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Muscle protein loss results from an imbalance between rates of proteolysis and protein synthesis. The ubiquitin proteasome dependent proteolytic system (UPS) is believed to be a major component of muscle protein wasting. This system involves an enzymatic cascade E1, E2, E3. E3 enzymes are responsible for selecting protein substrates but E2s generally possess the catalytic activity. E2-E3 interactions are therefore crucial as this determines life or death of the substrate.
Our main objective was to identify the E2s involved in the targeting of myofibrillar proteins in atrophying skeletal muscles. We focused on 13 E2 enzymes that are abundant in the skeletal muscle and/or up-regulated in atrophying skeletal muscles and determined the expression levels of these enzymes in catabolic fa-C2C12 myotubes (expressing flag-actin) treated or not with dexamethasone (Dex, 1 µM or 0.16 µM). One µM Dex increased mRNA levels of UBE2A, UBE2B, UBE2D1, UBE2D2 and UBE2G1. By contrast, only UBE2B mRNAs were upregulated within mild catabolic conditions. To further study the implication of UBE2B in myofibrillar proteins destabilization, we knocked down UBE2B in Dex-treated fa-C2C12 myotubes. This resulted in the stabilization of flag-actin in the soluble fraction (+50 %), and myosin in the soluble and myofibrillar fractions (+67 % and +65 % respectively). We also observed increased amounts of soluble proteins (+93 %). Our data suggests an important role of UBE2B in the processing of muscular proteins in catabolic myotubes.