Cleveland Clinic Innovations

PRODUCT
Cardiovascular disease risk panel

INDICATION
Cardiovascular Disease

VALUE PROPOSITION
Plasma detection of increased protein carbamylation is predictive of cardiovascular disease risk.

DEVELOPMENT STAGE
Approach validated in clinical studies.

INTELLECTUAL PROPERTY
Issued Patent (EP2409157B1) (UK, France, Germany)

RELATED PUBLICATIONS
Wang, Zeneng et al. “Protein carbamylation links inflammation, smoking, uremia and atherogenesis.” Nature medicine vol. 13,10 (2007): 1176-84.

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Carbamylated Proteins as Markers of Cardiovascular Disease Risk

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Cell Biology, Cardiovascular Medicine

UNMET NEED

Despite the centrality of cholesterol in the pathogenesis of atherosclerosis, the heightened risk for atherosclerotic coronary artery disease (CAD) in certain subpopulations is not easily explained by dyslipidemia. For example, traditional cardiovascular risk factors do not adequately explain the substantial increases in cardiovascular risks associated with either smoking or renal disease. Thus, in addition to dyslipidemia, exaggerated inflammatory and oxidative processes have been suggested to affect the pathogenesis of CAD in these high-risk subpopulations.

SOLUTION

In two separate clinical studies (1,000 patients combined), Cleveland Clinic researchers have discovered an association of elevated carbamylated protein levels with heightened long-term CVD risk as well as risk of experiencing CVD complications over the near to medium-term. These levels can be measured via blood draw and will allow physicians to monitor and stratify patients into risk categories to inform treatment decisions. Myeloperoxidase-catalyzed oxidation of thiocyanate, an anion abundant in blood whose levels are elevated in smokers, is the quantitatively dominant mechanism for cyanate formation and protein carbamylation at sites of inflammation and atherosclerotic plaque and facilitates multiple pro-atherosclerotic activities.

The current panel specifically measures levels of ε-carbamyllysine (homocitrulline, HCit) modification to albumin, apolipoprotein A, fibrinogen, and immunoglobulin (IgG) inpatient blood, serum, or plasma. Moreover, the panel can estimate risk of experiencing CVD complications over the next 1 month, 6 months, and/or 3 years and can help determine if a patient presenting with chest pain is at high risk for heart attack or other major adverse event. These results were independent of other traditionally used cardiovascular risk factors, renal function, and markers of inflammation.