Cardiac Actin: from molecules to Organisms

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Cardiovascular disease is the number one killer humans in the world. Cardiomyopathy is a group of diseases that contribute to heart disease and heart failure. Two examples of this are hypertrophic and dilated hearts. With a hypertrophic heart, the left ventricular wall increases in thickness. In the case of a dilated heart, the cardiac muscle becomes weakened and the ventricles become enlarged. At core of a contraction are two proteins, myosin and actin, which are present in all muscles. The “motor” protein is myosin, while the “track” protein as to which the motor protein relies on is actin. There are different types of myosin, ranging from standard myosin found in muscles, to myosin that provides the ability to walk backwards and some are located in the ear for hearing. Actin does not change much in different organisms, for example, the same actin located in yeast are 88% identical to human forms of actin. Actin is known as a hub protein that can interact with about 160 different actin bind proteins that are involved in every major physiological process. This plethora of actin binding proteins all interact with the same actin molecule. This causes an immense pressure for producing the actin protein’s sequence, to be usable by all needed actin bind protein like myosin. The structure actin as a free monomer, G-actin (“G” for globular) contains both a large and a small domain. The hinge or protein helices located at the center on the actin molecule allow the two domains to interact and cross over. The nucleotide binding cleft of actin is where either ATP or ADP binds. This binding keeps the structure functional. Twinfilin is a actin-monomer-binding protein that is composed of two ADF-homology domains; this protein is also structurally related to cofilin (binds G-actin-ADP), and play a role in sequestering actin monomers. Mutations in the twinfilin gene result in defects in the bipolar budding pattern in *S. cerevisiae*.