

# Identifying patient-specific differences to treat HCM with precision medicine

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Hypertrophic cardiomyopathy (HCM) is a cardiovascular disease characterized by thickening of the left ventricle, otherwise known as the main squeezing chamber of the heart. HCM is best known for causing sudden death in athletes but can occur in persons of any age, often without symptoms. While frequently discussed in the context of genetics, most patients with HCM do not have a known genetic variant. Investigators from Brigham and Women's Hospital uncovered a means to study the complexity of this disease beyond the identification of individual genes. This new approach offers a path toward treating HCM using individualized medicine. In a recent study, investigators analyzed the role protein-protein interactions (PPIs) play in differentiating individual cases of HCM. Their results are published in *Nature Communications*.

"While genes play a role in HCM, there is more information surrounding this condition that can't be explained with genetics alone," said corresponding author Bradley Maron, MD, a cardiologist in the Division of Cardiovascular Medicine at the Brigham. "This raises the question of whether there are other important components of the disease. With this project, we aim to provide an expanded view of the pathobiology of HCM in a way that doesn't hinge on understanding specific gene mutations."

The team collected tissue from 18 HCM patients recently recruited to receive myectomies, surgical procedures involving the excision of a portion of the heart muscle wall. To identify individual PPIs among the

HCM cohort, Maron, co-lead author Ruisheng Wang, Ph.D., and colleagues analyzed tissue contents using RNA-seq, a technique that allows researchers to identify patterns of where and when genes are active. Through a series of steps, they identified patient-specific PPIs (known as reticulotypes) corresponding to the unique biological characteristics of each patient's disease profile.

The group discovered that they could distinguish individualized protein networks in each patient in the HCM cohort.

"These findings represent a major step forward for precision medicine," said Maron. "With the identification of patient-specific biological wiring maps, researchers may one day develop personalized treatments informed by patients' protein networks."

The study is unique in that researchers studied affected tissue collected directly from HCM patients, allowing for a more robust, accurate way of studying patients' pathobiology than has been performed previously. Maron states, however, that in the future, he hopes to develop less invasive ways to perform this same test, whether it be through the collection of blood samples or through other biomarkers in the clinic. The team additionally aspires to apply this same procedure to other diseases as well, hoping to expand the number of opportunities for precision medicine.

"This study illustrates the complexity of HCM but also offers a clearer path forward for understanding the disease pathobiology with the promise of opportunity for precision [medicine](#) in this disease," said Maron.

**More information:** Bradley A. Maron et al, Individualized interactomes for network-based precision medicine in hypertrophic cardiomyopathy with implications for other clinical pathophenotypes,

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