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Redox derived damage associated molecular patterns (DAMPs) as pro-inflammatory triggers in human obesity.

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ABSTRACT. Obesity and related complications including insulin resistance and type II diabetes are characterized by low level chronic inflammation and redox imbalance. Dysregulation of lipid metabolic pathways in the presence of increased amounts of reactive oxygen species result in a generation of lipid peroxidation products (LPPs). LPPs can play different roles in adipose tissue pathogenesis. They can act as a secondary messengers in signal transduction pathways and/or as damage associate molecular pattern (DAMPs) recognized by a natural antibodies and different pattern recognition receptors (PRRs) on immune cells. Furthermore, electrophilic LPPs can react with various cellular and extracellular proteins to form even more stable DAMPs thus increasing overall proinflammatory status of the affected tissue. To understand the role of lipid-derived protein modifications and especially there proinflammatory potential, we performed analysis of reactive LPPs protein targets in subcutaneous and visceral adipose tissue from insulin sensitive and resistant obese patients. Using combination of immunoprecipitation, Wertern blot, ELISA and LC-MS/MS analysis LPP-derived DAMPs in adipose tissue were identified and relatively quantified. Furthermore, significant differences between types of adipose tissue (subcutaneous vs visceral) and metabolic states (insulin sensitive vs insulin resistant) were demonstrated. Analysis of the complex interplay between oxidized lipid and their protein targets will assist the discovery of early disease biomarkers and key molecules for the design of targeted intervention strategies.

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