Evaluation of human serum albumin sulfhydryl groups oxidation in plasma and atherosclerotic plaque extracts

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Human serum albumin (HSA) is the most abundant multifunctional plasma protein. It accounts for both transport and antioxidant functions, such as ROS/RNS scavenging, extracellular redox balance, redox active transition metal ion binding. Many of these functions are related to the high reactivity of the redox active free Cys34 residue, due to its low pKa. This residue accounts for 80% of total thiols in plasma. It is present primarily in the reduced form, although about 30-40% could be reversibly oxidized, as mixed disulfide with low molecular weight thiols (LMW-thiols), S-nitroso Cys, sulfenic acid, and reversibly oxidized, as sulfenic or sulfonic acid [1]. It has been described that the oxidation state of Cys34 is related to several physio-pathological conditions. Recently, by means of a proteomic approach on human carotid plaques, we have evidenced that the majority of extracted proteins were of plasma origin (about 70% of total proteins), being albumin the most represented [2]. Furthermore, we developed a highly sensitive method for quantification of all LMW thiols bound to circulating and plaque filtered albumin [3].

The aim of the present work was to evaluate the oxidation state of albumin-Cys34 in both plasma and plaque extracts of 27 patients undergoing carotid endarterectomy. We evaluated albumin-Cys34 total oxidation by non-reducing SDS-PAGE of fluorescein-5-maleimide adducts, and its thiolation level and pattern by capillary zonal electrophoresis [3]. Analysis of Cys34 total oxidation evidenced deep differences between plasma samples and the corresponding plaque extracts (p <0.001), indicating that circulating albumin, once filtered in the arterial wall, is subjected to Cys34 oxidative modifications. Data regarding albumin thiolation suggest that following tissue infiltration albumin releases Hcy in the plaque environment, and that the released quantities account for the bulk of total intra-plaque Hcy [4]. The relevance of albumin oxidative modifications in the patho-physiology of atherosclerotic plaque deserves further studies.

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References