COMMENT ON MATHEW ET AL.

Therapeutic Lifestyle Changes Improve HDL Function by Inhibiting Myeloperoxidase-Mediated Oxidation in Patients With Metabolic Syndrome. Diabetes Care 2018;41:2431–2437

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We read with great interest the study by Mathew et al. (1) on the impact of therapeutic lifestyle changes on HDL function. We agree with the authors that lifestyle changes used as a therapeutic strategy is a widely understudied subject and further studies are warranted. However, we do have concerns about the quality and interpretation of the proteomic data sets of isolated HDL. Unfortunately, the authors did not provide sufficient details (and provided no references) on the methodology they used to isolate HDL. When studying the proteome of HDL, it is critical to isolate HDL with high purity, since highly sensitive mass spectrometry measurements will detect any protein within the isolate. This can be achieved by a combination of techniques, e.g., sequential or density-gradient ultracentrifugation followed by size exclusion chromatography to remove unspecific lipid-carrying proteins or other impurities, such as albumin or LDL (2).

Looking at the raw data in the online Supplementary Data, it is apparent that HDL preparations contain significant amounts of albumin and apolipoprotein (apo)B, the main apolipoprotein of LDL. Based on the provided data, albumin was by far the most abundant protein (35% of all proteins), followed by apoA-I (9%) and apoB (5%). Given that apoA-I should account for about 70% in purified HDL (2–4), we speculate that many of the identified proteins are not HDL associated and represent impurities of the isolation process.

While we appreciate the authors' work and study design, we believe that their conclusion that the HDL proteome did not change during the intervention study cannot be drawn.

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