Development of a New Biomarker for Diagnosis of Cardiovascular Disease: Monoclonal Antibody to Oxidized Cholesteryl Esters

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BACKGROUND

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide. The primary prevention of CVD is dependent upon the ability to identify high-risk individuals long before the development of overt events. This highlights the need for accurate risk stratification. An increasing number of novel biomarkers have been identified to predict cardiovascular events. Biomarkers play a critical role in the definition, prognostication, and decision-making regarding the management of cardiovascular events. There are several promising biomarkers that might provide diagnostic and prognostic information. The myocardial tissue-specific biomarker cardiac troponin, high-sensitivity assays for cardiac troponin, and heart-type fatty acid binding potential help diagnose myocardial infarction (MI) in the early hours following symptoms. Inflammatory markers such as growth differentiation factor-15, high-sensitivity C-reactive protein, fibrinogen, and uric acid predict MI and death and many others. However, there is a high unmet medical need for the more specific biomarkers that reflect different aspects of the development of atherosclerosis.

TECHNOLOGY DESCRIPTION

Atherosclerosis is associated with increased lipid peroxidation, leading to generation of multiple oxidation-specific epitopes (OSEs), contributing to the pathogenesis of atherosclerosis and its clinical manifestation. Oxidized cholesteryl esters (OxCEs) are a major class of OSEs found in human plasma and atherosclerotic tissue.

Researchers at UC San Diego have developed a novel monoclonal antibody (mAb) to oxidized cholesteryl esters (OxCE). OxCE is a type of neo-epitope, which arise during the development of atherosclerosis, the underlying disease manifesting in heart attack or stroke. It belongs to the family of oxidation-specific epitopes (OSE), and it is involved in TLR4-mediated proinflammatory signaling.

The inventors optimized an assay where this mAb is used for measuring OxCE in apoB-100 and apoAI lipoproteins. In addition, there is the potential for molecular imaging and therapeutic applications of the new mAb and/or its derivatives in detecting and neutralizing proinflammatory and atherogenic OxCE epitopes.

Biomarkers to OxCE epitopes might be a good complement to oxidized phospholipid (OxPL). They have different distribution in plasma lipoproteins and could provide enhanced risk discrimination in addition to currently measured clinical variables. (Anti-OxPL antibody is being validated in the clinic and it also has the promising therapeutic potential.)

APPLICATIONS

Since OxCE is a target for diagnostic biomarkers and a therapeutic target, the invention is or will be used for a novel biomarker immunoassay and molecular imaging.

ADVANTAGES

OxPL has been shown to be a major biomarker for CVD and the anti-OxPL antibody has a robust therapeutic potential. Our data show that OxCE and OxPL levels in plasma do not correlate, suggesting that OxCE is an independent biomarker.

STATE OF DEVELOPMENT

Experimental data and a working prototype of a biomarker assay.

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

RELATED MATERIALS

- Gonen A, Choi SH, Miu P, Agatisa-Boyle C, Acks D, Taylor AM, McNamara CA, Tsimikas S, Witztum JL, Miller YI. A monoclonal antibody to assess oxidized cholesteryl esters associated with apoAI and apoB-100 lipoproteins in human plasma. J Lipid Res. 2019 Feb;60(2):436-445. doi: 10.1194/jlr.D090852. Epub 2018 Dec 18.DOI - 12/18/2018

PATENT STATUS

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Patent Cooperation Treaty	Published Application	WO 2020/092928	05/07/2020	2019-137

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OTHER INFORMATION

KEYWORDS

Atherosclerosis, biomarker, cardiovascular disease, cholesteryl ester, oxidized cholesteryl esters, oxidation-specific epitope

CATEGORIZED AS

- **Materials & Chemicals**
  - Biological
- **Medical**
  - Disease: Cardiovascular and Circulatory System
  - Therapeutics
- **Research Tools**
  - Antibodies

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