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REGULATION OF MICRORNAS ON CELLULAR EXPRESSION LEVELS OF MYOCARDIAL ANGIOTENSIN-CONVERTING ENZYME

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Objective To investigate the regulation of microRNAs (generally shorten as miRNAs) on the expression levels of angiotensin-converting enzyme (ACE), which is a key candidate gene in cerebrovascular and cardiovascular diseases. Methods Around 37 miRNAs that may regulate ACE were predicted based on the 'seed-region' principle. Among them, miR-27a and miR-27b are two ACE-regulating miRNAs matching 3'-UTR regions of both human and rodent origin and thereby were the focus of further tests. Rat myocardial cell line H9c2 (2-1) in culture was subjected to miR-27a and 27b enhancing and inhibiting treatments. MiR-27a and 27b precursor molecules were applied to boost the functional levels, while chemically modified miR-27a and 27b as antagonists were applied to blunt the activities of miR-27a and 27b, respectively. Each test was controlled with the treatment using corresponding negative control molecules. The precursor and inhibitor were introduced into cells using iFect mediated transfection. Cells were harvested for ACE immunoblotting after 48 h of treatments.

Results Enhancing of miR-27a or 27b with corresponding precursors significantly down-regulated cellular ACE protein levels, while inhibiting with corresponding antagonists significantly up-regulated ACE levels. According to ANOVA analysis, 48 hours treatments of miR-27a and miR-27b precursors reduced ACE levels by 35.98% ($p=0.022$) and 41.32% ($p=0.009$), respectively; meanwhile, 48 h treatments of miR-27a and miR-27b antagonists increased ACE levels by 46.11% ($p=0.047$) and 75.15% ($p=0.002$), respectively.

Conclusion miR-27a and miR-27b significantly regulate myocardial ACE levels in a negatively correlated pattern.