

**P049** The role of oxidative stress and muscle dysfunction with aging

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Skeletal muscle function deteriorates with aging. Our collaborative research team has developed several techniques to identify damaged proteins in muscle that may contribute to age-induced muscle dysfunction. This report describes how mass spectrometry was used to identify glycosylated (N<sup>ε</sup>-(carboxymethyl)lysine-modified; CML) and nitrated-proteins (3-NT) in skeletal muscle and a novel quantitative proteomic strategy to investigate carbonylation of mitochondrial proteins in fast-twitch muscles taken from young and old rats. The quantitation and identification of carbonylated proteins required affinity purification after derivatization with biotin hydrazide, followed by nano-HPLC-MS of the iTRAQ labeled peptides resulting from tryptic digestion of the purified proteins. The identified proteins were mapped against known biochemical pathways. A significant age-associated increase in 3-NT-modified sarcoplasmic reticulum Ca<sup>+2</sup>-ATPase, aconitase, β-enolase, triosephosphate isomerase and carbonic anhydrase III (CAIII) was observed. CML-modified proteins include creatine kinase, CAIII, β-enolase, actin and voltage-dependent anion-selective channel 1. seventy-eight carbonylated proteins were identified and quantitated, with 28 of the proteins showing age-related change in abundance. 13 non-unique pathways were matched with high confidence (P<0.001) using Ingenuity Pathway Analysis. These pathways include: degradation (hydrophobic amino acids and lysine); fatty acid metabolism and degradation; glutathione, propanoate, pyruvate, tryptophan, and beta-alanine metabolism; citrate cycle, oxidative phosphorylation, and mitochondrial dysfunction.