

Signaling pathway helps protect healthy tissue from overly active immune responses

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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 <u>autoimmune diseases</u>.

A better understanding of the mechanisms responsible for suppressing the <u>immune response</u> 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 <u>systemic lupus erythematosus</u>."

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."

Provided by American Society of Nephrology

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