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Advanced oxidation protein products are antagonists of the HDL receptor SR-BI

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Background: Advanced oxidation protein products (AOPPs) are carried by oxidized plasma proteins, especially albumin, and are important risk factors for cardiovascular events in patients with renal disease. Renal patients have a high prevalence of coronary and carotid arteriopathy and face an excessive cardiovascular mortality. Therefore the role(s) of AOPPs in the development of cardiovascular disease might be of great importance.

Results: Herein, we demonstrate that albumin isolated from hemodialysis (HD) patients and *in vitro*-generated AOPP-albumin binds with high affinity to the high-density lipoprotein (HDL) receptor scavenger receptor class B type-I (SR-BI). AOPP-albumin blocked HDL association to SR-BI and effectively inhibited SR-BI-mediated cholesterol ester (CE) uptake, dependent on the AOPP content of albumin. Furthermore, we demonstrate that AOPP-albumin effectively reduces SR-BI-mediated lipid tracer uptake in mice. AOPP-albumin administration increased the plasma half-life of [³H]CE-HDL in control mice 1.6-fold ($p = 0.01$) and 8-fold ($p = 0.0003$) in mice infected with adenoviral vectors encoding human SR-BI.

Conclusions: The observed inhibitory activity of albumin isolated from HD patients is of clear physiological relevance. Our data indicate that a physiological molar excess of HD-albumin over HDL may block up to 50% of HDL-CE delivery to SR-BI. Summing up, we provide strong *in vivo* and *in vitro* evidence that AOPPs are proinflammatory mediators that directly impair HDL metabolism and might therefore be potential key players in the development of cardiovascular disease.