SOUTHWESTERN NEWS

Media Contact: Scott Maier
214-648-3404
scott.maier@utsouthwestern.edu

EMBARGOED UNTIL 11 A.M. CST TUESDAY, DEC. 14, 2004

UT Southwestern researchers locate gene family involved in determining potential for acquiring lupus

DALLAS – Dec. 15, 2004 – Researchers at UT Southwestern Medical Center at Dallas have found a gene family involved in determining the potential for acquiring lupus, a debilitating autoimmune disease that affects more than one million Americans.

"Our findings indicate genetic susceptibility to lupus results from imbalance between genes that increase and genes that suppress the immune system's responsiveness," said Dr. Ward Wakeland, director of the Center for Immunology and the Harold C. Simmons Arthritis Research Center at UT Southwestern and senior author of the study in today's issue of *Immunity*. "Individuals with increased risk for lupus may simply have the misfortune of expressing a 'bad' combination of versions of genes that are 'good' for resistance to infectious diseases."

Systemic lupus erythematosus (SLE) is an autoimmune disease causing the immune system to attack the body's own tissue and organs, including the joints, kidneys, heart, lungs, brain, blood and skin. The Lupus Foundation of America estimates approximately 1.5 million Americans have the disease, which affects all age groups. It is 10 to 15 times more likely in adult women than adult men.

In its study of a mouse strain that develops autoimmunity similar to human SLE, Dr. Wakeland's research team identified a cluster of genes, the *SLAM/CD2* family, occurring in the same region of the human genome associated with genetic susceptibility to the disease. The genes played a crucial role in the disease's development in the mice, but only when they were expressed in specific combinations with other genes.

"The *SLAM/CD2* family interacts with sets of highly variable genes, which can provide a pathway toward disease," said Dr. Wakeland.

In addition, the researchers linked this gene family to resistance to infectious diseases. The latest findings follow an earlier discovery by Dr. Wakeland and his colleagues of four genes that can halt lupus. These "suppressor" genes – *Sles1*, *Sles2*, *Sles3* and *Sles4* – can block the disease even if the susceptibility

(MORE)

gene family is active.

"For example, *Sles1* specifically suppresses the autoimmune activity associated with the *SLAM/CD2* gene family found in the mouse model," Dr. Wakeland said. "With the identification of *SLAM/CD2*, we now have half of the combination of genes that can either lead to or suppress severe disease. Once we fully characterize *Sles1*, we'll have the complete picture."

Researchers in the Center for Immunology are currently working with faculty in the Division of Rheumatology and the Simmons Arthritis Research Center to expand analysis of these genes and their functions into humans with SLE, as well as individuals who may be at increased risk for developing the disease so they can be identified earlier.

"The way the disease is treated now is through a broad spectrum of drug therapies that basically suppress the entire immune system," Dr. Wakeland said. "Patients with lupus under this therapy are at risk to develop infectious diseases because their immune system is completely impaired. If we can understand what the suppressor gene is doing to block *SLAM/CD2*, we may be able to tweak the immune system back into normal balance."

Other Center for Immunology contributors to the *Immunity* study were Dr. Amy Wandstrat, assistant instructor; Xiang-Hong Tian, senior research associate; Charles Nguyen, Medical Scientist Training Program student; Alice Chan, MSTP student; Nisha Limaye, student research assistant; Srividya Subramanian, student research assistant; and Dr. Young-Sun Yim, former postdoctoral researcher. Dr. Harold Garner, professor of biochemistry, and Dr. Alexander Pertsemlidis, assistant professor in the Eugene McDermott Center for Growth and Development at UT Southwestern and Dr. Laurence Morel of the University of Florida School of Medicine also contributed.

Research was supported by grants from the National Institutes of Health, the Alliance for Lupus Research, the Lupus Research Institute, the Arthritis Foundation and the National Institute of Allergy and Infectious Diseases.

###