Researchers Identify 'Long-Sought Culprit' of Heart Failure

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The research, published in the journal Nature, revealed that an enzyme called PDE-9 interferes with the body's natural "braking" system needed to neutralise stress on the heart.

"Like a play with multiple characters, heart muscle function is the result of a complex but perfectly synchronised interaction of several proteins, enzymes and hormones," said lead investigator Dong Lee, cardiology research associate at the Johns Hopkins University School of Medicine in the US.

Naturally found in the gut, kidneys and brain, PDE-9 is already a prime suspect in neurodegenerative conditions such as Alzheimer's, the researchers said.

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But the new study shows that the enzyme's footprints are also present in heart cells and markedly elevated in patients with heart failure - evidence that PDE-9 is a multi-tasking "offender" and a key instigator of heart muscle demise, they added.

Working with lab animals and human heart cells, the scientists found that the enzyme PDE-9 wreaks mischief by gobbling up a signalling molecule, cGMP, which normally stimulates the production of a heart-protective protein called PKG.

The protein PKG is known to shield the heart muscle from the ravages of disease-causing stress, such as long-standing high blood pressure.

To understand the enzyme's role, the scientists exploited the knowledge that heart muscle health is safeguarded by two separate mechanisms, or signalling pathways.

Nearly a decade ago, researchers identified the culprit responsible for breakdown in one of the signalling pathways, an enzyme called PDE-5. Ever since then scientists have searched for the second "offender" that causes glitches in the other pathway.

The discovery of PDE-9 provides that long-sought break in the case, the researchers said.

In the current study, PDE-9 blockers not only stopped heart muscle enlargement and scarring in mice with heart failure, but they nearly reversed the effects of the disease.