Background: High-density lipoproteins (HDL) have been reported to exert a favorable impact on the artery wall. The factors that influence the ability of HDL to promote endothelial cell growth and migration have not been characterized.

Methods: Human umbilical vein endothelial cells (HUVECs) were co-incubated with increasing concentrations of native and reconstituted HDL (5-40 μg/mL) and their major apolipoproteins. The extent of HUVEC growth was evaluated using a 96-hour proliferation assay and migration using 12-hour wound healing model. These effects were further evaluated in the setting of dextrose (20 mM) and oxidative modification of HDL.

Results: (i) Increasing concentrations of both native HDL and reconstituted HDL containing apoA-I and PLPC resulted in a dose-dependent increase in HUVEC migration by 12.7-48.9% (p<0.05) and 42.8-46.9% (p<0.05) respectively. (ii) Similar benefits were observed with increasing concentrations of individual apoA-I (7.1-39.3%, p<0.05) and apoA-II (22.8-47.3%, p<0.05). (iii) Neither HDL nor its apolipoproteins had a beneficial effect on endothelial cell growth. (iv) HDL continued to promote HUVEC migration by 8.4-46.8% (p<0.05) and reversed the adverse impact on HUVEC growth in the setting of dextrose. (v) Modification of HDL by copper stimulated oxidation, acetylation and myeloperoxidase (MPO)-catalyzed chlorination reduced the ability of HDL to promote HUVEC migration by 34.5% (p<0.05), 26.7% (p<0.05) and 21.2% (p<0.05) respectively. Furthermore, HUVEC growth decreased by 46.6 % (p<0.05) in the setting of HDL that had been modified by MPO.

Conclusion: HDL and its major apolipoproteins have a favorable influence on endothelial cell growth and migration, even in the setting of hyperglycemia. This supports the role of HDL as a therapeutic target to promote repair of vascular injury in conditions including diabetes. Impairment of these functional activities in the setting of oxidative modification of HDL supports the role of MPO in the generation of dysfunctional HDL.