An often overlooked protein actually a potent regulator of cardiac hypertrophy

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A protein long thought to be a secondary regulator in the heart's response to stressors like hypertension actually appears to be a primary regulator according to researchers from the Center for Translational Medicine at Thomas Jefferson University. The data will be presented in the Late Breaking Science session at the American Heart Associations Scientific Sessions in Orlando, Fla.

According to Thomas Force, M.D., the James C. Wilson Professor of Medicine at Jefferson Medical College of Thomas Jefferson University, glycogen synthase kinase-3 (GSK-3) proteins include the isoforms GSK-3beta and GSK-3alpha. GSK-3beta has always been thought to be the regulator of cardiac hypertrophy, and GSK-3alpha has been largely ignored. But the ignored isoform is actually quite powerful.

"We found that knocking out GSK-3beta did not do much at all, but knocking out of GSK-3alpha caused a huge increase in hypertrophy," said Dr. Force, who led the study. "The standard theory was that beta is more potent than alpha, but alpha was far more important at regulating this process."

Hypertrophy is the heart's response to stressors such as hypertension. In hypertrophy, the heart muscle cells get larger, as does the heart itself. This process is a predictor of heart failure and death. The concept, according to Dr. Force, is to understand the pathways through which this happens, which would allow physicians to intervene and possibly prevent the heart failure.

In addition to regulating hypertrophy, the researchers also found that GSK-3alpha is a potent positive regulator of the beta-adrenergic system, which allows the heart to respond to stresses and helps failing hearts pump better. But when GSK-3alpha was knocked out in the mice models, the heart systems simply failed and were not able to stand up to the pressure of stressors like hypertension.

GSK-3 is targeted by a number of drugs in development for several diseases, including bipolar disorder, Alzheimer's disease and diabetes.

"If these inhibitors make it to clinical trials, patients being treated with them would need to be closely watched, especially if they have diseases like hypertension or underlying heart disease," Dr. Force said. "They could run into trouble if their hearts are unable to respond to stressors due to the inhibition of GSK-3alpha."

Lastly, the researchers also found that when GSK-3beta was knocked out, the heart progenitor cells started to proliferate. This could potentially serve as the basis for a regenerative therapy approach for patients with heart failure, according to Dr. Force. Inhibiting GSK-3beta increased the proliferation of myocytes in the heart by five- to 10-fold.

Source: Thomas Jefferson University (news : web)