Inhibition of GRK2 is protective against acute cardiac stress injuries

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Inhibition of a protein known to contribute to heart failure also appears to be protective of the heart in more acute cardiac stress injury, namely ischemia reperfusion, according to two studies conducted at the Center for Translational Medicine at Thomas Jefferson University. The studies will be presented at the American Heart Association Scientific Sessions 2009 in Orlando, Fla.

The first study was presented by Henriette Brinks, M.D., a postdoctoral fellow in the Center for Translational Medicine. The researchers, led by Walter J. Koch, Ph.D., director of the Center for Translational Medicine, examined mice that overexpressed the G-Protein coupled Receptor Kinase-2 (GRK2). This overexpression was deleterious in ischemic myocardium, according to Dr. Koch, in that these mice had larger areas of infarction or myocardial death. However, inhibition of GRK2 activity with the peptide GRK2 inhibitor, ?ARKct, was cardioprotective, and resulted in less cell death and increased AKT signaling, with more viable myocardium and improved post-ischemic cardiac function.

In the second study, Dr. Koch, who is also the W.W. Smith Professor of Medicine at Jefferson Medical College of Thomas Jefferson University, and his team looked at mice that had a heart-specific deletion of the GRK2 gene. This study was presented by Erhe Gao, M.D., Ph.D, research associate professor in the Center for Translational Medicine. This study revealed that when the GRK2 protein is absent from heart cells, there is limited damage to the myocardium after ischemic injury, including decreased cell death. This leads to improved recovery from acute cardiac damage.

"We know that levels of GRK2 are increased in chronic heart failure, but studies have also shown that increases of GRK2 levels are one of the first changes observed after acute heart damages such as heart attack and ischemia," Dr. Koch said. "Both of these studies show that the absence of GRK2 activity protects the cardiac myocytes against ischemic reperfusion."

The results of these studies show that inhibiting GRK2 is a viable therapeutic approach that reduces acute ischemia injury to the myocardium, and is a strategy to limit acute myocardial ischemia.

Source: Thomas Jefferson University (news : web)