

# DNA variations signal lupus risk

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Scientists have pinpointed a set of common variations in human DNA that signal a higher risk for lupus in women who carry them. Some of these variations are more common in relatives of lupus patients, which may help future studies examining whether lupus is more prevalent among certain racial and ethnic groups, according to a new study.

Also, the findings point to various drug targets important to the search for cutting-edge lupus treatments, according to an international consortium of genetics researchers that includes scientists at the University of Alabama at Birmingham (UAB).

“Building on this finding we hope to identify those at highest risk of lupus, diagnose the disease earlier and hopefully find a cure,” said Robert Kimberly, M.D., a professor of medicine in the UAB Division of Clinical Immunology and Rheumatology and co-author on the new study.

The findings are published in the journal *Nature Genetics*.

The study, the largest of its kind to date, is the work of the International Consortium for Systemic Lupus Erythematosus (SLEGEN), of which UAB is a member. SLE is the medical term for systemic lupus erythematosus, a common form of the disease.

Looking at the genomes of 6,728 people, the researchers found the variations located on various chromosomes in women of European ancestry. The variations may be linked to as many as 67 percent of all lupus cases in women, the study authors write.

“These findings underscore that numerous genes, which are often immune-function related, contribute to the risk of developing lupus,” said Carl D. Langefeld, Ph.D., of Wake Forest University School of Medicine in Winston-Salem, N.C., the senior author on the SLEGEN study.

The Lupus Foundation of America estimates 1.5 million to 2 million Americans have a form of lupus, but the actual number may be higher. More than 90 percent of people with lupus are women and lupus rates are higher in African-American, Latino, Asian and Native American women than in women of other races and ethnicities.

Systemic lupus is a chronic inflammatory disease that can involve many organs, and often strikes the joints, kidneys, heart, lungs brain and the blood. The interaction of genetic variants and environmental factors are thought to contribute lupus susceptibility and severity, so the variants are a diagnostic tool and not a confirmation of disease.

While there is no cure for lupus, early diagnosis and proper medical treatment can significantly reduce inflammation, pain and stop future complications.

In the *Nature Genetics* study, the nine DNA variants helped to identify those who had up to twice the risk of getting lupus compared to those who did not have the variants, the study authors said.

“In addition to the drug targets, this study will help in the understanding of the causes of lupus and in the development of new genetic tests to find those most at risk for the disease,” said Jeffrey Edberg, Ph.D., an associate professor of medicine in the UAB Division of Clinical Immunology and Rheumatology and co-author on the study.

Using the data from the study, UAB researchers and their SLEGEN

collaborators are developing further studies to determine if the same gene variants signal higher lupus risks in certain ethnic or racial groups. Also, the scientists are examining how these genetic pathways contribute to developing lupus.

The UAB research team included scientists from the departments of Medicine, Epidemiology and Biostatistics. The consortium includes investigators from the Oklahoma Medical Research Foundation in Oklahoma City, Wake Forest University, the University of Minnesota in Minneapolis, the University of California at San Francisco, the University of California at Los Angeles, the University of Southern California in Los Angeles, the Imperial College London and the University of Uppsala in Sweden.

Funding for the study came from the Alliance for Lupus Research, the National Institute of Arthritis, Musculoskeletal and Skin Diseases and the National Institute of Allergy and Infectious Diseases.

“We are hopeful this information will lead to new and better treatment possibilities and, eventually, a cure for lupus,” said Barbara Boyts, president of the Alliance for Lupus Research.

Source: University of Alabama at Birmingham

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