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## Significance of lipid peroxidation-cationic protein interactions in atherosclerosis in attenuation of inflammatory response

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Apolipoprotein (Apo A1) and apolipoprotein E (Apo E) mimetic peptides have attracted attention due to their ability to reduce atherosclerosis and exhibit antioxidant, anti-inflammatory and hypolipidemic properties. Based on the nature of the peptide, we predicted that these effects could be attributed to their positively charged amino acid residues and hydrophobicity. Accordingly, we designed and tested whether three distinct and unrelated cationic peptides would inhibit the oxidation of lipoproteins, neutralize the charge of negatively charged modified lipoproteins, and inhibit the latter's uptake by macrophages. As bacterial lipopolysaccharide (LPS) is also a highly negatively charged molecule, we also tested the peptides to affect LPS induced macrophage inflammatory response. 5F-mimetic peptide of apoA1, LL27 derived from the anti-microbial peptide CAMP, and a human glycodelin derived peptide was commercially synthesized. The number of positively charged amino acid residues (K+R) and negatively charged residues (D+E) were 4/4, 7/4, 6/2 respectively. Their abilities to reduce lipid peroxides (LOOH), inhibit the oxidation lipoproteins (LDL & HDL), interact with modified lipoproteins, and to inhibit macrophage uptake of modified LDL and inflammation were analyzed. Their abilities to inhibit LPS and Ox-LDL induced inflammatory responses also were determined. Cationic peptides decomposed 13-HPODE and inhibited the oxidation of LDL in a lysine dependent manner. Incubation of Ox-LDL and Ac-LDL with the peptides resulted in charge neutralization. Pre-incubation of the peptides with modified lipoproteins reduced the uptake of the latter by macrophages and foam cell formation as detected by Oil-Red O staining. Increased inflammatory gene expressions were observed in the presence of LPS/Ox-LDL. However, peptides inhibited the Ox-LDL-induced inflammatory gene expressions but showed a dual effect on LPS induced inflammatory response. In contrast, native LDL, which has several positively charged domains, formed complexes with Ox-LDL and increased macrophage cholesterol accumulation. Based on these studies, we suggested that cationic peptides could be a valuable tool for controlling Ox-LDL mediated inflammation and atherosclerotic progression. However, the Ox-LDL, in the presence of native LDL might be more atherogenic and suggest a potential competition between soluble peptides and intact lipoproteins.

### Biography

Sampath Parthasarathy MBA, PhD, was instrumental in the development of the concept of oxidized LDL and its contribution to atherosclerosis, a major form of cardiovascular disease. He is currently at the University of Central Florida as the Florida Hospital Chair in Cardiovascular Sciences and the Associate Dean of Research. He has published over 250 articles and has served on numerous Editorial Boards and NIH committees. He has been continuously funded by NIH and other agencies for over 30 years and was awarded the Distinguished Service Award by the American Heart Association, by the American Association of Cardiologists of Indian Origin and from SASAT International. He is also the recipient of the prestigious van Deenen Memorial Award for Lipids and the Ranbaxy Award for excellence in Cardiovascular Research.

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