Link found between immune system and high plasma lipid levels

April 12 2007

Researchers at the University of Chicago have found an unsuspected link between the immune system and high plasma lipid levels (cholesterol and triglycerides in the blood) in mice. The finding could lead to new ways to reduce the risk of heart disease by lowering elevated lipid levels.

In the April 13, 2007, issue of *Science*, the research team—led by James C. Lo, an MD, PhD student, in the laboratory of Yang-Xin Fu, MD, PhD, professor of pathology at the University of Chicago—suggest that an engineered protein could keep mice, and possibly humans, from developing high cholesterol and triglyceride levels, a key risk factor for coronary heart disease.

"Besides showing a link between the immune system and elevated lipids, this study also opens a new avenue for the study of the close and complex link between elevated blood lipid levels and chronic inflammation as manifest in coronary heart disease, ," said Fu, senior author on the paper. "It reveals a quite unexpected role of hepatic T cells in lipid metabolism."

"Those with inflammatory problems such as lupus, rheumatoid arthritis and inflammatory bowel syndrome have a higher incidence of cardiovascular disease, often associated with elevated lipid levels," added co-author Godfrey Getz, MD, PhD, professor of pathology, biochemistry and molecular biology at the University of Chicago. "This study may explain why. The next step would be to determine whether we can use this technique to manipulate the immune response and have a

favorable impact on lipid metabolism."

Using an assortment of engineered and non-engineered mice, the researchers looked specifically at the role of T cells (white blood cells that play a key role in immunity). They determined that altering the expression level of LIGHT (a specific type of molecule that binds to a receptor site of another cell) and also lymphotoxin (LT) on T cells significantly impacted the cholesterol and triglyceride levels.

When T cells expressing LIGHT were introduced into the mice, lipid levels rose, both when the mice were fed a regular diet, and also when fed a high-fat, high-cholesterol diet. However, if researchers blocked the LIGHT signaling, using an engineered protein (LTbR-Ig), lipid levels were lowered again.

Two organs believed to regulate lipid levels are the liver and the intestine. Researchers looked at the mouse livers – particularly at the enzyme, hepatic lipase. This enzyme is made in the liver and secreted into the blood where it plays a key role in lipid metabolism. The livers of mice with T cells expressing LIGHT made and secreted much less hepatic lipase – and consequently, had higher plasma lipid levels.

The authors write: "Our data may help to explain the long time dogma that chronic inflammation is associated with hyperlipidemia, the mechanisms of which have not been well defined. Whether this is an intended and advantageous product of inflammation or untoward consequences of combating pathogens or autoimmunity remains to be determined."

Source: University of Chicago Medical Center