ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

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Press Release

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SIGNALING PATHWAY HELPS PROTECT HEALTHY TISSUE FROM OVERLY ACTIVE IMMUNE RESPONSES

Findings may help improve treatment for a variety of autoimmune diseases

Highlights

- Researchers have shown that the messenger protein IL-6, which is rapidly produced at high levels during an acute inflammatory form of kidney disease, potently dampens activation of tissue-destructive immune cells called macrophages.
- The findings may have broad clinical implications because elevated IL-6 is observed in many different inflammatory diseases, and macrophages are often crucially involved in their pathogenesis.

Washington, DC (February 5, 2015) — Researchers have uncovered a pathway that's key for protecting healthy tissue from overly active immune responses. The findings, which are described in an upcoming issue of the *Journal of the American Society of Nephrology* (JASN), may help clinicians provide better treatments for patients with a variety of autoimmune diseases.

During inflammatory responses due to infection, trauma, or cancer, the body's immune system becomes highly activated in an attempt to fend off invading organisms, foreign bodies, or tumor cells. Excessive immune activation, however, often results in collateral damage to surrounding healthy tissues. Even worse, uncontrolled immune responses can lead to the development of self-destructive autoimmune diseases.

A better understanding of the mechanisms responsible for suppressing the immune response to prevent such damage could benefit many patients. Through studies conducted in mice, Oliver M. Steinmetz, MD (University Hospital Hamburg Eppendorf, in Germany) and his colleagues have shown that the messenger protein IL-6, which is rapidly produced at high levels during an acute inflammatory form of kidney disease, potently dampens activation of tissue-destructive immune cells called macrophages. Protection relies only on the IL-6 receptors that are bound on macrophage cell membranes.

The researchers note that elevated IL-6 is observed in many different inflammatory diseases (perhaps as the body's attempt to protect itself), and macrophages are often

crucially involved in disease pathogenesis. “We believe that the mechanism we have described might be more general in nature and extends to various other immune mediated diseases,” said Dr. Steinmetz. “Our observations are of great clinical importance since IL-6-directed therapies are increasingly being used or studied to treat various human autoimmune conditions such as rheumatoid arthritis and systemic lupus erythematosus.”

In an accompanying editorial, Alan Salama, PhD, MRCP (University College London Centre for Nephrology, in the UK) and Mark Little, FRCP, PhD (Tallaght Hospital, in Ireland) noted that the study presents “compelling data” using “elegant experiments”. They also stressed that IL-6’s role in inflammation “extends well beyond the immune system and the kidney, with high levels of expression in atherosclerotic plaques and elevated serum levels being associated with increased coronary artery disease and morbidity from hypertension, left ventricular hypertrophy, and development of insulin resistance.”

Study co-authors include M. Luig, PhD, M.A. Kluger, MD, B. Goerke, MD, M. Meyer, A. Nosko, I. Yan, J. Scheller, PhD, H.W. Mittruecker, PhD, S. Rose-John, PhD, R.A.K. Stahl, MD, and U. Panzer, MD.

Disclosures: Dr. Rose-John is a shareholder of the CONARIS Research Institute AG (Kiel, Germany), which is commercially developing sgp130Fc as a therapy for inflammatory diseases, and is an inventor on gp130 patents owned by CONARIS.

The article, entitled “Inflammation-Induced IL-6 Functions as a Natural Brake on Macrophages and Limits GN,” will appear online at http://jasn.asnjournals.org/ on February 5, 2015.

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Founded in 1966, and with more than 15,000 members, the American Society of Nephrology (ASN) leads the fight against kidney disease by educating health professionals, sharing new

knowledge, advancing research, and advocating the highest quality care for patients.

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