ATVB In Focus
HDL Structure, Function, Therapeutics and Imaging

Series Editor: Stanley Hazen

Articles in this series:
- Saddar S, Mineo C, Shaul PW. Signaling by the high-affinity HDL receptor scavenger receptor B type I. Arterioscler Thromb Vasc Biol 2010;30:144-150.

HDL Structure, Function, Therapeutics, and Imaging

Stanley Hazen

Despite significant advances in the treatment of dyslipidemia with high-potency statin therapy, there exist significant “residual” cardiovascular risk in patients. This has led to heightened interest in high-density lipoprotein (HDL) as a potential target for therapy. In parallel, research interest has intensified in studies aimed at better understanding the many biological functions of HDL and the partner proteins and receptors with which it interacts, as well as modifications to the particle that result in loss of specific biological functions involved in reverse cholesterol transport or gain in proatherosclerotic proinflammatory activities.

In this issue of Atherosclerosis, Thrombosis, and Vascular Biology, we present a series of review articles that highlight recent progress in numerous facets of HDL biology, structure/ function, and therapeutic mimetics and use of the lipoprotein as a functional imaging probe for atherosclerotic cardiovascular disease. The series begins with the biogenesis of the HDL particle in a review by Drs Yvan-Charvet, Wang, and Tall entitled “The Role of HDL, ABCA1, and ABCG1 Transporters in Cholesterol Efflux and Immune Responses.” In addition to discussing the role of ABC transporters in the formation and maturation of HDL, the authors review recent data showing that the traditional roles of HDL and ABC transporters in cholesterol efflux and reverse cholesterol transport are mechanistically linked to antiinflammatory and immunosuppressive functions of HDL. The review by Drs Saddar, Mineo, and Shaul entitled “Signaling by the High Affinity HDL Receptor Scavenger Receptor B Type 1” builds on this theme. Their discussion highlights recent observations indicating the HDL/SR-B1 interaction, particularly within endothelial cells, triggers specific antiinflammatory pathways through diverse kinase cascades with numerous biological functions, including those ultimately leading to enhanced nitric oxide synthesis and its pleiotropic effects. The role of inflammation in promoting oxidative modifications to apolipoprotein A1 of HDL, altering its atheroprotective properties, is the focus of the review by Dr Smith entitled “Dysfunctional HDL As a Diagnostic and Therapeutic Target.” Translation of proteomic and functional studies of genetically engineered forms of apolipoprotein A1 that are oxidant resistant and may serve as a potential therapeutic for atherosclerotic heart disease are discussed. In the review “Proteomics of Apolipoproteins and Associated Proteins From Plasma High-Density Lipoprotein,” by Drs Davidsson, Hulthe, Fagerberg, and Camejo, recent proteomics studies from multiple groups are discussed highlighting the complex and dynamic constellation of proteins associated with the HDL particle and differing patterns of HDL associated proteins identified within healthy subjects versus those with heart disease. The final two review articles focus on more applied topics related to HDL and atherosclerotic heart disease, spanning from basic research and animal model studies to early human clinical investigations. Dr Navab and colleagues discuss “Structure and function of HDL mimetics,” reviewing recent progress in the use of apolipoprotein A1 peptide mimetics as therapeutic agents for atherosclerosis. In the final review article, Dr Skajaa and colleagues describe the use of HDL as a molecular imaging agent for atherosclerosis in their review entitled “High-Density Lipoprotein–Based Contrast Agents for Multimodal Imaging of Atherosclerosis.” We anticipate two additional reviews on this subject to be published in later issues of ATVB.

In summary, this series of review articles by established leaders in the field serves as a valuable resource in the rapidly evolving research areas of HDL biology, diagnostics, and therapeutics. Each of the reviews also highlights critical areas where knowledge gaps exist and further research is needed.

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