SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS MOVE CLOSER TO EXPLAINING CYCLOSPORINE-INDUCED HYPERTENSION

DALLAS -- Aug. 15, 2000 -- Researchers at UT Southwestern Medical Center at Dallas have uncovered a potential explanation for how cyclosporine and related anti-rejection drugs can elevate blood pressure and cause hypertension in organ-transplant recipients.

The results of their study are published in today's issue of *Proceedings of the National Academy of Sciences*. The paper is available online at www.pnas.org.

"The mechanism seems to involve a specific protein that is present in sensory nerves of the kidney," said Dr. Ronald Victor, chief of hypertension and holder of the Dallas Heart Ball Chair in Hypertension and Heart Disease. "By understanding how this works, in the future we may be able to develop new drugs that block the bad effects of cyclosporine on blood pressure, while leaving intact its ability to prevent rejection of transplanted organs.

"This is one of the most important problems to solve in the transplant arena -- how to decrease the toxicity of cyclosporine and other immune-suppressive drugs that prevent the body from rejecting transplanted organs."

Victor and his UT Southwestern colleagues, including Dr. Weiguo Zhang, instructor of internal medicine, and Dr. Thomas Sudhof, director of the Center for Basic Neuroscience, used genetically altered mice to identify the molecules in sensory nerves that allow the nerves to sense the presence of cyclosporine.

(MORE)

The researchers found that when mice lacked a family of proteins called synapsins, their blood pressure did not go up when cyclosporine was administered.

Zhang, the principal investigator of the study, called the study "a wonderful marriage between cardiovascular physiology and molecular neuroscience."

Cyclosporine was introduced clinically in the 1980s, and it quickly revolutionized organ transplantation. The drug is credited for greatly improving the long-term survival of organ-transplant recipients.

But its chief side effect – high blood pressure -- has otherwise clouded its reputation. Almost 90 percent of heart-transplant patients, for example, develop cyclosporine-induced hypertension after the transplant, Victor said.

The drug also is administered following other organ transplants, including liver and bone marrow transplants.

A team of researchers led by Victor previously had used rats to show that cyclosporine caused the sympathetic nervous system to stimulate the nerves that cause blood vessels to contract, leading to an increase in blood pressure.

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