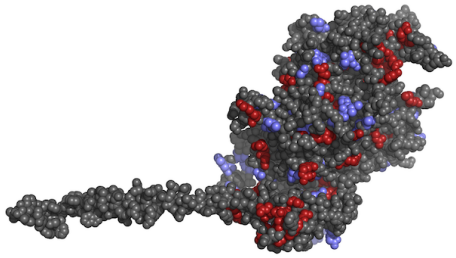
Study Summary

Mulitdimensional structure-function relationships in human B-cardiac myosin from population-scale genetic variations.

Myosin – The family of motor proteins that generate the force which causes muscles to contract
Phenotypic – The observable expression of a specific trait

"Myosin Motors are the fundamental force-generating elements of muscle contraction." Myosin is a protein, a class of large biological molecules that perform important physiological functions. Proteins are found throughout the body and occur in many different shapes and sizes – each with a different biological role. The myosin's job is to perform something called the myosin power stroke – an essential part of the biological cycle which causes muscles to contract. Myosin power strokes in the heart generate the force necessary for the heart beat – meaning these molecules have a very important job. Some, but not all, genetic changes in the heart's myosin molecule, known as MYH7, cause hypertrophic cardiomyopathy (HCM).



The image shows the molecular structure of the myosin molecule found in the human heart. This molecule is responsible for generating the force necessary to cause the heart to contract. Genetic changes throughout the myosin shown here may cause HCM. In the image, the locations within the myosin molecule of genetic changes seen in patients in the SHaRe registry are colored in red, while the locations within the myosin molecule of genetic changes seen only in other individuals are colored in blue.

In this study researchers looked at whether the genetic changes in the heart myosin that cause HCM tend to occur more often in certain areas of the molecule. In addition, the researchers looked at how different genetic changes contribute to differences in disease onset and disease outcomes of patients with Hypertrophic cardiomyopathy.

In order to do this they looked at genetic data from two population cohorts (groups) of more than 100,000 people as well as genetic and phenotypic data from 2,913 patients with HCM. Using this information they were able to compare the 3 dimensional locations of variation within the myosin molecule between patients and the population group and what it meant for disease onset.

The researchers observed that in patients with genetic variations on an area of the myosin called the myosin mesa had an earlier onset of the disease on average than those with variants in other areas.

This is the first published study to come out of the international SHaRe registry. Because the SHaRe Registry uses combined data from 12 different cardiac centers researchers were able to gather information from one of the largest study cohorts of HCM that has ever been put together.