Mechanisms of muscle atrophy: from UPS implication in rodent models to human biomarkers

Daniel Taillandier, Dulce Peris-Moreno, Cécile Polge

Mechanisms of muscle atrophy: from UPS implication in rodent models to human biomarkers

Daniel Taillandier, Dulce Peris Moreno, Cécile Polge

Université Clermont Auvergne, INRAE, UNH, Unité de Nutrition Humaine, F-63000 Clermont-Ferrand, France

The ubiquitin proteasome system (UPS) is a major player of skeletal muscle wasting, a common characteristic of many diseases (cancer, sepsis, heart failure, kidney diseases, etc.) that negatively impacts treatment and life prognosis. In the early 2000, the notion of "atrogenes" (atrophy-related genes) was proposed for genes that were systematically up regulated during catabolic situations in rodents, which included 2 founding members, the E3 ubiquitin ligases MAFbx/Atrogin-1 and MuRF1/TRIM63 [1]. Interestingly, MuRF1 is so far the only E3 ligase known for targeting several sarcomeric proteins (a-actin, MYHC, Troponin I, telethonin) and we recently identified the E2 ubiquitin conjugating enzymes that bring the catalytic activity for MuRF1-dependent protein degradation [2, 3].
Besides rodent models, we and others demonstrated that MAFbx and MuRF1 are also gold standard atrogenes in human pathologies and we recently found that numerous proteins may be part of a muscle atrophy program in chronic kidney disease and lung cancer patients [4]. In addition, we have identified blood markers that reflect skeletal muscle loss in patients suffering from several pathologies.

References

[1] Peris-Moreno, D.; Taillandier, D.; Polge, C. MuRF1/TRIM63, Master Regulator of Muscle Mass. Int. J. Mol. Sci. 2020, 21, 6663. *doi:10.3390/ijms21186663*

[2] Polge, C.; Cabantous, S.; Deval, C.; Claustre, A.; Hauvette, A.; Bouchenot, C.; Aniort, J.; Béchet, D.; Combaret,L.; Attaix, D.; Taillandier, D. A Muscle-Specific MuRF1-E2 Network Requires Stabilization of MuRF1-E2 Complexes by Telethonin, a Newly Identified Substrate. J. Cachexia Sarcopenia Muscle 2018, 9, 129–145. *DOI: 10.1002/jcsm.12249*

[3] Peris-Moreno, D.; Malige, M.; Claustre, A.; Armani, A.; Coudy-Gandilhon, C.; Deval, C.; Béchet, D.; Fafournoux, P.; Sandri, M.; Combaret, L.; Taillandier*, D; Polge, C*. UBE2L3, a Partner of MuRF1/TRIM63, Is Involved in the Degradation of Myofibrillar Actin and Myosin. Cells 2021, 10, 1974. *https://doi.org/10.3390/cells10081974*

[4] Aniort, J.; Stella A.; Philipponnet, C.; Poyet, A.; Polge, C.; Claustre, A.; Combaret, L.; Béchet, D.; Attaix, D.; Boisgard, S.; Filaire M.; Rosset E.; Burlet-Schiltz O.; Heng, A-E; Taillandier, D. Muscle wasting in patients with end-stage renal disease or early-stage lung cancer: common mechanisms at work. J. Cachexia Sarcopenia Muscle 2019, 9, 129–145. *DOI: 10.1002/jcsm.12376*