Medical Xpress

New immunological findings provide possible therapy for cardiovascular disease

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A new immunological mechanism in atherosclerosis and cardiovascular disease has been presented in a study from Karolinska Institutet in Sweden. The study is being published in the journal Arteriosclerosis, Thrombosis, and Vascular Biology, and also indicates a possible treatment method for these diseases.

Atherosclerosis is an inflammatory process where lipidsin the form of LDL cholesterol ('bad cholesterol') are stored in the artery walls. The activation of the immune system in the form of T-cells, among others, plays a vital role, particularly for rupturing the atherosclerotic plaques which, the primary cause of myocardial infarction and stroke.

LDL is only taken up in the artery wall after modification, a process where oxidation is one probable underlying cause. Enzymes in the artery walls can also modify LDL making it inflammatory. Most basic scientific studies in the field are based mouse models with genetic changes as mice cannot develop arteriosclerosis or cardiovascular disease .

Plaque cells and blood

Together with his research team, Dr. Johan Frostegård, Professor of Medicine at the Institute of Environmental Medicine at Karolinska Institutet, has studied inflammatory and immune defence reactions in atherosclerosis and cardiovascular disease using plaque cells and blood

from patients with cardiovascular disease. The researchers have observed that the lipids (phospholipids) in modified LDL appear to be one of the primary causes.

The research team has shown that LDL that is modified by enzymes in the artery walls can activate dendritic cells, which in turn play a key role in activating the T-cells. Non-modified, regular LDL on the other hand had no effect on these cells in the study. The research also indicates the possible existence of a mechanism, namely that stress proteins (also called heat shock proteins) are expressed, which is decisive when modified LDL activates the dendritic cells and T-cells. The study shows that a plasma protein Annexin A5 decreases inflammation and modulates immune reactions to modified LDL, which creates a protective effect.

"Studying the inflammatory process and immune reactions directly in cells from people with cardiovascular disease is a unique opportunity to discover the causes and new mechanisms behind the disease's progression. We have shown that modified LDL can play a key role and that stress proteins have a major significance to immune defence reaction," says Johan Frostegård.

Fighting inflammatory process

With the new results, Dr. Frostegård and his team hope to find a strategy for fighting the inflammatory process.

"We have shown that Annexin 5 is a possible new therapy for fighting inflammation and supports the immune defence system is a positive way. We hope to develop this protein into a new type of anti-inflammatory treatment for atherosclerotic disease," he says.

The study was funded with grants from the Torsten Söderberg Foundation, Vinnova, the EU, and RMR. Johan Frostegård is also

specialist consultant at the Emergency Clinic at Karolinska University Hospital, Huddinge in Stockholm County. The researchers and their European partners have applied for a larger EU grant to fund the continuing basic research studies and also treatment studies on patients with cardiovascular disease, which is backed by several patents.

More information: "Induction of dendritic cell-mediated T cell activation by modified but not native LDL in humans and inhibition by Annexin A5: involvement of heat shock proteins" Liu A, Ming J, Fiskesund R, Ninio E, Karabina S, Bergmark C, Frostegård AG, Frostegård *J Arteriosclerosis, Thrombosis, and Vascular Biology*, published online before print November 13, 2014,DOI: 10.1161/ATVBAHA.114.304342

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