



SMART Teams 2013-2014

Research and Design Phase

Cudahy High School SMART Team

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Mighty Myosin: Movement Generator

PDB: 1BR1

Primary Citation: R. Dominguez, Y. Freyzon, K. Trybus, C. Cohen (1998). Crystal Structure of a Vertebrate Smooth Muscle Myosin Motor Domain and Its Complex with the Essential Light Chain: Visualization of the Pre-Power Stroke State. *Cell*. 94: 559-571.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Muscle contraction is caused by the contractile protein myosin, which exists in various isoforms in different muscle types such as smooth, cardiac, and skeletal. Current data suggests smooth muscle myosin is in a non-functional conformation until light chain 20, which is associated with the myosin head, is phosphorylated. This allows either head to freely bind to actin, a protein also involved in contraction. The contractile process is initiated when ATP is hydrolyzed in the ATP binding region. The release of the products from ATP hydrolysis causes the "lever arm" portion of each myosin head to bend relative to the "motor domain," pulling the actin fibers closer together, shortening the muscle cells for movement. If the contractile process is disrupted, bodily function is impaired. These key areas were modeled by the Cudahy SMART (Students Modeling A Research Topic) Team using 3D printing technology. Aortic coarctation, a developmental problem, involves a constriction of proximal aorta which increases blood pressure by narrowing the aorta, changing vascular smooth muscle in this region of vessel. While surgery can correct this anatomical constriction and prolong life, there remain long-term consequences that reduce life span. Drug treatments for a specific smooth muscle problem can be complicated by also altering function of other smooth muscles, causing undesired side effects such as incontinence. The question researchers face is targeting of a drug to a specific smooth muscle. Further understanding of smooth muscle function and regulation helps to better treat, prevent, and or cure this and other smooth muscle diseases.



Specific Model Information:

- The entire myosin head (1-821) can be digested to give three components: the 25 (AA1-212) shown in green, 50 (AA213-645), shown in purple, and 20 (AA646-849), shown in yellow, kD fragments. The 25kD fragment includes the ATP binding site (177-184), which is shown in lime green. This area is responsible for ATP hydrolysis. The side chains of ATP binding site are also shown. The 50 KD fragment is the largest and most distal end and includes the actin binding sites which are shown in magenta and dark orchid on either side of the binding cleft. The last COOH 20 kD fragment (646-849) includes some amino acids that are close to the ATP binding site, the convertor domain (721-776), shown in red, and the lever arm (776-849), shown in blue. Lastly, Loop 1, seen in pink, indicates an area that shows the potential for a mutation of seven amino acids, which results in faster ATP hydrolysis.
- ATP is colored pale green.
- Hydrogen bonds within and between segments of the protein are colored lemon chiffon.
- Structural supports in the model are colored beige.

<http://cbm.msoe.edu/smartTeams/>

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