Researchers identify gene variants that may cause kidney problems in lupus patients

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Variants in a particular gene are linked with an increased risk for kidney complications in patients with lupus, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology* (*JASN*). The findings could lead to better treatments to protect the kidney health of patients with the disease.

Lupus is an autoimmune disease that affects many different body systems, including the central nervous system, joints, skin, heart, lungs, and kidneys. Kidney involvement—termed lupus nephritis—occurs in about 50% to 75% of patients, and up to 30% of those patients develop kidney failure. Currently, experts do not understand what makes some lupus patients susceptible to lupus nephritis.

David Powell, PhD, Dawn Caster, MD, and Erik Korte, MS (University of Louisville School of Medicine) led a team that looked at the role of a particular gene that may be involved. Their previous research conducted in collaboration with investigators in Scotland revealed that mice with an inactive form of the ABIN1 protein develop lupus-like disease and have enhanced activation of the NF-kappaB pathway. This pathway is involved with the control of inflammation.

In their current study, the researchers found that mice with inactive ABIN1 develop progressive kidney problems similar to lupus nephritis in humans. The investigators then sequenced the gene encoding ABIN1 in human samples. Comparing cases of lupus with nephritis and cases of lupus without nephritis revealed strong associations of lupus nephritis with a genetic variant called rs7708392 in European Americans and a variant called rs4958881 in African Americans. Comparing cases of lupus with nephritis and healthy controls revealed a stronger association at rs7708392 in European Americans, but not at rs4958881 in African Americans.

The findings suggest that variants in the gene that encodes ABIN1 are linked with an increased risk for lupus nephritis and could be mechanistically involved in disease development through aberrant regulation of NF-kappaB.

"Our studies identify genes of the NF-kappaB pathway as a focus for future work understanding the pathogenesis and therapy of lupus nephritis," said Dr. Powell. "Understanding the role of genes in the NF-kappaB pathway in the development and severity of lupus nephritis provides the hope that personalized therapy for the condition may be possible," he added. Current treatments for lupus nephritis consist of immunosuppressive drugs, which are effective in only about 50% of patients and are associated with undesirable short- and long-term side effects.

More information: The article, entitled "ABIN1 Dysfunction as a Genetic Basis for Lupus Nephritis," will appear online on August 22, 2013, DOI: 10.1681/ASN.2013020148

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