NEW METHOD FOR THE DIAGNOSIS OF ATHEROSCLEROSIS

Summary:

Inflammation is an active driver of atherosclerotic plaque development and a risk factor for atherosclerotic events. It is therefore of utmost importance to understand the mechanisms behind these inflammatory processes and to be able to develop new diagnostics and treatment modalities for atherosclerotic disorders. CNIC, FJD (Fundación Jiménez Díaz) and UAM (Universidad Autónoma de Madrid) researchers conducted a study to identify new antibodies that show reactivity against the atherosclerotic plaque. They have found that one of these antibodies recognizes a mitochondrial dehydrogenase of the proline metabolism (PRODH). The levels of this protein are increased in the plasma of atherosclerotic mice and humans with carotid disease, supporting the potential use of this PRODH as a biomarker for atherosclerosis.

Innovative aspects:

Atherosclerosis is a chronic inflammatory disease that causes atheroma plaque formation in the arteries, and is the major cause underlying thrombosis, ischemic heart disease and stroke. However, it can remain asymptomatic for long periods of time. Lesions of atherosclerosis contain macrophages, T cells and other cells of the immune response, together with cholesterol that infiltrates from the blood. Nevertheless, the immunogenic trigger and the impact of the antibody immune response during atherosclerosis are not well understood.

Atherosclerosis results from a complex interplay between inflammation and lipids. The accumulation of LDL and the inflammation of the arterial wall is the first stage of atherosclerosis. Immune cells are present within all atherosclerotic plaques, from early fatty streaks to complex atheromas. Distinct functions have been attached to B cells and the antibody immune response during atherosclerosis development.

CNIC, FJD and UAM researchers have performed a high-throughput single cell analysis of the antibody repertoire associated with atherosclerosis, because antibodies can be used as diagnostic and therapeutic agents. They found that one third of the antibodies showed reactivity against atherosclerotic plaques, indicating that a number of antigens in the lesion can trigger an antibody immune response

The researchers found, using deep proteomics analysis, that one of the antibodies recognizes a mitochondrial dehydrogenase of the proline metabolism (PRODH). Moreover, the distribution of this dehydrogenase is altered during atherosclerosis. The levels of this protein are increased in the plasma of atherosclerotic mice and humans with atherosclerosis, supporting the potential use of this PRODH as a biomarker for atherosclerosis. Measuring the levels of the PRODH or the levels of antibodies anti-PRODH in a sample, could be used as an *in vitro* method for the diagnosis of atherosclerosis.

Competitive advantages:

- This PRODH is a novel antigen associated with atherosclerosis and it shows reactivity for one specific antibody. Moreover, five additional antibodies have been identified to bind the PRODH.

- Proteomics analysis of human atherosclerotic tissue revealed an increased abundance of this protein as compared to normal aortic tissue.

- Patients with carotid atherosclerosis showed high levels of this PRODH, so it could be a valuable novel atherosclerosis biomarker.

Key words: Atherosclerosis, antibodies, LDLR-/- HFD mice, atheroma plaque.

Technology type: Atherosclerosis, diagnostic, therapy, biomarker.

Patent information: PCT/EP2020/076549

Stage of development: tested in animal models.

Scientific article: DOI 10.1038/s41586-020-2993-2

LEARN MORE:

Technology Transfer Office

tto@cnic.es
(+34) 914531200; Ext. 4236
www.cnic.es/en/investigacion/otri
TechID: OT66