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Review Article

Expression and Regulation of MuRF-1 and Atrogin-1 are Required for Skeletal Muscle Atrophy

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Abstract

Skeletal muscle atrophy is a debilitating consequence of many pathological conditions and diseases. The mechanisms for muscle atrophy could be attributed to an increase in protein degradation and/or a decrease in protein synthesis. The increase in protein degradation may be caused by the activation of the ubiquitin-proteasome proteolysis pathway. Many studies have confirmed the expression levels of two muscle-specific E3 ubiquitin ligases, MuRF-1 and atrogin-1, are increased in each type of skeletal muscle atrophy. However, the specific substrates for the MuRF-1 and atrogin-1 have not been clearly defined in the muscle degradation process. The expression of these two molecules are regulated by the activation of Nuclear Factor kappa B (NF-kB), forkhead type transcription factors (Foxo), and mitochondrial T3 receptor (p43). The expression and regulation of MuRF-1 and atrogin-1 in different diseases and conditions is the focus of this review. The aim of this review is to assist the research and therapy of skeletal muscle atrophy.

Keywords: MuRF-1; Atrogin-1; Gene expression; Gene regulation; Skeletal muscle atrophy

Introduction

Muscle atrophy is an important symptom of many neuromuscular diseases. The characteristics of muscle atrophy are muscle mass shrinkage and reduction or disappearance of muscle fibers, which are caused by myodystrophy. Skeletal muscle atrophy can be divided into the following three types: (i) Disuse muscle atrophy, the most common type, which is caused by systemic wasting disease or a long-term lack of exercise such as cancer cachexia, hyperthyroidism, weightlessness, aging, and so on [1-4]. (ii) Myogenic muscle atrophy caused by muscle lesions such as polymyositis and myasthenia gravis [5,6]. (iii) Neurogenic muscle atrophy, which is usually due to spinal cord or lower motor neuron lesions such as nerve injury [7]. These three types of muscle atrophy are sometimes related to each other and are all characterized by an increase in protein degradation and a decrease in protein synthesis [8]. Protein degradation was mainly carried out through the following 3 pathways, lysosomal protease pathway, calcium dependent protease/caspase-3 pathway, and the ubiquitin proteasome pathway. The last one is believed to play a major role in muscle atrophy [8-10].

Accumulating literatures suggest that two genes are required for skeletal muscle atrophy [11]. One is muscle ring finger-1 (MuRF-1) on the short arm of chromosome 2; another is muscle atrophy F-box (MAFbx/atrogin-1) on the long arm of chromosome 8. These two genes encode ubiquitin ligases (E3s). The E3s combine with ubiquitin-E2 to target proteins and release E2 to form specific ubiquitinated proteins. The ubiquitinated proteins are identified and combined by the specific proteasomes and then broken down into short peptides or amino acids by the enzyme [9,12]. The ability of the E3 protein to recognize its substrate is dependent on amino acid sequences and/or specifically phosphorylated structural domains of the target protein. Recent studies have identified elongation initiation factor 3 subunit f (eIF3-f), MyoD, and myogenin as targeted substrates of atrogin-1/MAFbx. Whereas titin, Myosin Heavy Chain (MHC) proteins, myosin-binding protein C, Myosin Light Chain-1 (MLC1), and MLC2 were identified as targeted substrates of MuRF-1 [13-16]. However, the specific substrates for the MuRF-1 and atrogin-1 in muscle degradation process have not been clearly defined.

MuRF-1 and atrogin-1 are key molecules involved in skeletal muscle atrophy [17]. They could be potentially used in research and in patient care as targets to prevent or to reverse skeletal muscle atrophy. Therefore, the purpose of this review is to summarize the current knowledge about the expression and regulation of MuRF-1 and atrogin-1 in different diseases and conditions. We hope that this work will be helpful to the research and targeted therapy of skeletal muscle atrophy.

The expression of MuRF-1 and atrogin-1 in neurogenic muscle atrophy

The study of Moriscot et al. [7] shows that MuRF-1 is preferentially induced in type II muscle fibers after denervation. Five to fourteen days after denervation, MuRF-1 protein was further elevated but remained preferentially expressed in type II muscle fibers. In MuRF-1 knockout mice, tibialis anterior muscle, which is rich in type II muscle fiber, was more protected from muscle wasting when compared to soleus muscle which has mixed fiber types. The authors concluded that MuRF-1 is not only just expressed during muscle atrophy but also required for the remodeling of type II muscle fibers under pathophysiological stress [7].

Researchers have found that expression of TNF-like weak inducer of apoptosis (TWEAK) receptor (fibroblast growth factor-inducible receptor 14, Fn14) is significantly increased in muscles under denervation conditions in mice. The up-regulation of this receptor allows TWEAK to activate NF-kB causing an increase in

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the expression of ubiquitin ligase MuRF-1 and resulting in skeletal muscle atrophy. This suggests that the TWEAK-Fn14 system is a crucial regulator of denervation-induced muscle atrophy [18]. Liu et al. [19] studied transplanted and de-nerved gracilis muscle in situ and found that the atrogin-1 mRNA expression of the experimental group peaked in two weeks after surgery and was seven times greater than that of the control group. The expression level gradually increased over four to fifteen weeks after operation accompanied by progressive muscular atrophy and gradually decreased from fifteen to thirty weeks resulting in gradual muscle mass restoration [19].

The expression of MuRF-1 and atrogin-1 in myogenic muscle atrophy

Limb Girdle Muscular Dystrophy 2A (LGMD2A) is a progressive genetic muscle disease caused by the deficiency of the muscle-specific protease calpain-3, resulting in a continuous turnover of sarcomeric proteins through sarcomere remodeling. The patients' muscles have higher levels of gene and protein expressions of MuRF-1 but not atrogin-1. The MuRF1 protein level is correlated significantly with both muscle fiber size and clinical disability score suggesting that muscle function and structural impairment are related [20].

Myasthenia Gravis (MG) is an autoimmune neuromuscular disease, in which circulating antibodies block acetylcholine receptors at the neuromuscular junction. A proportion of MG patients are Acetylcholine Receptor (AChR) antibodies negative but instead, carry antibodies to the Muscle Specific Tyrosine Kinase (MuSK), which is a receptor tyrosine kinase that plays an essential role during development of mature muscle. Patients with MuSK-MG often suffer from significant facial muscle weakness, some even with lingual muscle atrophy. The plasma of MuSK-MG patients, which contains MuSK antibodies, caused a moderate increase of MuRF-1 expression in cultured C2C12 cells. In vivo treatment using the MuSK antibodies to mouse masseter and facial muscle also resulted in increased MuRF-1 expression. This result suggests that the MuSK-MG antibody can affect expression of the atrophy related proteins and the facial muscle and masseter muscle is more susceptible to this influence[5]. However, in the experiment using acetylcholine receptor antibody positive MG mice, increased transcription levels of atrogin-1 and MuRF-1 were both detected in triceps, sternocleidomastoid, and masseter muscles [21]. These results suggest that the up-regulation of Atrogin-1 and MuRF-1 expression play a role in myogenic muscle atrophy.

Sporadic Inclusion Body Myositis (sIBM) is a rare idiopathic inflammatory myopathy that produces remarkable muscle weakness. Intracellular β -amyloid (Aβi), phosphorylated neurofilament protein, scattered white blood cell infiltration, and selective muscle atrophy is the characteristic of sIBM. In Polymyositis (PM), inflammation is more obvious and muscle wasting is symmetric and proximal. In both of these cases the forkhead family transcription factor Foxo3A is directed to the nucleus and atrogin-1 transcript is increased. Expression of Aβi in differentiated C2C12 myotubes and transgenic mice led to up-regulation of atrogin-1 mRNA and muscle wasting. Aβi decreased the levels of p-Akt and its downstream p-foxo3A, leading to Foxo3A translocation and atrogin-1 induction [6]. However, resistance training with vascular occlusion in inclusion body myositis can significantly decrease MuRF-1 expression and slightly alter atrogin-1 mRNA levels [22].

The expression of MuRF-1 and atrogin-1 in disuse muscle atrophy

Cancer cachexia is a severe wasting syndrome that results in muscle atrophy in cancer patients. Cachexia deletes muscle mass, which could lead to muscle asthenia. Previous studies using a lung cancer model has identified that the expression of NF-κ B, MuRF-1, and atrogin-1 are gradually increased with lung cancer progression, resulting in increased protein degradation and aggravated muscle atrophy. However, it was noted that the expression of the NF-κB, MuRF-1, and atrogin-1 became down-regulated after taking epigallocatechin-3-gallate, a cancer cachexia preventive reagent from green tea, suggesting that it can effectively attenuate skeletal muscle atrophy caused by cancer cachexia [4].

Studies of skeletal muscle atrophy in patients suffering with various degrees of diabetes showed that diabetes causes increased expression of MuRF-1 resulting in muscle wasting. The mechanism may involve oxidative stress-induced MuRF-1 up-regulation which can promote proteasome dependent protein degradation. However, exercise training can effectively improve muscle atrophy by inhibiting the oxidative stress-induced MuRF-1 up-regulation [23-27]. O'Neal injected Triiodothyronine (T3) into mice abdominal cavities to induce hyperthyroidism, which caused an increased expression of atrogin-1, MuRF1, and the ubiquitin proteasome dependent protein degradation. At the same time, T3 also stimulated the lysosomal pathway dependent protein degradation leading to muscle atrophy [23].

Du et al. [28] found, in a model of chronic kidney disease in rats, that caspase-3 can be used as a potential rate-limiting proteolytic enzyme that cleaves actomyosin or myofibrils to produce substrates degraded by ubiquitin-proteasome system. When caspase-3 is activated, it cleaves actomyosin to actin, myosin, and their fragments. This initial proteolytic step can be identified early because it leaves a specific 14-kDa actin band as a marker. The stimulation of caspase-3 activity depends on the inhibition of phosphatidylinositol-3 kinase (PI3K) activity. Inhibition of PI3K in muscle cells also leads to expression of a critical ubiquitin ligase E3 which is involved in muscle protein degradation (discussed above).

Studies have confirmed that the ubiquitin ligase Cbl-b (a highly conserved MuRF-1 family of E3 ubiquitin ligase) and atrogin-1 were significantly increased resulting in muscle mass loss in healthy volunteers after twenty days bed rest [29]. Another research team obtained a comprehensive understanding of human disuse muscle atrophy through complex adaptations and the underlying mechanisms. The experimental individuals were selected for two bed rest activities for 35 days or 24 days respectively. Vastus lateralis muscle samples were biopsied from them. The researchers founded the expression of MuRF-1 and atrogin-1 gradually increased along with the duration of bed rest [30]. Suetta et al. [3] found that regardless of age, the mRNA expression level of MuRF-1 and atrogin-1 increase with immobility-induced disuse in 2-4 days and muscle fiber size decrease 1-10% in 4 days. In skeletal muscle mass loss in elderlies caused by long-term immobility, the regulation of muscle wasting is age dependent [3]. Mice hind-limb suspension for 10 days resulted in an increased expression of MuRF-1 and muscle atrophy. But when the hind-limbs of the knockout mouse were hung for ten days, the MuRF-1 expression and muscle atrophy were not

obvious [1]. Furthermore, chicks fasted for twenty-four hours and then fed for two hours showed increased atrogin-1 expression and protein degradation but these changes were reversed by re-feeding [31].

Muscle atrophy can be induced by glucocorticoids. In this process, the increased expression of myostatin induces muscle atrophy by targeting sarcomeric protein (myosin heavy and light chains) which were ubiquiinized through mothers against decapentaplegic homolog 3 (Smad3) and then mediate the up-regulation of atrogin-1 and Foxo1. The atrogin-1 and Foxo1are involved in the NF-kB dependent pathway to the ubiquitin proteasome hydrolysis system. Myostatin can induce the increased expression of atrogin-1 while MuRF-1 remains constant. These findings suggest that the expression pathways of atrogin-1 and MuRF-1 are independent [32]. Statins induced the expression of atrogin-1, which caused atrophy in *Zebrafish* embryonic myocytes and in vitro cultured mice muscle cells. However, atrogin-1 knockout *Zebrafish* and mice prevented statins to induce skeletal muscle atrophy. This finding indicates that the muscle damage induced by statins is closely correlated with the increased expression of atrogin-1 [33]. Furthermore, investigators reported that the carcinogenic methionine receptor induction during fetal development and in adult mice caused muscle wasting with decreased muscle fiber size and loss of myosin heavy chain protein. Concomitantly, atrogin-1 and MuRF-1 mRNA expression were significantly increased in this case [17].

In chronic inflammatory diseases, Reactive Oxygen Species (ROS) can promote muscle atrophy. Li [34] used 100 µMol hydrogen peroxide to stimulate C2C12 myotubes for 24h. This led to ubiquitin conjugation to muscle proteins through transcriptional up-regulation of the enzymes (E2 and E3). This result suggests that hydrogen peroxide up-regulates the expression of specific E3 (atrogin-1, MuRF-1) proteins resulting in increased muscle protein degradation and myotube atrophy. It also shows that ROS stimulates protein catabolism in skeletal muscle by up-regulating the ubiquitin conjugation system [34].

Psychological stress can decrease lean body mass in rodents. Researchers subjected mice to a rotating cage which generated daily psychological pressure on the animals. This procedure led to an increased expression of atrogin-1 and muscle atrophy [35]. Li et al [36] defined fiber specificity of skeletal muscle abnormalities in Chronic Heart Failure (CHF). This study showed that transgenic mice with cardiac-specific overexpression of calsequestrin, a calcium binding protein in the sarcoplasmic reticulum, developed CHF and these animals have a dramatic induction of the atrogin-1 mRNA without significant change in muscle fiber-type composition. Carvalho showed that heart failure induced fiber type IIB specific atrophy and up-regulated atrogin-1 and MuRF-1 mRNA expression in the extensor digitorum longus muscle of monocrotaline treated rats [37]. This finding is not consistent with Li's.

In order to identify the muscle-specific molecular mechanisms of muscle atrophy in mice models suffering from acute lung injury, Files et al used the genetic approach to inactivate the MuRF-1 or atrogin-1 gene in order to identify their role in muscle atrophy associated with acute lung injury. The experimental results showed that the muscle-specific ubiquitin ligases (MuRF-1 and atrogin-1 mRNA) were increased in acute lung injury but only the MuRF-1 protein expression levels were up-regulated. When the MuRF-1 was suppressed by using the genetic approach muscle atrophy was prevented. However, the suppression of Atrogin-1 expression showed no effect. When the lung injury was resolved and MuRF-1 and atrogin-1 were down-regulated, the muscle strength was still inhibited [38]. This study showed that MuRF-1 is responsible for mediating muscle atrophy in acute lung injury in mice. These results also suggested that expression of the two E3s may be regulated by different mechanisms.

Levinee used prolonged disused diaphragm to research proteolysis in muscle dystrophy. In the fractions of cytoplasm the researcher found increased ubiquitin protein conjugates, enhanced the 26S proteasome activity, and significantly decreased myosin heavy chain and α-actin. In the nuclear fractions, the phosphorylations of Akt and Foxo1 were both decreased whereas binding to consensus DNA sequence for atrogin-1 and MuRF-1 was increased. In whole muscle fibers lysates, increased atrogin-1 and MuRF-1 transcripts were found [39].

Skeletal muscle protein breakdown could be induced by burn injuries. Ghrelin normalized plasma glucocorticoid levels are elevated after a burn injury. Expression of the ubiquitin ligases MuRF-1 and Atrogin-1 were markedly elevated in both Extensor Digitorum Longus (EDL) and gastrocnemius in ghrelin normalized plasma of rats [40]. Another study also demonstrated that 24 hour continuous administration of Des-Acyl Ghrelin (DAG) could attenuate the proteolysis induced by burns and markedly reduce the elevated mRNA expression of TNF-α in EDL muscle. These results suggest that DAG can attenuate the atrophy signal. Since the expression of Atrogin-1 and MuRF-1 mRNA are up-regulated by TNF-α in C2C12 myotubes, DAG may be useful in treating wasting disorders [41].

In addition, atrophy conditions such as sepsis cause a decrease in protein synthesis, and an increase in skeletal muscle atrophy. Van Hees used plasma samples obtained from septic patients within 24 hours after ICU admission on cultured mice skeletal myotubes and found increased expression of NF- κB, MuRF-1, and atrogin-1 but decreased expression of myosin [42]. West African patients with Buruli ulcers demonstrated that Mycobacterium ulcerans infection can cause significant skeletal muscle contracture, atrophy, and dysfunction. Subcutaneous injection of Mycobacterium ulcerans in the C57BL/6 male mice and 42 days post-injection observation found that there was an increased expression of muscle specific ubiquitin ligases (MuRF-1 and Atrogin-1). The isometric muscle contraction force and muscle fiber cross-sectional area is reduced by 31% and 29% respectively [43].

The regulation of MuRF-1 and atrogin-1 expression by NF-kB

NF-kB is one of the most important transcription factors involved in muscle atrophy. Its activation can cause increased expression of proteasome subunits and ubiquitin ligase MuRF-1 resulting in myofibrillar protein hydrolysis. Tumor necrosis factor-α (TNF-α), Proteolysis Inducing Factor (PIF), and angiotensin II (Ang II) all induce the activation of NF-kB through reactive oxygen species causing the expression of MuRF-1 or atrogin-1 [8]. Activation of NF-kB can inhibit myoblast determination protein (MyoD) expression and block the skeletal muscle from differentiation and repair [44].

The activation of NF-kB by TNF-α

Previous studies have shown that the expression of TNF-α is significantly increased in cancer, AIDS, congestive heart failure, and chronic obstructive pulmonary disease. When TNF-α is combined with Reactive Oxygen Species (ROS) surface receptors, it may increase ROS activity and activate the redox sensitive transcription factors and protein kinase including NF-kB, which induced the increased expression of MuRF-1 resulting in muscle atrophy [45,46]. TNF-α may also act via MAPK-P38 to increase MAFbx/atrogin-1 gene expression and cause muscle protein degradation [47]. In the fasting condition, TNF-α can be induced by Foxo4 leading to atrogin-1 expression increase. This is not the traditional Akt-Foxo1/3 approach [48]. When mice hind-limb was immobilization for 7 days, TNF-α expression level was significantly increased as well as the expression levels of MuRF-1 and atrogin-1, which in turn, cause the increase of NF-kB expression. However, the transcription of NF-kB can be prevented by subcutaneous injection of proteasome inhibitor (MG132), which inhibits the expression levels of MuRF-1 and atrogin-1. These results suggest that the NF-kB pathway plays a central role in protease hydrolysis [49].

The regulation of MuRF-1 and atrogin-1 expression by PIF and Ang II

Proteolysis inducing factor is a glycoprotein with a molecular mass of 24 kDa. It is detected in the urine of cachexia patients and the blood of mice with induced tumors [50,51]. Some investigators have demonstrated that tumor is the source of the PIF, which passed through the blood circulation and excreted in urine [52]. Previous study has shown that PIF inhibited muscle protein synthesis and induced proteolysis in the following steps: The activation of PKR leads to the activation of NF-κB, which increases the expression of main components of ubiquitin proteasome pathway including the increased expression of MuRF-1 and atrogin-1. However, Ang II can directly increase the formation of reactive oxygen species and induce the activation of PKC. Formation of reactive oxygen species leads to up-regulation of the MuRF-1 and atrogin-1 of ubiquitin-proteasome proteolytic pathways through increased transcription of the NF-κB induction of skeletal muscle degeneration [53]. In conclusion, both PIF and Ang II could induce the activation of PKC. The key step to induce muscle protein degradation is to increase the transient formation of reactive oxygen species through the activation of NADPH oxidase II by arachidonic acid and PKC. PKR may be involved in the release of arachidonic acid and subsequent activation of PKC. Therefore, PKR and PKC may have a common role which results in the activation of NF-kB and increases the expression of MuRF1 and Atrogin-1 leading to skeletal muscle protein degradation.

The regulation of MuRF-1 and atrogin-1 expression by Foxo

The Foxo family members are involved in the regulation of many cellular processes including cell cycle, apoptosis, DNA repair, stress response, and metabolic processes. The Foxo gene is one of the main downstream mediators of PI3K/Akt signal transduction pathway. The role of Foxo has a significant inhibition on tumors. Recent study demonstrates that dexamethasone can lead to the Foxo dephosphorylation in cultured myotubes. This process may cause Foxo to translocate to the nucleus and increase the expression level of myostatin resulting in the increased expression levels of MuRF-1 and atrogin-1 [54]. Another study has shown that the muscle atrophy in acidosis, insulin deficiency, hunger, and septic state can be inhibited when resecting animals adrenal gland or administering glucocorticoid receptor blocker. Interestingly, when it was again administered in a higher than physiological dose of glucocorticoid, the Foxo gene can be activated and increases expression levels of myostatin, MuRF-1, atrogin-1, and then muscle atrophy were observed [55]. These findings suggest that Foxo regulates the expression levels of MuRF-1 and atrogin-1 which could be attributed to the expression of myostatin. In addition, the atrogin-1 promoter has been shown to be activated by Foxo3 to cause an increase in transcription, while expression was suppressed by IGF-I acting through the Phosphatidylinositol 3-Kinase (PI3K)/Akt pathway [8,56].

The regulation of MuRF-1 and atrogin-1 expression by Mitochondrial T3 receptor (p43)

P43 is a mitochondrial T3 (triiodothyronine) receptor which can stimulate T3 induced mitochondrial transcription and protein synthesis [57,58]. In C2C12 myoblasts, p43 overexpression can stimulate mitochondrial activation and oxidative stress [59,60]. Furthermore, p43 overexpression not only induces oxidative stress but also stimulates the anti-oxidative enzyme activity. In oxidative stress processes, the up regulation of these two muscle specific ubiquitin ligase E3s in ubiquitin proteasome pathway results in an increase in muscle protein hydrolysis [61,62]. Therefore, p43 expression is noteworthy because it is one of the targets of muscle atrophy. The imbalance of p43 expression may lead to mitochondrial diseases.

Conclusions and Prospect

In general, the expression levels of the MuRF-1 and atrogin-1 are increased in all three types of muscle atrophy, but the substrate targets and the regulatory mechanisms of MuRF-1 and atrogin-1 remain unclear. However, these two molecules have been considered to be the key enzymes of skeletal muscle atrophy. Therefore, with the study on the mechanisms of expression and regulation, they could be the molecular targets for prevention and treatment of skeletal muscle atrophy in the future. However, it is unclear whether the regulatory pathways induce muscle protein degradation or block its synthesis. Fortunately, researchers have begun to filter enzyme inhibitors which have therapeutic efficacy of muscle atrophy and hope that they are helpful to inhibit the MuRF-1 and atrogin-1 gene products. There are also efforts to obtain some proteins that are specific to and can degrade the products of the two genes. These works may achieve a major breakthrough in the treatment of muscle atrophy.

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References

1. Labeit S, Kohl CH, Witt CC, Labeit D, Jung J, Granzier H. Modulation of Muscle Atrophy, Fatigue and MLC Phosphorylation by MuRF1 as Indicated by Hindlimb Suspension Studies on MuRF1-KO Mice. J Biomed Biotechnol. 2010; 2010: 693741.

2. O'Neal P, Alamdari N, Smith I, Poylin V, Menconi M, Hasselgren PO. Experimental hyperthyroidism in rats increases the expression of the ubiquitin

ligases atrogin-1 and MuRF1 and stimulates multiple proteolytic pathways in skeletal muscle. J Cell Biochem. 2009; 108: 963-973.

3. Suetta C, Frandsen U, Jensen L, Jensen MM, Jespersen JG, Hvid LG, et al. Aging affects the transcriptional regulation of human skeletal muscle disuse atrophy. PLoS One. 2012; 7: e51238.
4. Wang H, Lai YJ, Chan YL, Li TL, Wu CJ. Epigallocatechin-3-gallate effectively attenuates skeletal muscle atrophy caused by cancer cachexia. Cancer Letters. 2011; 305: 40-49.
5. Benveniste O, Jacobson L, Farrugia ME, Clover L, Vincent A. MuSK antibody positive myasthenia gravis plasma modifies MURF-1 expression in C2C12 cultures and mouse muscle in vivo. J Neuroimmunol. 2005; 170: 41-48.
6. Lee HK, Rocnik E, Fu Q, Kwon B, Zeng L, Walsh K, et al. Foxo/atrogin induction in human and experimental myositis. Neurobiol. 2012; 46: 463-475.
7. Moriscot AS, Baptista IL, Bogomolovas J, Witt C, Hirner S, Granzier H, et al. MuRF1 is a muscle fiber type II associated factor and together with MuRF2 regulates type II fiber trophicity and maintenance. J Struct Biol. 2010; 170: 344-353.
8. Tisdale MJ. Is there a common mechanism linking muscle wasting in various disease types? Curr Opin Support Palliat Care. 2007; 1: 287-292.
9. Marco Sandri. Protein breakdown in muscle wasting: Role of autophagy-lysosome and ubiquitin-proteasome. Int J Biochem Cell Biol. 2013; 45: 2121–2129.
10. Ventadour S, Attaix D. Mechanisms of skeletal muscle atrophy. Curr Opin Rheumatol. 2006; 18: 631-635.
11. Bodine SC, Latres E, Baumhueter S, Lai VK, Nunez L, Clarke BA, et al. Identification of ubiquitin ligases required for skeletal muscle atrophy. Science. 2001; 294: 1704-1708.
12. Lecker SH, Solomon V, Mitch WE, Goldberg AL. Muscle protein breakdown and the critical role of the ubiquitin-proteasome pathway in normal and disease states. J Nutr. 1999; 129: S227- S237.
13. Lagirand-Cantaloube J, Offner N, Csibi A, Leibovitch MP, Batonnet-Pichon S, Tintignac LA, et al. The initiation factor eIF3-f is a major target for atrogin1/MAFbx function in skeletal muscle atrophy. EMBO J. 2008; 7: 1266-1276.
14. Tintignac LA, Lagirand J, Batonnet S, Sirri V, Leibovitch MP, Leibovitch SA. Degradation of MyoD mediated by the SCF (MAFbx) ubiquitin ligase. J Biol Chem. 2005; 280: 2847-2856.
15. Centner T, Yano J, Kimura E, McElhinny AS, Pelin K, Witt CC, et al. Identification of muscle specific ring finger proteins as potential regulators of the titin kinase domain. J Mol Biol. 2001; 306: 717-726.
16. Cohen S, Brault JJ, Gygi SP, Glass DJ, Valenzuela DM, Gartner C, et al. During muscle atrophy, thick, but not thin, filament components are degraded by MuRF1-dependent ubiquitylation. J Cell Biol. 2009; 185: 1083-1095.
17. Crepaldi T, Bersani F, Scuoppo C, Accornero P, Prunotto C, Taulli R, et al. Conditional activation of MET in differentiated skeletal muscle induces a trophy. J Biol Chem. 2007; 282: 6812-6822.
18. Mittal A, Bhatnagar S, Kumar A, Lach-Trifilieff E, Wauters S, Li H, et al. The TWEAK-Fn14 system is a critical regulator of denervation-induced skeletal muscle atrophy in mice. J Cell Biol. 2010; 188: 833-849.
19. Liu A, Yu D, Zhang Y, Zhu L, Chen H, Ren A, et al. MAFbx expression after free muscle transplantation and its relationship with muscle function. Chung Kuo Hsiu Fu Chung Chien Wai Ko Tsa Chih. 2009; 23: 969-973.
20. Fanin M, Nascimbeni A, Angelini C. Muscle Atrophy in Limb Girdle Muscular Dystrophy 2a: a Morphometric and Molecular Study. Neuropathol Appl Neurobiol. 2013; 18. doi: 10.1111/nan.12034.
21. Meinen S, Lin S, Rüegg MA, Punga AR. Fatigue and muscle atrophy in a mouse model of myasthenia gravis is paralleled by loss of sarcolemmal nNOS. PLoS One. 2012; 7: e44148.
22. Gualano B, Neves M Jr, Lima FR, Pinto AL, Laurentino G, Borges C, et al. Resistance training with vascular occlusion in inclusion body myositis: a case study. Med Sci Sports Exerc. 2010; 42: 250-254.
23. Chen GQ, Lü KR, Yang YQ, Wang S, Bie MJ. Effects of oxidative stress on MuRF1 expression in skeletal muscle of diabetic rats. Sichuan Da Xue Xue Bao Yi Xue Ban. 2011; 42: 349-352.
24. Chen GQ, Mou CY, Yang YQ, Wang S, Zhao ZW. Exercise training has beneficial anti-atrophy effects by inhibiting oxidative stress-induced MuRF1 upregulation in rats with diabetes. Life Sci. 2011; 89: 44-49.
25. Foletta VC, White LJ, Larsen AE, Léger B, Russell AP. The role and regulation of MAFbx/atrogin-1 and MuRF1 in skeletal muscle atrophy. Pflugers Arch. 2011; 461: 325-335.
26. Mastrocola R, Reffo P, Penna F, Tomasinelli CE, Boccuzzi G, Baccino FM, et al. Muscle wasting in diabetic and in tumor-bearing rats: role of oxidative stress. Free Radic Biol Med. 2008; 44: 584-593.
27. Vignaud A, Ramond F, Hourdé C, Keller A, Butler-Browne G, Ferry A. Diabetes provides an unfavorable environment for muscle mass and function after muscle injury in mice. Pathobiology. 2007; 74: 291-300.
28. Du J, Hu Z, Mitch WE. Molecular mechanisms activating muscle protein degradation in chronic kidney disease and other catabolic conditions. Eur J Clin Invest. 2005; 35: 157-163.
29. Ogawa T, Furochi H, Mameoka M, Hirasaka K, Onishi Y, Suzue N, et al. Ubiquitin ligase gene expression in healthy volunteers with 20-day bedrest. Muscle Nerve. 2006; 34: 463-469.
30. Brocca L, Cannavino J, Coletto L, Biolo G, Sandri M, Bottinelli R, et al. The time course of the adaptations of human muscle proteome to bed rest and the underlying mechanisms. J Physiolm. 2012; 590: 5211-2530.
31. Nakashima K, Yakabe Y, Yamazaki M, Abe H. Effects of Fasting and Refeeding on Expression of atrogin-1 and Akt/Foxo Signaling Pathway in Skeletal Muscle of Chicks. Biosci Biotechnol Biochem. 2006; 70: 2775-2778.
32. Lokireddy S, McFarlane C, Ge X, Zhang H, Sze SK, Sharma M, et al. Myostatin induces degradation of sarcomeric proteins through a Smad3 signaling mechanism during skeletal muscle wasting. Mol Endocrinol. 2011; 25: 1936-1949.
33. Hanai J, Cao P, Tanksale P, Imamura S, Koshimizu E, Zhao J, et al. The muscle-specific ubiquitin ligase atrogin-1/MAFbx mediates statin induced muscle toxicity. J Clin Invest. 2007; 117: 3940-3951.
34. Li YP, Chen Y, Li AS, Reid MB. Hydrogen peroxide stimulates ubiquitin-conjugating activity and expression of genes for specific E2 and E3 proteins in skeletal muscle myotubes. Am J Physiol Cell Physiol. 2003; 285: C806-C812.
35. Allen DL, McCall GE, Loh AS, Madden MC, Mehan RS. Acute daily psychological stress causes increased atrophic gene expression and myostatin dependent muscle atrophy. Am J Physiol Regul Integr Comp Physiol. 2010; 299: R889-R898.
36. Li P, Waters RE, Redfern SI, Zhang M, Mao L, Annex BH, et al. Oxidative phenotype protects myofibers from pathological insults induced by chronic heart failure in mice. Am J Pathol. 2007; 170: 599-608.
37. Carvalho RF, Castan EP, Coelho CA, Lopes FS, Almeida FL, Michelin A, et al. Heart failure increases atrogin-1 and MuRF1 gene expression in skeletal muscle with fiber type-specific atrophy. J Mol Histol. 2010; 41: 81-87.
38. Files DC, D'Alessio FR, Johnston LF, Kesari P, Aggarwal NR, Garibaldi BT, et al. A critical role for muscle ring finger-1 in acute lung injury-associated skeletal muscle wasting. Am J Respir Crit Care Med. 2012; 185: 825-834.
39. Levine S, Biswas C, Dierov J, Barsotti R, Shrager JB, Nguyen T, et al. Increased proteolysis, myosin depletion, and atrophic AKT-FOXO signaling in human diaphragm disuse. Am J Respir Crit Care Med. 2011; 183: 483-490.
40. Sheriff S, Kadeer N, Joshi R, Friend LA, James JH, Balasubramaniam A. Des-acyl ghrelin exhibits pro-anabolic and anti-catabolic effects on C2C12 myotubes exposed to cytokines and reduces burn-induced muscle proteolysis in rats. Mol Cell Endocrinol. 2012; 351: 286-295.
41. Balasubramaniam A, Joshi R, Su C, Friend LA, Sheriff S, Kagan RJ, et al. Ghrelin inhibits skeletal muscle protein breakdown in rats with thermal injury through normalizing elevated expression of E3 ubiquitin ligases MuRF1 and MAFbx. Am J Physiol Regul Integr Comp Physiol. 2009; 296: R893-R901.

42. Van Hees HW, Schellekens WJ, Linkels M, Leenders F, Zoll J, Donders R, et al. Plasma from septic shock patients induces loss of muscle protein. Crit Care. 2011; 15: R233.

43. Houngbédji GM, Bouchard P, Frenette J. Mycobacterium ulcerans infections cause progressive muscle atrophy and dysfunction, and mycolactone impairs satellite cell proliferation. Am J Physiol Regul Integr Comp Physiol. 2011; 300: R724-R732.

44. Di Marco S, Mazroui R, Dallaire P, Chittur S, Tenenbaum SA, Radzioch D, et al. NF-kB-mediated MyoD decay during muscle wasting requires nitric oxide synthase mRNA stabilization, HuRprotein, and nitric oxide release. Mol Cell Biol. 2005; 25: 6533-6545.

45. Li X, Moody MR, Engel D, Walker S, Clubb FJ Jr, Sivasubramanian N, et al. Cardiac-specific overexpression of TNF-α causes oxidative stressand contractile dysfunction in mouse diaphragm. Circulation. 2000; 102: 1690-1696.

46. Garg AK, Aggarwal B B. Reactive oxygen intermediates in TNF signaling. Mol Immunol. 2002; 39: 509-517.

47. Li YP, Chen Y, John J, Moylan J, Jin B, Mann DL, et al. TNF-[alpha] acts via p38 MAPK to stimulate expression of the ubiquitin ligase atrogin1/MAFbx in skeletal muscle. FASEB J. 2005; 19: 362-370.

48. Moylan JS, Smith JD, Chambers MA, McLoughlin TJ, Reid MB. TNF induction of atrogin-1/MAFbx mRNA depends on Foxo4 expression but not AKT-Foxo1/3 signaling. Am J Physiol Cell Physiol. 2008; 295: C986-C993.

49. Caron AZ, Haroun S, Leblanc E, Trensz F, Guindi C, Amrani A, et al. The proteasome inhibitor MG132 reduces immobilization-induced skeletal muscle atrophy in mice. BMC Musculoskeletal Disorders. 2011; 12: 185. doi: 10.1186/1471-2474-12-185.

50. Todorov P, Cariuk P, McDevitt T, Coles B, Fearon K, Tisdale M. Characterization of a cancer cachetic factor. Nature. 1996; 379: 739-742.

51. Todorov PT, McDevitt TM, Cariuk P, Coles B, Deacon M, Tisdale MJ. Induction of muscle protein degradation and weight loss by a tumour product. Cancer Res. 1996; 56: 1256-1261.

52. Cabal-Manzano R, Bhargava P, Torres-Duarte A, Marshall J, Bhargava P, Wainer IW. Proteolysis-inducing factor is expressed in tumours of patientswith gastro-intestinal cancer and correlates with weight loss. Br J Cancer. 2001; 84: 1599-1601.

53. Eley HL, Tisdale MJ. Skeletal muscle atrophy, a link bet ween depression of protein synthesis and increase in degradation. J Biol Chem. 2007; 282: 7087-7097.

54. Stitt TN, Drujan D, Clarke BA, Panaro F, Timofeyva Y, Kline WO, et al. The IGF-I/PI3K/Aktpathway prevents expression of muscle atrophy-induced ubiquitin ligases by inhibiting FOXO transcription factors. Mol Cell. 2004; 14: 395-403.

55. Mitch WE, Bailey JL, Wang X, Jurkovitz C, Newby D, Price SR. Evaluation of signals ctivating ubiquitin proteasome proteolysis in a model of muscle wasting. Am J Physiol. 1999; 276: C1132-C1138.

56. Penner G, Gang G, Sun X, Wray C, Hasselgren PO. C/EBP DNA-binding activity is upregulated by a glucocorticoid-dependent mechanism in septic muscle. Am J Physiol Regul Integr Comp Physiol. 2002; 282: R439-R444.

57. Casas F, Rochard P, Rodier A, Cassar-Malek I, Marchal-Victorion S, Wiesner RJ, et al. A variant form of the nuclear triiodothyronine receptor c-ErbAalpha1 plays a direct role in regulation of mitochondrial RNA synthesis. Mol Cell Biol. 1999; 19: 7913-7924.

58. Pessemesse L, Schlernitzauer A, Sar C, Levin J, Grandemange S, Seyer P, et al. Depletion of the p43 mitochondrial T3 receptor in mice affects skeletal muscle development and activity. FASEB J. 2012; 26: 748-756

59. Rochard P, Rodier A, Casas F, Cassar-Malek I, Marchal-Victorion S, Daury L, et al. Mitochondrial activity is involved in the regulation of myoblast differentiation through myogenin expression and activity of myogenic factors. J Biol Chem. 2000; 275: 2733-2744.

60. Seyer P, Grandemange S, Busson M, Carazo A, Gamaléri F, Pessemesse L, et al. Mitochondrial activity regulates myoblast differentiation by control of c-Myc expression. J Cell Physiol. 2006; 207: 75-86.

61. Sandri M, Lin J, Handschin C, Yang W, Arany ZP, Lecker SH, et al. PGC-1alpha protects skeletal muscle from atrophy by suppressing Foxo3 action and atrophy-specific gene transcription. Proc Natl Acad Sci USA. 2006; 103:16260-16265.

62. Casas F, Pessemesse L, Grandemange S, Seyer P, Baris O, Gueguen N, et al. Overexpression of the Mitochondrial T3 Receptor Induces Skeletal Muscle Atrophy during Aging. PLoS One. 2009; 4: e5631.

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