Cleveland Clinic Innovations

Trymethyllysine: A TMAO Precursor as a Predictor of CVD Risk

Stanley Hazen, MD, PhD – Cleveland Clinic, Lerner Research Institute

PRODUCT
Plasma metabolite biomarker that predicts cardiovascular risk

INDICATIONS
Identification of patients at high risk and prevention of adverse CVD-related events

VALUE PROPOSITION
- Method to detect TML levels
- TML as a predictive biomarker for CVD risk
- TML in combination with TMAO can help provide near- and long-term cardiovascular risk assessment

DEVELOPMENT STAGE
Validated in patient cohort

INTELLECTUAL PROPERTY
U.S. Patent Application Submitted

CONTACT INFORMATION
Saqib Sachani, PhD, MBA
Associate Director, Business Development and Licensing
sachans@ccf.org
(216) 672-1913

IDF 2018-018

OPPORTUNITY

Each year in North America and Europe, approximately 20M patients are seen in emergency departments with symptoms of acute coronary syndrome (ACS), which can cause a number of adverse effects, including myocardial infarction, stroke, and death. Cardiovascular risk factors used for long-term risk prediction (e.g., cholesterol, triglycerides, high-sensitivity C-reactive protein) are not typically used in the ACS setting because they do not provide significant prognostic value for near-term risks.

Identifying circulating biomarkers that provide both near- and long-term prognostic value in both ACS and stable subjects alike could help to uncover pathways relevant to cardiovascular disease (CVD) pathogenesis and improve potential preventive cardiovascular risk reduction efforts. In the past decade, the gut microbiota-derived metabolite trimethylamine N-oxide (TMAO) has emerged as a novel predictor of adverse events and death associated with cardiovascular disease. Research performed at Cleveland Clinic has identified a nutrient precursor to TMAO—trimethyllysine (TML)—that is also associated with adverse events and mortality in patients with ACS and, taken together with TMAO plasma levels, is a strong predictor of poor outcomes in patients.

SOLUTION/PRODUCT

The technology described would allow identification of patients with high plasma levels of TML or a combination of TML/TMAO and determination of their risk of CVD based on these levels. High-risk patients may be flagged for therapeutic intervention. Inhibitors of the TML/TMAO pathway are in development, b) agent or procedure to prevent adverse effects or c) antimicrobial agent to reduce TML production in the gut.

In conclusion, plasma TML levels, alone and together with TMAO, are associated with both near- and long-term CV events in patients with chest pain and ACS

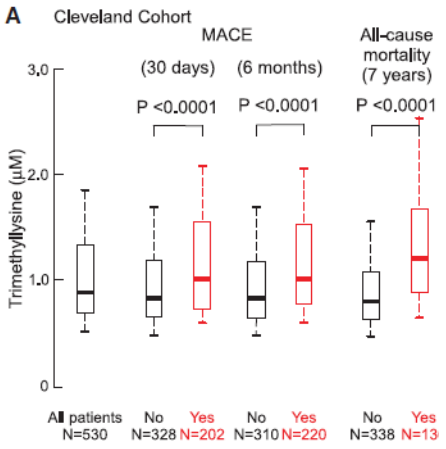

Fig 1: Data showing patients exhibiting chest pain with correlating TML levels. Patients with chest pain (yes) and mortality exhibit higher TML levels.