

Intrarenal dopamine and Hypertension

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Although the kidney synthesizes dopamine through the actions of aromatic amino acid decarboxylase (AADC) in the proximal tubule, discrimination between the role of extrarenal and intrarenal dopamine in the overall regulation of renal function has not previously been definitively addressed. We generated mice with selective deletion of AADC in the kidney proximal tubules by crossing AADC^{flax/flax} mice with γ -GT Cre mice (ptAADC^{-/-}), which led to selective decreases in kidney and urinary dopamine. The ptAADC^{-/-} mice exhibited increased expression of nephron sodium transporters, decreased natriuresis and diuresis in response to L-DOPA, decreased medullary COX-2 expression and urinary PGE2 excretion and salt-sensitive hypertension. They had increased renin expression and altered renal angiotensin receptor expression, with increased AT1b and decreased AT2 and Mas expression, associated with increased renal injury in response to angiotensin II. They also exhibited a significantly shorter life span compared to wild type mice. At 20 months of age, only 9 of 19 ptAADC^{-/-} mice still survived while 19 out of 20 wild type mice were alive. These results demonstrate the importance of the intrarenal dopaminergic system in salt and water homeostasis and blood pressure control. Decreasing intrarenal dopamine subjects the kidney to unbuffered responses to angiotensin II and results in the development of hypertension and a dramatic decrease in longevity.

Biography

Mingzhi Zhang got his M.D. degree from Xuzhou Medical College and finished his postdoctoral training in Department of Cell Biology at Vanderbilt University. He is now an Assistant Professor of Medicine and Cancer Biology at Vanderbilt University School of Medicine. He has focused his research on the interactions of intrarenal hormones and the cyclooxygenase-2 (COX-2) pathway, the interactions of intrarenal dopaminergic system and the renin angiotensin system. More recently, he has also studied the role of resident macrophages in recovery from acute kidney injury. He has published more than 40 peer-reviewed scientific papers in reputed journals.

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