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CKIP-1 PLAYS AN IMPORTANT ROLE IN THE REGULATION OF CARDIAC REMODELING INDUCED BY SIMULATED MICROGRAVITY

Abstract

Objectives: Physiological adaptations to microgravity involve alterations in cardiovascular, neuromuscular, and neuroendocrine systems. These adaptations result in cardiac remodeling and orthostatic hypotension. However, the mechanism of cardiac remodeling induced microgravity remains to be disclosed. We previously showed casein kinase-2 interacting protein-1 (CKIP-1) was an inhibitor of cardiac remodeling induced by pressure-overload by up-regulating the dephosphorylation of HDAC4 through the recruitment of protein phosphatase 2A. However, the role of CKIP-1 in the cardiac remodeling induced by microgravity is unknown. The purpose of this study was to determine whether CKIP-1 was also involved in the regulation of cardiac remodeling induced by microgravity.

Methods: To evaluate the role of CKIP-1 in the cardiac remodeling induced by microgravity, we first detected the expression of CKIP-1 and phosphorylation of HDAC4 in the heart from mice which were exercised by hindlimb unloading (HU) for 28 days using Q-PCR and western blotting. Then myocardial specific CKIP-1 transgenic (TG) mice were under simulated microgravity. We assessed the heart alterations in morphology and function by histological analysis and echocardiography. Finally, we detected the phosphorylation of HDAC4 in the heart from wild type and CKIP-1 transgenic mice after HU.

Results: The results of Q-PCR and western blotting revealed the lower levels of CKIP-1 in the heart from HU mice. The results of echocardiography and histology demonstrated that CKIP-1–TG inhibited pathological cardiac remodeling induced by simulated microgravity. The phosphorylation of HDAC4 in the heart of CKIP-1 TG mice, a key molecule in the signaling cascade of pathological hypertrophy, increased less than that in wild type controls.

Conclusions: These results indicate that simulated microgravity can induced cardiac remodeling via upregulated of the phosphorylation of HDAC4. Moreover, CKIP-1 can inhibt simulated microgravity-induced cardiac remodeling by up-regulating the dephosphorylation of HDAC4.