Elevated blood pressure linked to primary hyperaldosteronism and impaired vasodilation in BK channel-deficient mice.

BACKGROUND: Abnormally elevated blood pressure is the most prevalent risk factor for cardiovascular disease. The large-conductance, voltage- and Ca2+-dependent K+ (BK) channel has been proposed as an important effector in the control of vascular tone by linking membrane depolarization and local increases in cytosolic Ca2+ to hyperpolarizing K+ outward currents. However, the BK channel may also affect blood pressure by regulating salt and fluid homeostasis, particularly by adjusting the renin-angiotensin-aldosterone system.

METHODS AND RESULTS: Here we report that deletion of the pore-forming BK channel alpha subunit leads to a significant blood pressure elevation resulting from hyperaldosteronism accompanied by decreased serum K+ levels as well as increased vascular tone in small arteries. In smooth muscle from small arteries, deletion of the BK channel leads to a depolarized membrane potential, a complete lack of membrane hyperpolarizing spontaneous K+ outward currents, and an attenuated cGMP vasorelaxation associated with a reduced suppression of Ca2+ transients by cGMP. The high level of BK channel expression observed in wild-type adrenal glomerulosa cells,
together with unaltered serum renin activities and corticotropin levels in mutant mice, suggests that the hyperaldosteronism results from abnormal adrenal cortical function in BK(-/-) mice.

CONCLUSIONS: These results identify previously unknown roles of BK channels in blood pressure regulation and raise the possibility that BK channel dysfunction may underlie specific forms of hyperaldosteronism.