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Statins Can Stimulate Cardiac Muscle Cell Regeneration, Improve Heart Function

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(PhysOrg.com) -- Statins, used widely to treat elevated cholesterol, have been shown to prevent progression of coronary narrowing and to have other beneficial effects on the heart, such as reducing inflammation, that are independent of cholesterol.

Now, adding to this list of multiple effects, researchers at the University at Buffalo have shown that the drug pravastatin, one of the oldest statins, may be able to prevent the development of heart disease by regenerating diseased heart muscle.

In a paper published in the January 2009 issue of *Circulation Research*, the investigators report that pravastatin mobilizes bone marrow progenitor cells -- blood stem cells that are able to transform into many different types of cells -- which infiltrate the heart and develop into cardiac muscle cells, or myocytes, improving cardiac function.

The research was carried out in UB's Center for Research in Cardiovascular Medicine, using the center's unique swine model of hibernating myocardium -- a condition in which myocytes reduce their contraction yet remain viable in areas that have received reduced blood flow over an extended period of time due to narrowed arteries.

"The finding that a drug with an excellent safety profile used widely to lower blood cholesterol is effective in improving cardiac function in hibernating myocardium is a welcome finding," said Gen Suzuki, M.D., Ph.D., UB research assistant professor of medicine and first author on

the study.

"This provides a new strategy for treating patients with ischemic heart failure who are not candidates for coronary artery bypass graft surgery (CABG) or coronary balloon angioplasty."

John M. Canty Jr., M.D., Albert and Elizabeth Rekate Professor and chief of the Division of Cardiovascular Medicine in UB's School of Medicine and Biomedical Sciences, and director of the cardiology research center, developed the swine model and is a coauthor on the study.

"Pravastatin increased the number of progenitor cells in bone marrow in proportion to the dose of the drug, which correspondingly increased the number of progenitor cells circulating in the blood stream and ultimately localizing in the heart," said Suzuki.

"This occurred in as little as five weeks after treatment with pravastatin, using animals that had chronic coronary artery narrowings and dysfunctional hearts, with completely normal cholesterol levels. The number of cardiac myocytes increased in the hibernating hearts after pravastatin, and this 'new' population of myocytes was remarkably smaller than the existing myocytes, suggesting they arose from myocyte regeneration."

Suzuki noted that, importantly, animals with normal hearts that received pravastatin showed no increase in new myocytes, even though the drug increased the number of circulating and cardiac progenitor cells.

"This finding suggests that the new myocytes formed directly in response to need and to the presence of the heart's diseased state, preventing uncontrolled cardiac muscle growth and proliferation in otherwise normal hearts.

Earlier small clinical studies using a variety of older statins had suggested the possibility that the drugs improved heart function and symptoms in patients with congestive heart failure. Canty noted that this contrasts with randomized clinical trials completed recently to test the effects of the newer and extremely potent drug rosuvastatin, which failed to demonstrate a beneficial effect on survival or symptoms.

"Our current preclinical study now raises the possibility that this difference is associated with age-related changes in progenitor cells in patients, or perhaps with a proinflammatory state that prevents the beneficial actions of statins," said Canty. "An alternative possibility could be that the ability of individual statins to mobilize bone marrow stem cells may vary, and may not be a 'class' effect, like their actions to lower cholesterol."

To determine if the latter possibility is at work, researchers at the UB Center for Research in Cardiovascular Medicine now are investigating, as they did with pravastatin, if rosuvastatin (shown to have no major effect in large clinical studies in patients with heart failure) can mobilize bone marrow stem cells and aid cardiac repair in their porcine model of ischemic heart disease.

Provided by University at Buffalo