UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Erin Prather Stafford
214-648-3404
erin.pratherstafford@utsouthwestern.edu

Preclinical study suggests organ-transplant drug may aid in lupus fight

DALLAS – Aug. 15, 2007 – A compound related to a drug used in humans to prevent organ-transplant rejection attacks a key biochemical process in the faulty immune cells of lupus-prone mice, suggesting a possible new approach to combating the disease, UT Southwestern Medical Center researchers have found.

"We found that an analog of rapamycin is very effective in improving all aspects of the disease in lupus-prone mice," said Dr. Chandra Mohan, professor of internal medicine and senior author of a study appearing in the August issue of the *Journal of Clinical Investigation*. "Our next step will be to see if the same biochemical pathways exist in humans. If they do, this research and treatment could prove very significant."

Lupus is a chronic autoimmune disease in which the immune system attacks the body's cells and tissues. In a normal immune system, foreign intruders are recognized by special immune cells called B-cells, which produce antibodies. In patients with lupus, however, the antibodies created by the B-cells start to attack the body itself.

Certain genetic strains of mice are prone to developing lupus. In the current study, a research team led by Dr. Mohan discovered that an analog of rapamycin shuts down specific biochemical processes in the B-cells of the mice. Rapamycin has been used in humans to prevent organ transplant rejection and for treating cancer. The analog of rapamycin halted production of antibodies and the development of lupus in all the strains of lupus-prone mice, as well as improved symptoms, despite each animal having a different genetic makeup that led to the disease.

"Though lupus in different mouse models may originate from different genetic triggers, those triggers ultimately funnel through a shared series of biochemical pathways that lead to the disease," Dr. Mohan said. "These shared biochemical pathways represent an attractive target for future therapeutic intervention in lupus patients."

In humans, lupus can cause life-threatening damage to the kidneys, lungs, heart, central nervous system, joints, blood vessels and skin. It can be associated with severe fatigue, joint pain,

(MORE)

skin rashes, hair loss and neurological problems. Although treatable symptomatically, there is currently no cure for the disease, which affects up to 1 million people in the U.S.

Other UT Southwestern researchers involved with the study were Dr. Tianfu Wu, assistant instructor of immunology; Xiangmei Qin, research assistant in immunology; Zoran Kurepa, immunology resident; Kirthi Raman Kumar, postdoctoral trainee in internal medicine; Dr. Kui Liu, instructor of internal medicine; Hasna Kanta, research assistant in internal medicine; Dr. Xin J. Zhou, professor of pathology; Dr. Anne Satterthwaite, assistant professor of immunology; and Dr. Laurie Davis, associate professor of immunology.

The research was funded by the National Institutes of Health and the Alliance for Lupus Research.

###