



NEWS

For more information:
Cathy Yarbrough
press@ashg.org
sciencematter@yahoo.com
858-243-1814

Embargo: 3:30 p.m. ET, Thursday, Oct. 24, 2013

First gene implicated in most common form of mitral valve prolapse disrupts heart valve development & growth, scientists report at ASHG 2013

Research on the DNA of a large multi-generational family has provided a genetic clue that enabled scientists to pinpoint a gene that plays a role in mitral valve prolapse (MVP), a common cardiac disease that is a leading cause of heart failure, according to a study presented today (Thursday, Oct. 24) at the American Society of Human Genetics 2013 meeting in Boston.

The scientists who located the gene, named *DCSH1*, also determined how mutations in this gene disrupt the normal embryonic development of the mitral valve, one of the valves that controls blood flow in the heart.

“This work provides insights into the pathways regulating valve growth and development,” said Susan Slaugenaupt, Ph.D., Professor of Neurology in the Center for Human Genetic Research at Massachusetts General Hospital and Harvard Medical School and one of the lead scientists in the collaborative group that conducted the research.

“The results implicate a previously unrecognized paradigm in the development of long-term structural integrity in the mitral valve,” said Ronen Y. Durst, M.D., former member of Dr. Slaugenaupt’s lab and now a senior cardiologist at Hebrew University and Hadassah Medical Center in Jerusalem. Dr. Durst presented the study this afternoon at ASHG 2013.

The researchers’ first step was to link MVP to a region on human chromosome 11 in the DNA of the group of relatives with the heart disorder. By sequencing that DNA region in family members, the scientists were able to link mutations in *DCSH1* to MVP.

To understand the normal biological functions altered by the mutated copy of *DCSH1*, the researchers turned to two animal models, zebrafish and mice. Experimentally reducing the expression level of the zebrafish version of *DCSH1* resulted in abnormal heart development.

“Treating the zebrafish embryos with the normal copy of the *DCSH1* gene rescued the lesion, while the mutated human *DCSH1* gene did not,” said Dr. Slaugenaupt. “This finding constitutes strong evidence that the mutation disrupts the normal function of *DCSH1*.”

To begin to understand the normal function of *DCSH1* in the valve, the researchers obliterated, or knocked out, the gene in mice. The mice were born with excessive connective tissue in the mitral valve that was elongated, thickened, and the valve prolapsed into the left atrium, as in the human disease.

(more)

The scientists then traced the excessive connective tissue to developmental errors in the alignment of interstitial cells responsible for proper heart valve development and growth. “These developmental errors cause mitral valve prolapse and regurgitation in adult mice,” said Dr. Slaughaupt.

DCHS1 is the first gene implicated in the most common form of MVP, which is not associated with other syndromes. MVP is the most common indication for surgical intervention to repair the mitral valve.

Dr. Slaughaupt said that the research was an interdisciplinary collaboration among scientists specializing in human genetics, cardiac imaging, zebrafish modeling and developmental biology with mouse modeling, with funding provided by the Leducq Foundation Transatlantic Network of Excellence for Mitral Valve Disease.

The scientists’ ASHG abstract is titled, “[Mutations in the DCHS1 Gene Cause Mitral Valve Prolapse In Humans.](#)”

About ASHG

The American Society of Human Genetics is the primary professional membership organization for nearly 8,000 human genetics specialists worldwide. The ASHG Annual Meeting is the world's largest gathering of human genetics professionals and a forum for renowned experts in the field. For more information about ASHG, visit: <http://www.ashg.org>.