

BIOMARKERS FOR THE EARLY DETECTION OF SUBCLINICAL ATHEROSCLEROSIS

Summary:

One of the main problems of atherosclerosis disease is that it is diagnosed too late. Primary prevention is currently based on the evaluation of modifiable risk factors according to standardized recommendations. There is a need to find new biomarkers for subclinical atherosclerosis, which are independent of traditional cardiovascular risk factors and scores. CNIC, UAM and IIS-FJD researchers have discovered a panel of proteins, which are accumulated in the atheroma plaques themselves even in their earliest stages of formation. Moreover, the plasma abundance levels of these proteins could be used to predict the presence of subclinical atherosclerosis. Diagnosis/biotech companies are sought for a license agreement.

Innovative aspects:

One of the challenges associated to the clinical management of atherosclerotic disease is that it is diagnosed usually when the condition is very advanced and lesions are already irreversible, or when it has caused clinical signs or events in organs or territories vascularized by the diseased arteries. Non-invasive measurement by imaging methods of the subclinical atherosclerotic burden in middle-aged people has the potential to improve assessment of cardiovascular risk and might contribute to a more effective prevention of

cardiovascular events. Nevertheless, it was only recommended in asymptomatic adults considered at moderate risk.

Very few studies have assessed potential plasma protein biomarkers of subclinical atherosclerosis. There is a need to find new biomarkers for the screening, diagnosis and/or monitoring of individuals presenting subclinical atherosclerosis. Moreover, it is particularly desirable to identify markers, which are independent of traditional cardiovascular risk factors and scores.

CNIC, UAM and IIS-FJD researchers have carried out the deepest and largest mass spectrometry-based plasma proteomics analysis to date in the search for atherosclerosis-related biomarkers. Firstly, they did a first analysis using a proteomics platform in samples of 444 asymptomatic middle-aged individuals and a second analysis in a 3-year follow-up, identifying a set of putative biomarker proteins whose association with atherosclerosis remained stable over time. In addition, they validated this panel in another cohorts from Europe (3000 subjects) and USA (6000 subjects). As a result, the researchers have discovered a set of protein biomarkers in plasma that are associated to subclinical atherosclerotic disease independently of each other, and of established cardiovascular risk factors.

Almost 60% of the asymptomatic individuals classified as low risk by

traditional risks scores such as Framingham Heart Study 10-year (FHS) have subclinical atherosclerosis. The protein panel was able to predict the presence of subclinical

atherosclerosis even in this low risk population. The use of this biomarker panel could improve the prediction of the presence of atheroma plaques.

Competitive advantages:

- A panel of protein biomarkers were associated with subclinical atherosclerosis disease independently of each other and of established cardiovascular risk factors. Moreover, these proteins accumulate in the atheroma plaques themselves even in their earliest stages of formation.
- The combination of at least 3 of these biomarkers is a new tool for the screening, diagnosis and/or monitoring of subclinical atherosclerosis.
- The protein levels could be measured using a kit, which could be incorporated in hospitals and in companies that offer biochemical analysis of plasma samples. The commercial kit would include an algorithm that, once measured the levels of the proteins, determines whether the subject has atherosclerosis.

Key words: subclinical atherosclerosis, protein biomarkers, cardiovascular risk factors, atheroma plaques.

Technology type: prevention, diagnostics, biomarkers, biochemical analysis.

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Stage of development: successfully tested in almost 10000 individuals

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