Apolipoprotein(a): A natural regulator of inflammation

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In a study to be published in the January 09 issue of *Experimental Biology and Medicine*, Hoover-Plow and co-workers in seeking to define a role of apo(a) in leukocyte recruitment have identified a novel activity of apo(a) apolipoprotein that may function as a natural and cell specific suppressor of the inflammatory response in vivo. In addition, a mechanism for this novel function of apo(a) was also identified: its selective regulation of cytokine production. These effects of apo(a) are independent of its molecular mimicry of Plg.

Lipoprotein(a) (Lp(a)) is similar to low density lipoprotein (LDL), but contains an additional apolipoprotein, apo(a). Numerous clinical studies conducted over the past 40 years have identified Lp(a) as a risk factor independent from LDL for a variety of cardiovascular pathologies. Much of the focus of apo(a) pathogenic activities has centered on its strong resemblance to plasminogen, the zymogen for plasmin, the primary enzyme for blood clot degradation. In addition to its important role in clot lysis, plasmin is required for leukocyte recruitment in inflammation. While several in vitro studies have demonstrated the interference of apo(a) in plasminogen leukocyte recruitment, evidence for this in vivo has been lacking.

In vivo investigation of Lp(a) function has been impeded by the lack of availability of small animal models. Lp(a) is expressed only in humans, nonhuman primates and the European hedgehog. In this study Hoover-Plow's group utilized mice with apo(a) in a plasminogen deficient or replete background to study leukocyte recruitment in three models of

inflammation. Hoover-Plow said "In this study apo(a) impeded neutrophil recruitment in two of the models of inflammation, thioglycollate and lipopolysaccharide induced peritonitis. Apo(a) also inhibited neutrophil chemoattractants, and neutrophil recruitment was restored in mice administered neutrophil chemoattractants.

The impaired neutrophil recruitment occurred by a mechanism independent of plasminogen. While the clinical studies point to pathogenic functions of apo(a), a physiological role of Lp(a) has been elusive, but must exist to account for its role in humans and non-human primates, but not most other species. Our results indicate for the first time that apo(a), independent of plasminogen interaction, inhibits neutrophil recruitment in vivo and functions as a cell specific suppressor of the inflammatory response."

Dr. Steven R. Goodman, Editor-in-Chief of Experimental Biology and Medicine, said "Hoover-Plow and colleagues have demonstrated a novel role for apo(a) as a regulator of inflammation. This represents an important contribution to our understanding of the regulation of neutrophil recruitment during the inflammatory response". Experimental Biology and Medicine is a journal dedicated to the publication of multidisciplinary and interdisciplinary research in the biomedical sciences.

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