

MICRORNA-155 REGULATES HUMAN ANGIOTENSIN II TYPE 1 RECEPTOR EXPRESSION IN FIBROBLASTS

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A large number of studies have demonstrated that the expression of the angiotensin II type 1 receptor (AT₁R) is regulated predominantly by post-transcriptional mechanisms. Recently, it has been suggested that 10% of human genes may be regulated, in part, by a novel post-transcriptional mechanism involving microRNAs (miRNAs). MiRNAs are small RNAs that regulate gene expression primarily through translational repression. The aim of this study was to determine whether miRNAs could regulate human AT₁R expression. Luciferase reporter assays demonstrated that miR-155 could directly interact with the 3'-UTR of the hAT₁R mRNA. Functional studies demonstrated that transfection of miR-155 into human primary lung fibroblasts (hPFBs) reduced the endogenous expression of the hAT₁R compared with nontransfected cells. Additionally, miR-155 transfected cells showed a significant reduction in Ang II-induced extracellular receptor kinase 1/2 (ERK1/2) activation. Furthermore, when hPFBs were transfected with an antisense miR-155 inhibitor, anti-miR-155, endogenous hAT₁R expression and Ang II-induced ERK1/2 activation was significantly increased. Finally, TGF- β_1 treatment of hPFBs resulted in the decreased expression of miR-155 and the increased expression of the hAT₁R. In summary, our studies suggest that miR-155 can bind to the 3'-UTR of hAT₁R mRNAs and translationally repress the expression of this protein *in vivo*. Importantly, the translational repression mediated by miR-155 can be regulated by physiological stimuli.