PEROXYNITRITE INDUCES DEGRADATION OF MYOSIN HEAVY CHAIN VIA P38 MAPK AND MUSCLE-SPECIFIC E3 UBIQUITIN LIGASES IN C2 SKELETAL MYOTUBES

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Recently, it has been shown that cigarette smoke (CS) exposure stimulated catabolism of skeletal muscle by activation of p38 MAPK and up-regulation of muscle-specific E3 ubiquitin ligases (E3s). Peroxynitrite (ONOO-), an oxidative ingredient of CS, has been previously shown to induce ubiquitination and degradation of muscle proteins.To examine whether ONOO- may be one of the components of CS that stimulates muscle catabolism, C2 myotubes, differentiated from a myoblast cell line, were exposed to ONOO- (25 microM) in a time-dependent manner. Following exposure, degradation of muscle contractile proteins myosin heavy chain (MyHC) and actin, activation of p38 MAPK and up-regulation of muscle-specific E3s atrogin-1 and MuRF were studied by Western blotting. Peak phosphorylation of p38 MAPK was evident at 1 h of ONOO- exposure. A significant increase in atrogin-1 and MuRF1 levels was found starting from 1 h and lasted until 6 h of ONOO- exposure. In accordance, MyHC level decreased significantly in a time-dependent manner. In conclusion, ONOO-, an oxidative component of CS, induces degradation of muscle proteins by activation of p38 MAPK and up-regulation of atrogin-1 and MuRF1. These findings are consistent with previous studies in which the catabolic effects of ONOO- were shown.