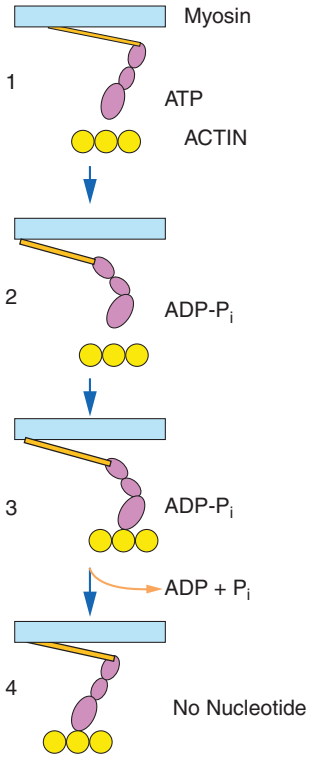

FIGURE 5C

The Actomyosin Cycle in Skeletal Muscle

(Step 1:) The myosin head has bound an ATP within the nucleotide-binding site and has detached from actin. (Step 2:) ATP hydrolysis causes the myosin head to become "cocked." (This is the energy-transducing event.) (Step 3:) Myosin binds weakly to actin. (Step 4:) Release of ADP and P_i causes the myosin head to bind tightly to actin, which is followed by the power stroke. The conformational change in the myosin head (the leverlike swinging motion) causes the myosin filament to move along the actin filament.

SUMMARY: ATP-induced conformational changes in myosin cause a leverlike swinging motion that results in the movement of the myosin head domain along the actin filament in muscle cells.