Why 'lazy Susan' has a weak heart

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When young, apparently healthy athletes suddenly collapse, it can be due to hereditary cardiac disease. Researchers at the Heidelberg University Hospital have now discovered a genetic modification that leads to cardiac weakness in an animal model. Just one "false" amino acid can give zebrafish a heart condition. Since the fish have a genetic makeup similar to that of humans, these defects could be critical for humans as well.

Cardiac insufficiency is not just a disease that results from a heart attack or myocarditis. For young people in particular there is often an underlying genetic cause (cardiomyopathy). Some 30,000 people in Germany are affected and the disease often remains undetected for a long time. The tragic cases of athletes who suddenly collapse during training or competition are well known. The cardiology department at the Heidelberg University Hospital (Medical Director Prof. Hugo Katus) is one of the major centers in Germany for the treatment and research of cardiac insufficiency.

For many years, the researchers in Heidelberg have been studying the zebrafish. The genetic variant that suffers from cardiomyopathy is called "Lazy Susan" and got its nickname because of its slow blood flow. Dr. Benjamin Meder and Christina Laufer from Dr. Wolfgang Rottbauer's research group (Department of Cardiology) examined its muscle protein myosin light chain-1, which is involved in contraction of the heart muscle. They discovered the crucial change in the amino acid Serine 195, which was lost through mutation. This single change is sufficient to severely limit heart function.

Some 70 percent of the genes of zebrafish and humans are identical

Can these research results be transferred from zebrafish to humans? In the next step, the Heidelberg cardiologists plan to search for the same mutation in patients' genes. Since approximately 70 percent of human genes are identical with those of zebrafish, the researchers are confident that a Serine 195 mutation will have a similar affect in human hearts. The researchers also hope to develop new therapies for patients. A targeted modification of the amino acid Serine could increase the activity of the actin-myosin complex and result in an increase of cardiac contractility.

More information: Benjamin Meder, Christina Laufer, David Hassel, Steffen Just, Sabine Marquart, Britta Vogel, Alexander Hess, Mark C. Fishman, Hugo A. Katus and Wolfgang Rottbauer. "A Single Serine in the Carboxy-terminus of Cardiac Essential Myosin Light Chain-1 Controls Cardiomyocyte Contractility in-Vivo", *Circulation Research*, published online Jan 22, 2009, DOI:10.1161/CIRCRESAHA.108.186676

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