Researchers examine molecular relationships between diabetes and heart disease

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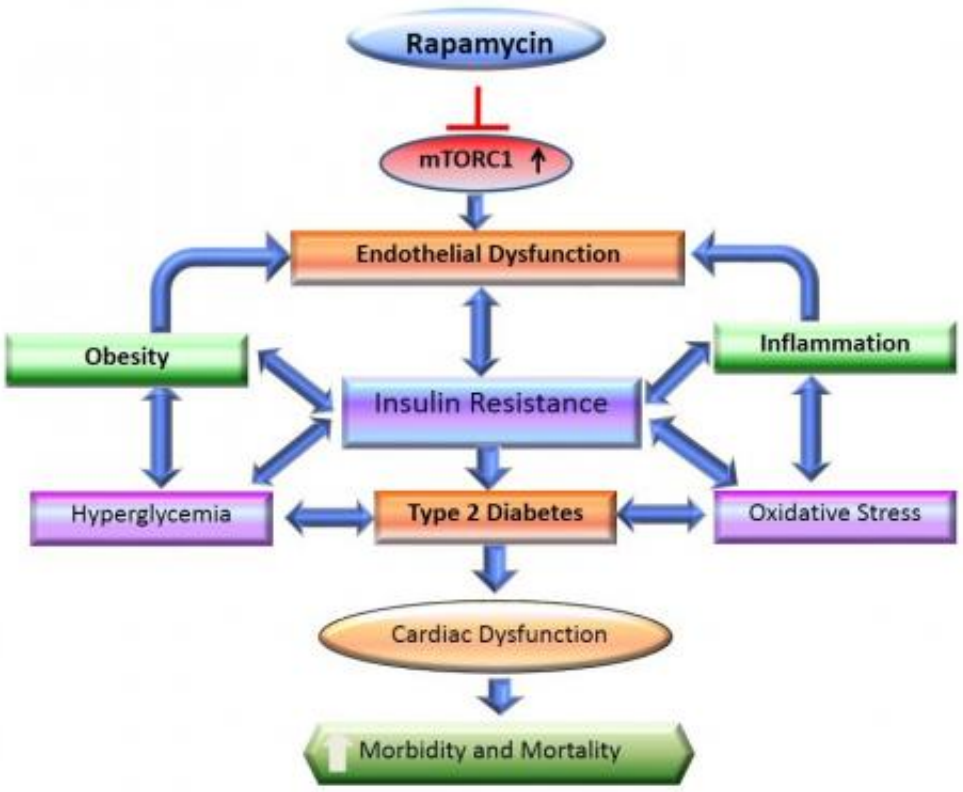

Proposed mechanisms of cardio protection by rapamycin in type 2 diabetes. Rapamycin inhibits mTOR signaling and subsequently prevents endothelial dysfunction, obesity, hyperglycemia, insulin resistance, inflammation and oxidative stresses. This eventually prevents diabetic-induced cardiac dysfunction in type 2 diabetes. Credit: Anindita Das, Ph.D./ VCU.

(Medical Xpress)—Chronic treatment with low doses of a drug used to

boost organ survival in transplant patients has been found to improve metabolism and heart dysfunction in an animal model, according to a new study from Virginia Commonwealth University.

As the number of patients with type 2 diabetes reaches epidemic proportions worldwide – and is expected to double during the next 20 years – researchers are working to gain a basic understanding of the molecular relationships between diabetes and heart disease to identify new drug targets. Diabetes is associated with heart attack, and patients with elevated fasting glucose are at a three-fold increased risk of mortality following a heart attack.

In a study published Feb. 14in the *Journal of Biological Chemistry*, researchers report that rapamycin, an antibiotic used to boost organ survival in transplant patients, may protect the heart against complications associated with type 2 diabetes in an animal model.

Using cutting-edge physiological, molecular and proteomic approaches, the team closely examined a key signaling pathway called mammalian target of rapamycin (mTOR). It is a signaling pathway responsible for the regulation of cell growth and metabolism, and has been implicated in a number of human diseases, including diabetes.

"Rapamycin treatment improves metabolism in diabetic mice with significant reduction in body weight, heart weight, plasma glucose, insulin levels and triglyceride levels," said contributing author Rakesh C. Kukreja, Ph.D., professor of medicine, Eric Lipman Chair of Cardiology and Scientific Director at the Virginia Commonwealth University Pauley Heart Center.

"In addition, the drug prevents cardiac dysfunction in diabetic mice, possibly through reducing oxidative stress and altering proteins that assist in maintaining the contractility of the diabetic heart," said Anindita

Das, Ph.D., assistant professor of medicine at VCU, who led the study.

In 2006, in a study published in the *Journal of Molecular and Cellular Cardiology*, the team reported a protective role of rapamycin against heart disease in a non-diabetic animal model.

According to Das and Kukreja, further research is needed to understand the molecular mechanisms underlying metabolic and heart function benefits of rapamycin in patients with diabetes. The team has plans for new studies in translational animal models of type 2 diabetes to show that rapamycin can minimize damage to the heart after an acute heart attack.

"These investigations may help in rapid initiation of clinical trials for safe development of this promising therapy in patients," Kukreja said.

Provided by Virginia Commonwealth University