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 Cys^{34} 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 variably both reversibly oxidized, as mixed disulfide with low molecular weigth thiols (LMW-thiols), S-nitroso Cys, sulfenic acid, and irreversibly oxidized, as sulfinic or sulfonic acid [1]. It has been described that the oxidation state of Cys^{34} 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-Cys^{34} in both plasma and plaque extracts of 27 patients undergoing carotid endarterectomy.

We evaluated albumin-Cys^{34} 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 Cys^{34} 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 Cys^{34} 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

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