THYMOSIN BETA-4 ALTERS MIR-139-5p EXPRESSION IN THE HYPOXIC MAMMALIAN HEART

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Although myocardial infarction (MI) occurs approximately every forty seconds in the U.S. alone, medical research still lacks the key to fully support post-hypoxic myocardial regeneration. Thymosin beta-4 (TB4), a 43 amino acid long secreted peptide, was proven to possess a beneficial impact regarding myocardial cell survival, coronary re-growth and progenitor cell activation following myocardial infarction (MI) in adult mammals. The primary aim of our study was to identify novel molecular contributors responsible for the impact of TB4 in the hypoxic heart.
16-week-old male C57BL6 mice underwent permanent left anterior descendent (LAD) coronary ligation and received TB4 or PBS treatment. miRNA profiling, real-time qPCR, western blot and immunohistochemical analyses were performed in search of target proteins, to confirm results and to unveil the potential mechanisms.
miRNA microarray results revealed a significant increase in mmu-mir-139-5p expression. We identified ROCK1 as a potential target protein aligned to mmu-mir-139-5p. Western blot analyses confirmed significant ROCK1 protein downregulation among infarcted adult mouse hearts 24 hours following ligation. Immunohistochemical studies utilizing ROCK1 specific antibody imply hypoxic myocardial and remote vascular endothelial cells are primarily responsible for the distinct alterations observed in protein levels.
Our results demonstrate downregulation of ROCK1 protein in the hypoxic mammalian myocardium in response to systemic TB4 treatment in vivo. We hypothesize these alterations are primarily due to elevated mmu-mir-139-5p expression. Given the beneficial effects of ROCK1 inhibition in various cardiac pathologies, we propose a potential utilization for TB4 as a ROCK1 inhibitor in the future.

Keywords: Cardiac regeneration, miRNA-139-5p, Thymosin beta-4, ROCK1

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