SOUTHWESTERN NEWS

Media Contact: Amy Shields
214-648-3404
amy.shields@utsouthwestern.edu

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UT SOUTHWESTERN RESEARCHERS REVEAL FUNCTION OF CALCIUM TRANSPORT PROTEIN THAT REGULATES HEARTBEAT FREQUENCY, STRENGTH

DALLAS – Feb. 5, 2004 – A membrane protein, NCX1, that transports sodium and calcium into and out of cells, may determine the frequency as well as strength of the heartbeat, researchers at UT Southwestern Medical Center at Dallas report.

The findings are published in today's issue of *Nature*.

"This calcium transporter really is an important key to understanding how the heart is regulated," said Dr. Donald Hilgemann, professor of physiology and senior author of the study. "At every beat, calcium in heart cells increases. And it's calcium that is the messenger to the heart to get it to contract.

"We knew for a long time that NCX1 brings calcium into and out of heart cells by exchanging it for sodium. And in doing so it generates important electrical currents in the heart. The surprise is that this transporter dances more than just that old waltz from Vienna. It knows Salsa!"

The research reveals two new modes of operation of NCX1. First, the membrane protein can move sodium into heart cells without moving calcium out. This mode generates an electrical current independent of calcium transport that contributes to excitation of the heart. The second mode is to move calcium into heart cells without generating any electrical current. This mode, Dr. Hilgemann said, may determine the calcium that remains in heart cells after each beat and thereby determines the strength of cardiac contraction over many beats.

Using so-called "giant membrane patch" techniques together with highly sensitive ion detection techniques, both developed and implemented by Dr. Hilgemann, UT Southwestern researchers were able to determine precisely how NCX1 works as an ion exchanger, how many calcium and sodium ions move across the membrane, when they are exchanged, and, surprisingly, when they move together.

(MORE)

"Transporters move ions across membranes by grabbing hold of them and transferring the energy of one type of ion to another type, just one or a few at a time, backwards and forward, together or in exchange for one another," Dr. Hilgemann said. "This is a much bigger biophysical problem to get a handle on than ion channels. Ion channels, when they are open, let millions of ions slip through them each second. You measure the electrical current, and you know what's going on."

UT Southwestern researchers over the last three years spearheaded new approaches to measure ion transfer across microscopic patches of membrane, independent of the electrical current. The "giant patch" system is essentially a large piece of cell membrane glued to the end of a glass pipette. This method has been used by numerous groups to study ion transporters and channels that could not be studied with conventional techniques. It can measure the properties of these systems in a millionth of a second, at least 10 times faster than the previous methods.

"Seeing now that NCX1, in some instances, moves an extra calcium or an extra sodium ion lets us predict much better how this system works in the heart and how it affects the function of the heart," Dr. Hilgemann said. "There are many, many more important transporters – many of them involved in human disease – to be studied with this kind of resolution in the kidney, in the pancreas, in the brain, everywhere. NCX1 is just the tip of the iceberg."

In 1997 Dr. Hilgemann was named Young Investigator of the Year by the International Biophysical Society in recognition of his studies of transport systems that move molecules across cell membranes.

Dr. Tong Mook Kang, a former fellow at UT Southwestern who is now at the Sungkyunkwan University School of Medicine in South Korea, is coauthor of the study.

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