The role of myeloperoxidase in the formation of cholesterol ozonolysis products *in vivo*

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Atheronal-A (3β-hydroxy-5-oxo-5,6-secocholestan-6-al) and its aldolization product atheronal-B (3β-hydroxy-5β-hydroxy-B-norcholestane-6β-carboxaldehyde) can be formed *in vivo* due either to ozone-mediated oxidation of cholesterol or Hock cleavage of cholesterol-5α-hydroperoxide. These atheronals have been reported to be present in human atherosclerotic plaques and brain tissues of patients with Alzheimer's disease and to exert much stronger cytotoxic activities on various cells than four other known oxysterols such as 7β-hydroxycholesterol, 7-ketocholesterol and 5β,6β-epoxycholesterol. These findings suggest that atheronals may contribute to the development of several oxidative stress-related disorders. However, the mechanism for the formation of atheronals in human tissues is unknown. We have recently reported that atheronals are formed by the reaction of cholesterol with human myeloperoxidase (MPO) in the presence of its substrates H_2O_2 and Cl^-. Furthermore, the formation of atheronals by the MPO-H_2O_2-Cl^- system was inhibited by a MPO inhibitor (sodium azide) and singlet oxygen scavengers such as methionine and β-carotene. In this study, we have analyzed the levels of atheronals in the plasma samples collected from wild-type and MPO-deficient mice, after intraperitoneal administration of lipopolysaccharide (LPS). We found the levels of atheronal-A and atheronal-B in the plasma collected from WT mice after the treatment with LPS were increased significantly in a time-dependent manner. However the levels of atheronals in plasma sample of MPO-KO mice were not increased significantly. These results strongly suggest that MPO plays a pivotal role in the formation of atheronals *in vivo*.