

## **Advanced Oxidation Protein Products Block the HDL Receptor SR-BI**

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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. 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 [<sup>3</sup>H]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.

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.