MedicalXpress

Highly-sensitive detection method makes close monitoring of HDL kinetics possible

April 11 2016

High-density lipoprotein (HDL) is often referred to as good cholesterol: high levels of HDL are associated with lower risk of cardiovascular disease. But many clinical outcome trials for drugs that raise HDL levels have failed to show significant benefits for trial participants. However, current HDL detection methods usually measure only total HDL cholesterol - a more sensitive detection method could allow investigators to measure the subfractions of HDL, and more precisely pinpoint which of these subfractions should be raised to help protect against cardiovascular events.

In a paper published in the April 1 print edition of the *Journal of Lipid Research*, Brigham and Women's Hospital investigators and collaborators at the Harvard T.H. Chan School of Public Health describe a mass spectromeric approach that has allowed them to identify HDL subfractions of various sizes and distribution. The new technique for monitoring HDL kinetics has helped reveal new lipid biology and may help pharmaceutical companies better design and test lipid modulators in the future.

Using this technique for proteomic analysis, the multidisciplinary team led by Masanori Aikawa, MD, PhD, Director of the Center for Interdisciplinary Cardiovascular Sciences at BWH and Associate Professor at Harvard Medical School, and Frank Sacks, MD, Professor at the Harvard T.H. Chan School of Public Health was able to identify 58 proteins in HDL that were shared among three humans. Co-first authors Sasha A. Singh, PhD, Director of Proteomics at CICS, and

Allison B. Andraski, PhD student at HSPH, followed up on seven of these proteins, monitoring their kinetics to better understand apolipoprotein metabolism and the formation of HDL particles. Their results suggest that the traditional view of the role of HDL in reverse cholesterol transport may oversimplify the roles and contributions of various components of HDL.

"Our study demonstrates the feasibility of closer monitoring of HDL kinetics. We believe that establishing new, high-resolution methods that can monitor HDL kinetics is critical to examine the desired effects of new drugs," said Aikawa.

Sacks, co-senior author, also underscored the importance of this technique for future drug development. "This approach not only revealed novel evidence for the formation of HDL particles, but also found that each HDL subfraction has a unique proteome, which may help to discover new therapeutic targets."

More information: Sasha A. Singh et al. Multiple apolipoprotein kinetics measured in human HDL by high-resolution/accurate mass parallel reaction monitoring, *Journal of Lipid Research* (2016). DOI: 10.1194/jlr.D061432

Provided by Brigham and Women's Hospital