

I. Myosin Matters

Walking over to this poster probably required minimal effort for you because of the protein myosin. Myosin binds with actin and causes muscles to contract, pulling on the skeletal system and propelling your body forward. This protein is found in all muscle groups and is the reason we are able to function normally. A problem in the myosin protein can also be the cause of various diseases, including coarctation of the aorta. These diseases may be the result of a mutation that occurs within the myosin protein. Phosphorylation normally causes the active site on either of the myosin heads to bind to the active site on actin (the protein that myosin binds to, to allow for muscle contractions), and this process regulates the muscle contractions.

II. Methods

The structure of our model was determined using electron cryomicroscopy. A crystallized myosin structure was developed using a positively charged lipid monolayer system and these crystalline samples were examined using an electron microscope. The structure was determined by matching the electron density from the cryomicroscopy program to the x-ray crystal structure, homology models, and an α -helical coiled-coil simulation program. We then designed the model in a program called JMOL, which created a virtual representation of myosin that we were able to print. A Zcorp printer was used to print our JMOL model. The printer formed the model out of layers of plaster and then soaked it in glue to hold the layers together.

III. The Molecular Story

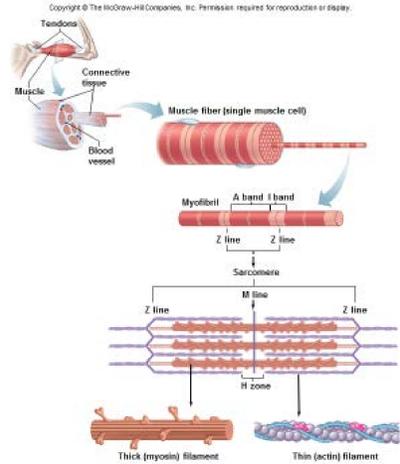


Figure 1

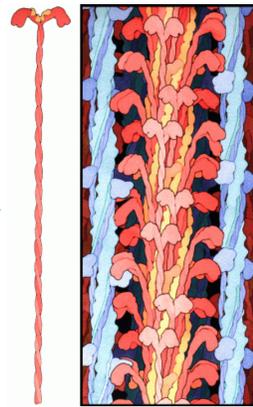


Figure 2

Coarctation of the aorta

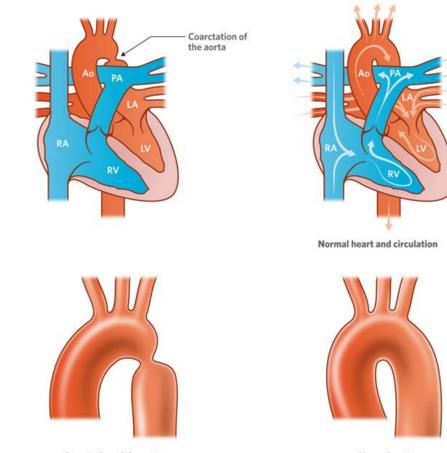


Figure 3

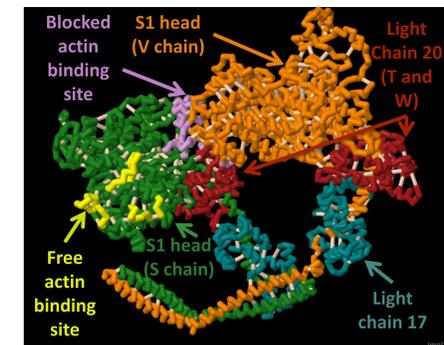


Figure 4
PDB File: 1184

Figure 1 depicts a "zoom-in" progression of where myosin is found, starting at the macro scale. The first image of the arm leads into the muscle, in which we find muscle fibers. In those muscle fibers are myofibrils, and in those sarcomeres. Sarcomeres are split into two parts, the thick myosin filament as well as the thin actin filament.

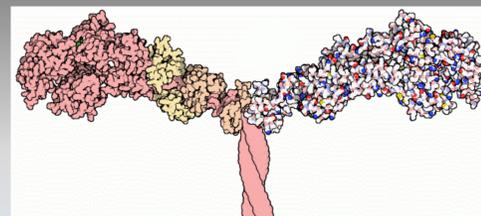
Figure 2 details the myosin filaments within smooth muscle in red. Myosin filaments are composed of roughly 300 myosin molecules that are bound together by their long tails. Next to the myosin filament is an actin filament, which is pictured in blue and green. The myosin heads work together to "climb" the actin filament, allowing for muscle contraction.

Figure 3 portrays a coarctation of the aorta (CoA). Our mentor, Dr. Eddinger of Marquette University, hypothesizes that myosin may be one of the main determining factors of this birth defect. This is evidenced by the increased expression of nonmuscle (NM) myosin molecules that are found in the thickened aorta walls characteristic of individuals with CoA. During normal development, the NM myosin is down regulated and smooth muscle (SM) myosin becomes the prevalent myosin isoform; however, in a person with CoA, this does not occur.

The Brookfield East SMART Team built a model of smooth muscle (SM) myosin using 3D printing technology. The model (Figure 4) focuses on the structure of dephosphorylated (unregulated) SM myosin S1 and S2 regions which interact with actin and generate contraction. The active sites for actin binding and ATP hydrolysis are on the S1 heads. Phosphorylation of myosin light chain 20 that associates with the S1 head regulates its function. When dephosphorylated, the two myosin heads bind to each other, blocking the actin binding sites, thereby preventing acto-myosin interaction and muscle contraction. Knowing the structure of myosin in more detail allows us to determine its function as well as its role in CoA.

IV. Science Behind the Story

An experiment that was instrumental in understanding myosin's function was a paper by Dr. Ivan Rayment of UW-Madison, published in 1993. Dr. Rayment's paper played a vital role in our understanding of both the structure and function of the S1 head and also explained how myosin binds to actin. He created the first 3-D structure of the S1 head using crystal x-ray diffraction. The S1 fragment was the basis of a majority of this experiment, and thus very important. Using the crystal structure of the S1 head, scientists have determined that the S1 head contains binding sites for actin and ATP, allowing for motion. Dr. Rayment's work was critical in subsequent studies such as this one.



Myosin S1 Head

V. Important Take Away

Myosin is one of the key proteins involved in muscle contractions; it enables humans to do anything involving motion, from running and jumping, to moving food through the digestive tract, to keeping the heart beating without having to think about it. Important studies have shown that dephosphorylation results in the binding of one of the myosin heads to the other. This process inhibits the ability of myosin to interact with actin filaments and thus regulates muscle contractions. In effect, dephosphorylation keeps our muscles from constantly contracting. As myosin is found in nearly all systems of the human body, mutations in this protein can lead to many severe diseases such as coarctation of the aorta. Though much has been learned about the structure and function of myosin, it is important to continue studying in order to gain a better understanding of how myosin plays a role in these diseases and to find a cure for those affected by them.

VI. References

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