Dexamethasone-induced autophagy mediates muscle atrophy through mitochondrial clearance

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Glucocorticoids, such as dexamethasone, enhance protein breakdown via ubiquitin-proteasome system. However, the role of autophagy in organelle and protein turnover in the glucocorticoid-dependent atrophy program remains unknown. Here, we show that dexamethasone stimulates an early activation of autophagy in L6 myotubes depending on protein kinase, AMPK, and glucocorticoid receptor activity. Dexamethasone increases expression of several autophagy genes, including ATG5, LC3, BECN1, and SQSTM1 and triggers AMPK-dependent mitochondrial fragmentation associated with increased DNM1L protein levels. This process is required for mitophagy induced by dexamethasone. Inhibition of mitochondrial fragmentation by Mdivi-1 results in disrupted dexamethasone- induced autophagy/mitophagy. Furthermore, Mdivi-1 increases the expression of genes associated with the atrophy program, suggesting that mitophagy may serve as part of the quality control process in dexamethasone-treated L6 myotubes. Collectively