骨格筋肥大・萎縮の制御に長寿遺伝子はどのように関わるのか

豊橋創造大学大学院　江川達郎
（共同研究者）同　後藤勝正
同　後藤亜由美
同　大野善隆
京都大学大学院　林達也

How Do Longevity-related Genes Regulate Skeletal Muscle Hypertrophy and Atrophy?

by

Tatsuro Egawa, Katsumasa Goto, Ayumi Goto
Graduate School of Health Sciences,
Toyohashi SOZO University
Yoshitaka Ohno
School of Health Sciences,
Toyohashi SOZO University
Tatsuya Hayashi
Graduate School of Human and Environmental Studies,
Kyoto University

ABSTRACT

5'AMP-activated protein kinase（AMPK）is one of longevity-related genes, which promotes health and wellbeing by regulating glucose, lipid, and energy metabolisms. Recently, it has been revealed that AMPK is also associated with regulating skeletal muscle mass. However, the precise mechanism of AMPK-mediated regulation of

muscle mass is not fully clarified. In the present study, we examined mechanisms by which AMPK coordinates muscle mass. Wild type mice（WT）and muscle-specific AMPK inactivated mice（AMPK-DN）were used in this experiment, and soleus muscle atrophy was induced by 2-week hindlimb suspension. Soleus muscle atrophy was greater in WT group than AMPK-DN group. In WT group, mRNA of muscle-Ring finger 1, which promotes protein degradation in muscle, was upregulated, but not in AMPK-DN group. In addition, Akt/mammalian target of rapamycin/p70 s6 kinase pathway, which promotes protein synthesis in muscle, is activated more in AMPK-DN group compared with WT group. In conclusion, a longevity-related gene, AMPK negatively regulates skeletal muscle mass through upregulating protein synthesis pathways and downregulating protein degradation pathways.

要　旨

5'AMP-activated protein kinase（AMPK）は糖・脂質・エネルギー代謝を調節して健康増進をもたらす長寿関連遺伝子の１つであるが，骨格筋量の調節に関与することも示唆されている．本研究ではAMPKが骨格筋量を制御するメカニズムについて，骨格筋AMPKを特異的に不活性化したマウスを用いて検討した．野生型マウス（WT）と骨格筋特異的AMPK不活性化マウス（AMPK-DN）に対し，２週間の後肢懸垂処置によるヒラメ筋への負荷除去および後肢懸垂後に１および２週間の通常飼育による再荷重を行ったところ，AMPK-DNはWTに比べて筋萎縮の程度が軽減された．WTではタンパク質分解を促進するmuscle Ring-finger 1のmRNA発現が増加したが，AMPK-DNでは変化がなかった．また，タンパク質合成を促進するAkt/p70 s6 kinase経路はAMPK-DNにおいてWTに比べてより活性化していた．以上より，長寿関連遺伝子AMPKはタンパク質合成・分解を調節して，骨格筋量を負に制御することが明らかになった．