Dietary intake of long-chain fatty acids (LCFA, C>16) plays a causative role in insulin resistance and risk of diabetes. Whereas LCFA promote lipid accumulation and have detrimental effects on metabolic health, diets rich in medium-chain fatty acids (MCFA; C8–C14) have been associated with increased oxidative metabolism and reduced adiposity, with little effect on insulin action in vivo. The molecular mechanisms underlying these differences are poorly understood. To shed light into this question, we have treated L6 myotubes with specific MCFA (capric acid, 10:0 and lauric acid, 12:0) and LCFA (palmitic acid, 16:0 and oleic acid, 18:1) and determined the effect of fatty acid treatment on metabolic parameters including triglyceride accumulation and insulin-stimulated glycogen synthesis as a measure of insulin sensitivity. A potential mechanism linking lipid accumulation and insulin resistance is increased oxidative stress within the insulin-sensitive tissue. Therefore, these studies were extended by measuring reactive oxygen species (ROS) production and oxidative damage in muscle cells treated with different fatty acids.

Incubation of myotubes with LCFA led to lipid accumulation (+90% with palmitic acid vs. control BSA-treated cells, p<0.01), impaired glycogen synthesis (−40%, p<0.05) and decreased succinate dehydrogenase activity (−40–55% vs. control, p<0.05), however these deleterious effects were not observed in the MCFA-treated myotubes. Furthermore, ROS generation (both superoxide and hydrogen peroxide), measured using HPLC and spectrophotometry, was not significantly altered with MCFA, but was significantly greater in the LCFA-treated cells (+500% vs. control, p<0.001), suggesting that MCFA might prevent the induction of oxidative stress. Increased oxidative stress with LCFA, but not MCFA, was confirmed by measuring a marker of lipidoxidative damage, lipid hydroperoxides, which were increased by LCFA (+40% vs. control, p<0.01), but remained unchanged in the MCFA-treated cells.

These results show that treatment of muscle cells with MCFA does not produce the detrimental metabolic effects observed when cells are exposed to LCFA. A potential mechanism is the differential effects observed in ROS production and oxidative damage in the MCFA- and LCFA-treated L6 myotubes.