Study links patrolling monocytes to lupus-related kidney disease

April 30 2019

This work shows for the first time that a type of immune cell called a patrolling monocyte plays a critical role in lupus-related kidney disease. Authors Vanessa Redecke, M.D., Ph.D., Hans Haecker, M.D., Ph.D., and Jeeba Kuriakose, Ph.D. Credit: St. Jude Children's Research Hospital

A study led by St. Jude Children's Research Hospital has found evidence suggesting that patrolling monocytes may drive glomerulonephritis,

inflammation of the kidneys, in patients with lupus. The findings overturn the previously held notion that lupus is solely the result of B cell dysfunction. The work appears as an advance online publication today in the *Journal of Clinical Investigation*.

"The thinking has been that to be lupus, it has to be caused by B cell dysfunction," said senior investigator and corresponding author Hans Haecker, M.D., Ph.D., an associate member of the St. Jude Department of Infectious Diseases. "Now, we know that lupus and its varied symptoms are not all the same. In glomerulonephritis, patrolling monocytes appear to play a significant role, possibly even independent of B cells, at least during the early phase of disease."

Lupus is a chronic autoimmune disease that affects adults as well as children and adolescents. There are a range of symptoms associated with lupus, including fatigue and pain in numerous tissues in the body such as the joints, kidneys, brain, heart and lungs. Among patients with lupus, 40-70% develop nephritis—and 10-30% of those individuals progress to end-stage kidney disease requiring dialysis or kidney transplantation.

The current therapeutic approach for lupus-related glomerulonephritis is based on general immuno-suppressive agents with significant side effects. Experimental therapies target B cells; however, such treatments have proven largely ineffective in clinical testing and therefore have not been approved for use. Patrolling monocytes are a type of immune cell previously linked to inflammation in blood vessels. Their dominance in glomerulonephritis opens the door for novel treatment strategies.

"Our findings indicate that treatments for glomerulonephritis that do not address the patrolling monocytes may be ineffective," said co-first author Jeeba Kuriakose, Ph.D., of the St. Jude Department of Infectious Diseases. "We are looking at the immune signaling pathways and the genetic regulation of patrolling monocytes to identify new therapeutic

targets."

A unique research model yields insight

The researchers developed a mouse model based on the human lupus susceptibility locus TNFAIP3-interacting protein 1 (TNIP1, also called ABIN1). This gene is the same between humans and mice, producing a disease model that closely mimics human lupus. In addition to this work, the researchers confirmed their findings in patient samples.

"It was an interest in immune signaling related to TNIP1 that led us to this model and our study in lupus," said co-first author Vanessa Redecke, M.D., Ph.D., of the St. Jude Department of Infectious Diseases. "This gene plays a role in other diseases, such as psoriasis, which our model helps us study."

To figure out which cells were appearing in the kidney glomeruli, the investigators conducted an antibody screen, using cellular markers to identify cell types. This effort found that the cells in question were marked with CD43, a hallmark of patrolling monocytes.

"There is more work to do to understand why these cells get stuck in the kidneys in patients with lupus," Haecker said. "Exploring these mechanisms may lead us to new drug targets, while continuing to inform our view of lupus and the biology that underlies symptoms associated with the disease."

St. Jude does not have a treatment program for lupus but does conduct research as part of scientific efforts to advance immunology.

More information: Jeeba Kuriakose et al. Patrolling monocytes promote the pathogenesis of early lupus-like glomerulonephritis, *Journal of Clinical Investigation* (2019). DOI: 10.1172/JCI125116

Provided by St. Jude Children's Research Hospital