Researchers identify genes linked to stress-triggered heart disease

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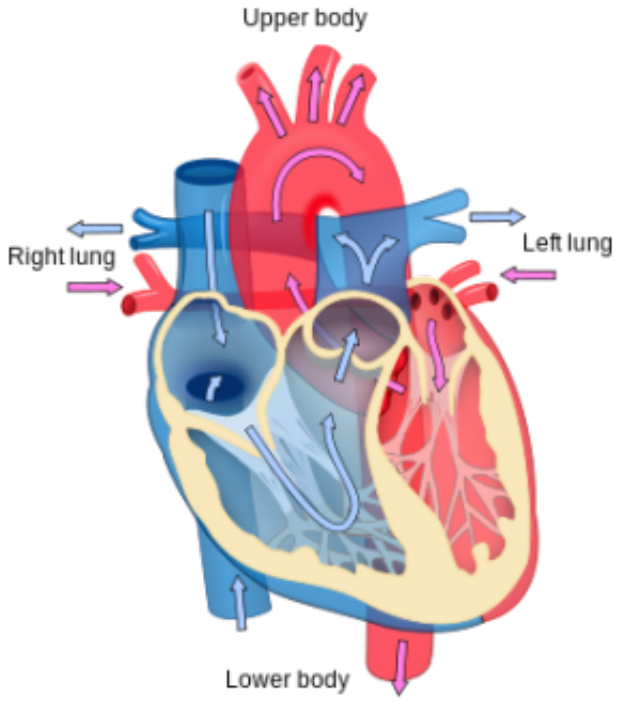

Heart diagram. Credit: Wikipedia

Researchers at the Translational Genomics Research Institute (TGen) and Barrow Neurological Institute have for the first time identified genetic risk factors that are linked to stress-induced cardiomyopathy (SIC), a rare type of heart disease.

Patients with SIC generally show no symptoms until they suffer some

form of intense emotional or physiological distress. For this reason the disorder is sometimes referred to as "broken heart syndrome," and because of its unusual presentation has captured the attention of physicians for centuries.

In a study published Nov. 24 in the journal *Neurosurgery*, researchers report on the identification of new genetic risk factors through the use of the powerful approach of genomic sequencing. Knowing which patients harbor the genes associated with SIC could help guide their care and treatment before, and after, they suffer a life-threatening stressor that induces SIC.

Using ultra-high resolution cameras and supercomputers, researchers identified the suspect genes by next generation DNA sequencing, essentially by spelling out the billions of bits of information in the genomes of seven women who exhibited SIC following a brain aneurysm.

"We hypothesize that patients at highest risk for SIC likely live in a compensated state of cardiac dysfunction that manifests clinically only after the heart muscle is stressed," said Matt Huentelman, Ph.D., Associate Professor of TGen's Neurogenomics Division, and the senior author of the study. "We have identified a series of rare genetic changes associated with this disease that may be used for early identification of patients at risk."

Patients who volunteered for the study were among the 21 victims of hemorrhagic stroke treated at Barrow between 2005-13, and who were diagnosed with SIC. None of the patients had significant prior cardiac history. Barrow is a leading neurotrama center with more than 300 hemorrhagic stroke patients each year.

"We propose that SIC is an example of a hidden heart disease with a

distinct physiological trigger, and suggest that alternative clinical approaches to these patients may be warranted," said Yashar Kalani, M.D. and Ph.D., a chief resident in Neurological Surgery, assistant professor at Barrow at Dignity Health St. Joseph's Hospital and Medical Center, and the study's lead author.

Among the gene variants identified in the study as associated with SIC are MYLK2, DSG2, FKTN, and LDB3. Importantly, all of these genes were previously known to play a role in other cardiac diseases, but not in SIC.

All of these variants are extremely rare. Among the 65,000 publicly available human genomes, MYLK2 had previous been seen in only 1,539 individuals (1.3 percent), DSG2 in 224 (0.1 percent), FKTN in just 3 (0.002 percent), and LDB3 had never before been sequenced.

SIC, also known as or Takotsubo cardiomyopathy, is a poorly understood, and likely under-diagnosed, phenomenon.

"Clinically, SIC is challenging to treat in the critically ill patient, in part because the treatment may exacerbate the sickness," Dr. Kalani said. "A blood-based biomarker for SIC has been elusive until recently and could greatly aid with early identification of patients at risk."

In some cases, the very drug used to treat a heart attack could worsen the condition of patients with SIC.

"Identification of patients at risk for SIC, based on genetic predispositions, would allow for tailored treatment upon admission of these patients to the intensive care unit, and perhaps prior to a decline of the heart and brain," said Dr. Huentelman. "The panel of genes identified by our analysis provides a means of identifying patients who may be at risk for developing this type of heart disorder, and may also be

useful in helping those at the highest risk avoid SIC altogether."

More information: M. Yashar S. Kalani et al. Rare Variants in Cardiomyopathy Genes Associated With Stress-Induced Cardiomyopathy, *Neurosurgery* (2015). DOI: 10.1227/NEU.0000000000001152

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