Protein carbonylation and adipocyte mitochondrial function

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Carbonylation is the covalent, non-reversible modification of the side chains of cysteine, histidine, and lysine residues by lipid peroxidation end products such as 4-hydroxy- and 4-oxononenal. In adipose tissue the effects of such modifications are associated with increased oxidative stress and metabolic dysregulation centered on mitochondrial energy metabolism. To address the role of protein carbonylation in the pathogenesis of mitochondrial dysfunction, quantitative proteomics was employed to identify specific targets of carbonylation in GSTA4-silenced or overexpressing 3T3-L1 adipocytes. GSTA4-silenced adipocytes displayed elevated carbonylation of several key mitochondrial proteins including the phosphate carrier protein, NADH dehydrogenase 1? subcomplexes 2 and 3, translocase of inner mitochondrial membrane 50, and valyl-tRNA synthetase. Elevated protein carbonylation is accompanied by diminished complex I activity, impaired respiration, increased superoxide production, and a red