Possible role of mTORC1 in the regulation of ribosome biogenesis in rat soleus muscle at the initial stage of mechanical unloading

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It is well known that disuse-induced muscle atrophy caused by immobilization or real/simulated microgravity is associated with a downregulation of protein synthesis and a corresponding loss in muscle mass and size. The rate of protein synthesis in skeletal muscles is determined by both protein synthesis per unit RNA (translational efficiency) and the amount of ribosomes per unit tissue (translational capacity). mTORC1 is considered to be one of the key regulators of both abovementioned factors. Therefore, using a specific mTORC1 inhibitor (rapamycin) we aimed to determine to what extent mTORC1 would influence ribosome biogenesis in rat soleus muscle at the early stage of mechanical unloading (24 h).

Wistar rats were divided into the 4 groups: vivarium control + saline injection (C); vivarium control + rapamycin injection (400 mg/kg) (CR); 1-day hindlimb suspension (HS) + saline injection (HS); 1-day HS + rapamycin injection (400 mg/kg) (HSR). The expression levels of both c-Myc and 45S pre-rRNA were assessed by RT-PCR. 18S rRNA and 28S rRNA contents were determined by 1.2%-agarose gel electrophoresis.

RT-PCR analysis revealed that c-Myc mRNA expression did not change in the CR group compared with the C group, but declined by almost 50% ($p < 0.05$) in the HS and HSR groups relative to the C group. The expression levels of 45S pre-rRNA showed an 80% ($p < 0.05$) increase in the CR group vs. the C group, and almost a 30% decrease in the HS group and a 50% ($p < 0.05$) increase in the HSR group in comparison with the C group. The pattern of changes between the groups for the content of 18S and 28S rRNAs was similar to that observed for 45S pre-rRNA expression.

Thus, the results of our study suggest that at the initial stage of mechanical unloading of the rat soleus muscle (24 h) the expression of 45S pre-rRNA, but not c-Myc expression, is apparently dependent on the activity of mTORC1. The study was supported by the Russian Science Foundation (project No. 17-75-20152).

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