

## Carvedilol shown to have unique characteristics among beta blockers

## November 20 2009

In a new study, researchers report that a class of heart medications called beta-blockers can have a helpful, or harmful, effect on the heart, depending on their molecular activity.

The study, which appears in the journal *Circulation Research*, found that beta-blockers that target both the alpha- and beta-receptors on the heart muscle offer the most benefit to cardiac patients, while those that target only the beta-receptors can actually undermine the structure and function of the heart.

Circulation Research is published by the American Heart Association.

Heart disease is the leading cause of death in the United States. Patients with heart disease usually have higher levels of catecholamines - hormones that activate the beta-adrenergic receptors to stimulate cardiac muscle contraction. In this process, the heart initially grows to become a more efficient pump. Unfortunately, the researchers found, this growth also predisposes the heart to eventual failure.

Traditionally, beta-blockers targeting the beta-adrenergic receptors have been utilized as a long-term therapy for heart failure.

Interestingly, blocking adrenergic receptors has been widely used clinically for nearly 50 years without a full understanding of the molecular consequences of these drugs, said co-author and graduate student David Cervantes. Kevin Xiang, a professor of molecular and



integrative physiology at the University of Illinois led the study. The research team also included researcher Catherine Crosby.

A previous study in 2003 showed that the beta-blocker carvedilol produced a greater survival benefit than another drug, metoprolol tartrate. Carvedilol targets both the beta- and alpha-adrenergic receptors.

The new study unveiled an elegant intracellular signaling system in which beta-receptor activation modulates alpha-adrenergic signaling. It showed that blocking the beta-receptor alone promotes cardiac remodeling via growth of cardiac fibroblasts induced by alpha-adrenergic receptor signaling. The growth of fibroblasts in the heart further damages the integrity and function of the heart.

This observation suggests that the use of carvedilol in combination with inhibitors of angiotensin-converting enzyme (ACE inhibitors) may be of the greatest benefit to cardiac patients, and has significant clinical implications on which beta-blockers patients should take.

"I think this is really good stuff," Xiang says. "It's a surprise project. It's not what we initially intended looking into. But it's a very nice, elegant study and a very beautiful cellular mechanism. It definitely will help people along the way to understand how to further manipulate this system. Beta blockers are still the most commonly used drug for heart disease."

Source: University of Illinois at Urbana-Champaign (<u>news</u>: <u>web</u>)

Citation: Carvedilol shown to have unique characteristics among beta blockers (2009, November 20) retrieved 5 May 2024 from <a href="https://medicalxpress.com/news/2009-11-carvedilol-shown-unique-characteristics-beta.html">https://medicalxpress.com/news/2009-11-carvedilol-shown-unique-characteristics-beta.html</a>



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