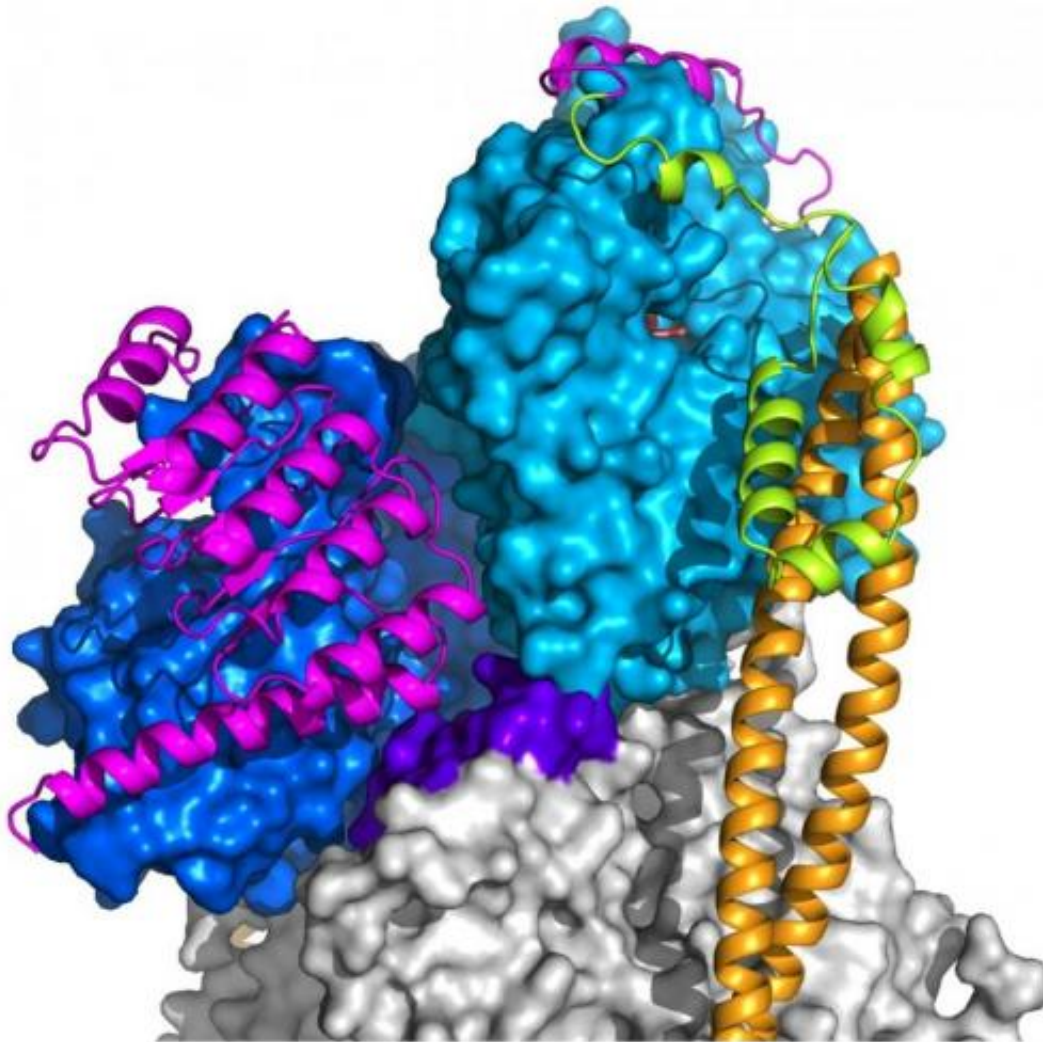


Atomic structure of key muscle component revealed

July 24 2014



This is a representation of the atomic structure of tropomodulin at the minus end of the actin filament in muscle sarcomeres. Tropomodulin interacts with the first three actin subunits of the filament. The regions of tropomodulin that interact with actin are colored magenta, and the three actin subunits involved in this

interaction are represented by two shades of blue, and purple for the interacting surface of the third subunit. Other subunits of the filament are colored gray. The actin filament also has two tropomyosin coiled coils bound symmetrically on each side (orange). At the minus end, tropomodulin also interacts with the tropomyosin coiled coils, and the region responsible for this interaction is colored green. Credit: Yadaiah Madasu, Ph.D., Perelman School of Medicine at the University of Pennsylvania, *Science*

Actin is the most abundant protein in the body, and when you look more closely at its fundamental role in life, it's easy to see why. It is the basis of most movement in the body, and all cells and components within them have the capacity to move: muscle contracting, heart beating, blood clotting, and nerve cells communicating, among many other functions. And, movement can turn harmful when cancer cells break away from tumors to set up shop in distant tissues.

Adding to the growing fundamental understanding of the machinery of [muscle cells](#), a group of biophysicists from the Perelman School of Medicine at the University of Pennsylvania describe in the journal *Science* this week – in minute detail—how actin filaments are stabilized at one of their ends to form a basic muscle structure called the sarcomere.

With the help of many other proteins, actin molecules polymerize to form filaments that give rise to structures of many different shapes. The actin filaments have a polarity, with a plus and minus end, reflecting their natural tendency to gain or lose subunits when not stabilized.

Actin is one of the two major proteins (together with myosin) that form the sarcomere—the contractile structures of cardiac, skeletal, and [smooth muscle cells](#). In sarcomeres, actin filaments are stabilized at both ends by capping proteins. At the minus end of the filament, the universal

capping protein is tropomodulin.

"While the existence of this protein has been known for almost 30 years, we still did not know how it actually works," says senior author Roberto Dominguez, PhD, professor of Physiology. His lab is dedicated to deciphering the fundamental mechanisms of proteins responsible for movement, and how these components fit together at the atomic level.

"We describe how tropomodulin interacts with the slow-growing end of [actin filaments](#)," says coauthor Yadaiah Madasu, PhD, a postdoctoral fellow in the Dominguez lab. "From a clinical point of view, we know that mutations in tropomodulin can trigger an accumulation of irregular actin filament bundles, which contribute to nemaline myopathy or other skeletal muscle disorders typified by delayed motor development and muscle weakness."

"The lack of structural information for the minus end of the actin filament severely limits our understanding of how tropomodulin caps actin," says Dominguez. The team described atomic crystal structures of tropomodulin complexes with actin. The structures and biochemical analysis of engineered tropomodulin variants show how one tropomodulin molecule winds around the minus end of an actin filament, making highly specific interactions with three actin subunits and two tropomyosin molecules (another protein characteristic of muscle sarcomeres) on each end of the actin filament. The detailed picture emerging from this study will help shed light on how mutations in tropomodulin, actin, and tropomyosin can cause heart disorders.

The team is now studying another [muscle protein](#) called leiomodulin. It was discovered more recently and resembles tropomodulin, but appears to have a completely different function, by participating in the development and repair of muscle sarcomeres.

More information: [www.sciencemag.org/lookup/doi/...
1126/science.1256159](http://www.sciencemag.org/lookup/doi/10.1126/science.1256159)

Provided by University of Pennsylvania School of Medicine

Citation: Atomic structure of key muscle component revealed (2014, July 24) retrieved 26 April 2024 from <https://phys.org/news/2014-07-atomic-key-muscle-component-revealed.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.