MYOSTATIN AND AUTOPHAGY EXPRESSION IN PHYSIOLOGICAL CARDIAC HYPERTROPHY AND ITS RELATION WITH MIRNA-MEDIATED REGULATION.

Trabalho selecionado para concorrer ao prêmio Prof. Antonio Belló

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Introduction: Myostatin and autophagy are involved in muscle growth regulation. However, there are few studies exploring their role in physiological cardiac hypertrophy. **Aim:** Evaluate myostatin and autophagy in mice subjected to a swimming protocol to induce physiological cardiac hypertrophy. **Methods:** Adult (8 weeks-old) male BALB/c mice (*n*=52) divided in sedentary (S) and trained (T) groups were evaluated in 7 (S7 or T7) and 28 (S28 or T28) days. Left ventricular/tibial length ratio (LV/TL) and cardiomyocyte diameter were used to assess cardiac hypertrophy. Gene expression was evaluated by RT-qPCR, while protein expression was analyzed by western blot. Bioinformatics analysis was performed by TargetScan to predict potential miRNAs' targets and Genemania to create an interaction network between miRNAs and genes. All results are expressed as mean ± SEM and comparisons were performed with Student T test. **Results:** Myocardial hypertrophy was confirmed in trained group either by the increase in LV/TL ratio in 28 days (13%, p=0.0001) and cardiomyocyte diameter in 7 days (20%, p=0.04) and 28 days (30%, p=0.002). There was a reduction in myostatin levels only in T7 compared to S7 (0.8 ± 0.1 *vs* 1.2 ± 0.1, p=0.01). Conversely, mTOR was increased only in T28 compared to S28 (397±95 *vs* 90±23 AU; p=0.02). Autophagic genes showed reduced levels in T7 and T28 (19% and 10% for *Lc3* and *Beclin1,* 22% and 11% for *P62* in T7 and T28; p<0.05 compared to sedentary), but there was no difference at protein levels. Bioinformatics analysis showed that miR-30a, - 221, -27a/b and 208a/b potentially regulate autophagic and myostatin genes. **Conclusions:** Taken together, reduced myostatin during initial hypertrophy and increased mTOR phosphorylation in the established hypertrophic phenotype might favor muscular growth and reduce autophagy. Candidate miRNAs identified might be regulating this process and should be further validated in this scenario.

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