Human angiotensinogen +11525 C/A polymorphism modulates its gene expression through microRNA binding

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Abstract

Hypertension is a serious risk factor for cardiovascular disease. Like other complex disease, hypertension is caused by a combination of genetic and environmental factors. The renin–angiotensin system plays an important role in the regulation of blood pressure. Angiotensinogen (AGT) gene is associated with essential hypertension in Caucasians, Japanese, and Asian-Indian subjects. AGT gene may also be associated with cardiac hypertrophy, coronary atherosclerosis, and microangiopathy related cerebral damage. Human AGT gene has a C/A polymorphism at nucleoside 11525 (rs7079) that is located in the 3′-untranslated region (3′-UTR) and is modestly associated with increased blood pressure. We show here that miR-31 and miR-584 bind strongly to the hAGT 3′-UTR containing 11525C allele compared with 11525A allele. We also show that transfection of miR-31 and miR-584 downregulates the hAGT mRNA and protein levels in human liver cells. These studies may provide new therapeutic approach to reduce hypertension.