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A Novel Kidney-Specific Bmal1 Knockout Model Reveals Circadian Control of Renal Physiology

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Objectives : The kidney contains a high number of circadian clock genes, but the impact of circadian disruption on renal physiology and disease progression remains unclear. This study aimed to establish a kidney-specific circadian clock gene knockout model and investigate its effects on renal function.
Methods : An inducible, kidney-specific Bmal1 knockout mouse model was generated using the Cre-loxP system. Three transgenic mouse lines—Pax8-rtTA, tetO-Cre, and floxed Bmal1—were bred, allowing doxycycline-inducible postnatal gene deletion. After doxycycline administration, the expression of central (brain) and peripheral (kidney, liver, lung, heart) clock genes was assessed.
Results : A two-week doxycycline treatment selectively deleted Bmal1, a key molecule that controls the mammalian molecular clock, in renal proximal and distal tubules as well as the collecting duct system. This loss disrupted diurnal variations in key physiological parameters, including glomerular filtration rate and urinary electrolyte excretion (sodium, potassium, chloride). Furthermore, the expression of key tubular transporter genes—NHE3, OAT3, SGLT2 (proximal tubules), V2 receptor (collecting ducts), and Na+/K+-ATPase—exhibited altered circadian patterns. These findings indicate that kidney Bmal1 is essential for maintaining normal renal function rhythmicity.
Conclusions : We developed a novel, inducible kidney-specific circadian disruption model and demonstrated that the endogenous renal clock is critical for kidney function. This study provides new insights into how circadian rhythm disturbances affect kidney physiology and disease progression, potentially guiding future therapeutic strategies.