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Slowing the Racing Heart
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Scientists have discovered how we put the brakes on a racing heartbeat.

Researchers at the University of Illinois at Chicago explain in the May 11 issue of *Circulation Research* how an enzyme acts on the heart's pacemaker to slow the rapid beating of the heart's "fight-or-flight" reaction to adrenaline.

A single cell in the upper right chamber is responsible for setting the pace of the beating heart, triggering its neighbor cells to beat. In the human heart, one cell -- the pacemaker cell -- beats faster or slower to induce a rhythmic heartbeat that varies to increase or decrease the blood flow to the body as we eat, sleep or exercise.

"Disturbances of pacemaker control are common in heart diseases. When the heartbeat becomes non-rhythmic and chaotic, it can result in fatal arrhythmias and stroke," said R. John Solaro, UIC distinguished university professor and principal investigator of the study.

Current treatment of arrhythmia requires destruction of tissue surrounding a chaotic pacemaker, followed by insertion of a mechanical pacemaker that can regulate the heartbeat.

"Understanding the molecular regulation of the heart's pacemaker opens the possibility of less drastic treatment options, including drug interventions," said Solaro, who is also director of the center for cardiovascular research and head of physiology and biophysics at UIC.

Solaro worked with Yunbo Ke, UIC research assistant professor of physiology and biophysics and first author of the paper, and colleagues in England at Oxford and Manchester on characterizing and isolating the pacemaker cell.

The UIC researchers demonstrated that an enzyme called Pak 1, present in high concentrations in the heart, signals depression in the action of adrenaline and adrenaline-like chemicals on the pacemaker cell, playing an important role in slowing down the heart rate.

"The enzyme works through calcium and potassium channels that we know to be key players in the generation and regulation of the pacemaker activity," said Ke.

"Although adrenaline and other mechanisms that accelerate the heart rate have been well studied, mechanisms that might act as a brake are poorly understood," said Solaro.

"Identification of this previously unknown molecular mechanism for slowing the heartbeat may offer new avenues of diagnosis, drug design and treatment of many common heart diseases," said Solaro.

"Further, now that we know something of how this enzyme works in the pacemaker

cell, we may discover it is involved in the regulation of other processes, particularly in the brain, where it is also highly expressed," added Ke.

Other contributors include Dr. Derek Tarrar, Thomas Collins, Stevan Rakovic, Paul Mattick and Michiko Yamasaki at Oxford; Dr. Ming Lei at the University of Manchester; and Mark Brodie at UIC.

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[Editors Note: Extended interview as MP3 audio file available at www.uic.edu/depts/paff/newsbureau/podcasts.html]
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