Hypertension affects ~80 million adults in the United States (US), making it a leading risk factor for the development of coronary heart disease, cerebrovascular disease and kidney failure. It is a major burden for the US health care system (annual cost over $300 billion) and its treatments are often ineffective. Moreover, the incidence of hypertension is predicted to rise as the rate of obesity and life expectancy increase. Therefore, new strategies to prevent, limit or reverse hypertension are needed. Long-term regulation of blood pressure has fundamental kidney components; loss of the kidney ability to maintain sodium (Na+) balance due to defects in tubular transport of Na+ associates with hypertension. Recently, we have shown that a Ca2+-binding protein, the Calcineurin Homologous Protein-1 (CHP1), is a regulatory binding partner of a key player in the control of renal Na+ homeostasis, the epithelial brush-border Na+/H+ exchanger-3 (NHE3). CHP1 bound to NHE3 regulates NHE3 surface activity and protein expression and controls blood pressure as a regulatory co-factor of NHE3 transport. Indeed, a reduction in renal protein expression of CHP1 in mice associates with hypotension, diuresis and natriuresis. Overall, our observations support a CHP1 action on BP via the regulation of Na+ transport. Our findings provide new insights into the action of CHP1 on renal tubular Na+ transport and propose CHP1 expression as a novel tool to significantly control blood pressure.