The Rho exchange factor Arhgef1 mediates the effects of angiotensin II on vascular tone and blood pressure

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Résumé en anglais	Hypertension is one of the most frequent pathologies in the industrialized world. Although recognized to be dependent on a combination of genetic and environmental factors, its molecular basis remains elusive. Increased activity of the monomeric G protein RhoA in arteries is a common feature of hypertension. However, how RhoA is activated and whether it has a causative role in hypertension remains unclear. Here we provide evidence that Arhgef1 is the RhoA guanine exchange factor specifically responsible for angiotensin II-induced activation of RhoA signaling in arterial smooth muscle cells. We found that angiotensin II activates Arhgef1 through a previously undescribed mechanism in which Jak2 phosphorylates Tyr738 of Arhgef1. Arhgef1 inactivation in smooth muscle induced resistance to angiotensin II-dependent hypertension in mice, but did not affect normal blood pressure regulation. Our results show that control of RhoA signaling through Arhgef1 is central to the development of angiotensin II-dependent hypertension and identify Arhgef1 as a potential target for the treatment of hypertension.

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