Two beta blockers found to also protect heart tissue

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(PhysOrg.com) -- A newly discovered chemical pathway that helps protect heart tissue can be stimulated by two of 20 common beta-blockers, drugs that are prescribed to millions of patients who have experienced heart failure.

Researchers from Duke University Medical Center tested 20 beta blockers and found that two of them -- alprenolol and carvedilol -- could stimulate a pathway recently found to protect heart tissue.

This finding could guide future drug development and in particular help heart failure patients, says Howard Rockman, M.D., senior author of the study and chief of the Duke Cardiology Division.

"To our surprise, we found that these two beta blockers can actually stimulate the beta receptor to activate a pathway in the cell that promotes cell survival. We have the first evidence that these two drugs have greater potential to repair the heart and to protect it, and possibly even to reverse some heart damage," Dr. Rockman said.

Until now, scientists believed that all beta-blockers worked by binding to and blocking the beta-adrenergic receptor, a molecule on the cell surface that responds to the hormone adrenalin. Blocking the receptor moderates increases in heart rate and heart function that could be damaging to patients whose hearts are already overstressed.

The two beta-blockers identified by the current study also serve to

stimulate a different signaling beta-arrestin pathway. Beta arrestin is a protein known as an "off-switch" for beta-adrenergic receptors. These two drugs activated a beta-arrestin pathway that produces beneficial effects in the heart tissue.

"These two drugs were found to stimulate the pathway that produces certain proteins that are protective to the heart," Rockman said.

The new study, published online in *Proceedings of the National Academy of Sciences,* was funded by that National Institutes of Health.

"Based on these findings, we hope to design drugs that strongly bind in this way and activate this pathway," Rockman said. "We call these drugs biased-ligands or super receptor blockers, because they are designed to block the harmful actions of adrenalin at the beta receptor, but at a molecular level will activate other pathways that protect the cell." Rockman and colleagues discovered the heart-protection factors in a study published last year.

He noted that carvedilol (marketed for many years as Coreg and now as available in generic forms) is known as a very effective beta blocker, but alprenolol has not been fully developed as a beta blocker drug for heart failure patients. Beta blockers now are part of a standard of care for heart failure patients, who have weakened hearts and cannot tolerate much adrenalin, which is released all day long in people as they perform any exertion, even reading an exciting novel. Every year, 400,000 new cases of heart failure are diagnosed and the number is growing as the population ages.

"The next step is to test the drugs in animals to learn which might promote protection and which might cause more negative effects," Rockman said. "Cell studies can be tricky to replicate in organisms and we will have to see what happens, but these cellular results are very

exciting and encouraging and could be a boon to heart failure patients."

Provided by Duke University Medical Center