Response to Letter Regarding Article “Atherosclerosis 2005: Recent Discoveries and Novel Hypotheses”

We thank Drs Williams and Tabas for their interest in our work and agree that there is a substantial body of evidence supporting the role of hyperlipidemia in atherogenesis. In our review, we addressed this point and indicated that cholesterol may be sufficient to alter the homeostasis of the arterial wall in susceptible individuals even at levels previously considered “normal.” To explain the spectrum of atherosclerotic lesions at any given lipid level, we hypothesized that some individuals might have robust repair capability, rendering them resistant to aggressive lipidic offense, whereas others may be particularly vulnerable to hyperlipidemia. Furthermore, the lipidic injury may not only damage the arterial wall but also affect the repair mechanisms. Indeed, we have demonstrated that the supply of progenitor cells is prematurely exhausted in the marrow of vulnerable individuals even at levels previously considered “normal.” To explain the spectrum of atherosclerotic lesions in all the above disorders independent of elevated lipid levels.

Williams and Tabas make the point that there are no cases of atherosclerosis resulting from a lack of progenitor cells. This statement may not adequately reflect the current state of knowledge. First, a loss of endothelial progenitor cells (EPCs) has been observed in the circulation of patients with atherosclerosis. Higher levels of circulating EPCs were associated with a reduced risk of major cardiovascular events. Importantly, the development of vascular lesions and other manifestations can be affected by the administration of progenitor cells. Indeed, children with severe Hurler syndrome usually die before age 20, with autopsy showing valvular involvement and coronary artery narrowing. After umbilical cord blood transplantation, the lifespan of these patients is remarkably prolonged, with no clinical signs of cardiovascular lesions.

Notably, our review was designed to address recent hypotheses related to the role of progenitor cells, or lack thereof, in arterial disorders. It was by no means a comprehensive review, nor was it intended to downplay the importance of existing work on the arterial injury triggered by abnormal lipids.

Disclosures

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Pascal J. Goldschmidt-Clermont, MD
Gregory K.W. Lam, MD
Victor J. Dzau, MD
Chunnong Dong, MD
Cardiology Division
Department of Medicine
Duke University Medical Center
Durham, NC

Joanne Kurtzberg, MD
Pediatric Blood and Marrow Transplant Program
Duke University Medical Center
Durham, NC

Mark A. Creager, MD
Cardiovascular Division
Brigham and Women’s Hospital
Harvard Medical School
Boston, Mass

Douglas W. Lorsordo, MD
Division of Cardiovascular Research
St Elizabeth’s Medical Center
Tufts University School of Medicine
Boston, Mass

Montaz Wassef, PhD
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Bethesda, Md

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Pascal J. Goldschmidt-Clermont, Gregory K.W. Lam, Victor J. Dzau, Chunming Dong, Joanne Kurtzberg, Mark A. Creager, Douglas W. Losordo and Momtaz Wassef

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