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Investigation of Pathophysiological Role of Novel Interacting Molecule with Angiotensin II Receptor in Salt Sensitive Hypertension

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Summary

We have been shown that ATRAP (angiotensin II type 1 receptor-associated protein) interacts with the angiotensin II type 1 receptor and promotes constitutive internalization of the angiotensin II type 1 receptor so as to inhibit its downstream signaling. The present study was designed to investigate the putatively beneficial role of renal ATRAP in angiotensin II-dependent hypertension. We generated transgenic mice dominantly expressing ATRAP in the renal distal tubules. In the renal ATRAP transgenic mice compared with the wild-type mice, the development of high blood pressure in response to angiotensin II infusion was suppressed based on radiotelemetry, with a concomitant increase in urinary sodium excretion. The renal mRNA and protein inductions of the α-subunit of the epithelial sodium channel (αENaC) by angiotensin II infusion were decreased in the renal ATRAP transgenic mice compared with the wild-type mice. Furthermore, overexpression of ATRAP by adenoviral gene transfer suppressed the angiotensin II-mediated increase in the expression of the αENaC in mouse distal convoluted tubule cells. These results demonstrate that kidney-dominant overexpression of ATRAP *in vivo* suppresses angiotensin II-dependent hypertension, thereby suggesting ATRAP is a target of interest in hypertension.