MedicalXpress

Study helps advance heart-related research

December 4 2009

Using a new mathematical model of heart cells, University of Iowa investigators have shown how activation of a critical enzyme, calmodulin kinase II (CaM kinase), disrupts the electrical activity of heart cells.

The study, which also involved Columbia University, was published online Dec. 3 in the journal PLoS Computational Biology.

"Recently, researchers have developed great interest in calmodulin kinase II as a critical regulator of the heart's response to injury. By targeting this enzyme's activity, it may be possible to prevent or treat heart disease and associated electrical rhythm disturbances," said Thomas Hund, Ph.D., associate in internal medicine at the University of Iowa Roy J. and Lucille A. Carver College of Medicine and the paper's senior author.

"CaM kinase is activated when the heart experiences injury, for example, when an artery providing blood to the heart becomes blocked. In the short-term, this increase in activity may be the heart's attempt to increase blood flow," Hund said. "However, unfortunately, the initial response results in a vicious cycle that likely advances heart disease."

In this study, the team analyzed tissue from injured hearts from animals, in which a coronary artery had been blocked. They found a dramatic increase in the levels of oxidized CaM kinase in specific heart regions where potentially lethal electrical activity occurs.

Using the mathematical model of the cardiac cell, the researchers were

able to predict, through computer simulation, the effects of oxidized CaM kinase on cardiac electrical activity.

Oxidation activates the enzyme by modifying key chemical groups. In heart disease, oxidation is overactive, and CaM kinase is turned on too much.

"Oxidation appears to be a critical pathway for activation of CaM kinase in disease," Hund said. "Heart cells are very difficult to study, so improving our research tools -- as we did by creating the mathematical model -- is critical for generating new insight into heart disease mechanisms."

The study also included significant contributions from Peter Mohler, Ph.D., University of Iowa associate professor of internal medicine, Mark Anderson, M.D., Ph.D., University of Iowa professor and head of internal medicine, and Penelope Bodyen, Ph.D., professor of pharmacology, at Columbia University.

More information: The published study can be read online at www.ploscompbiol.org/article/info%3Adoi%2F10.1371%2Fjournal.pcbi.1000583 .

Source: University of Iowa (news : web)