Role of a RhoA/ROCK-dependent pathway on renal connexin43 regulation in the angiotensin ii-induced renal damage

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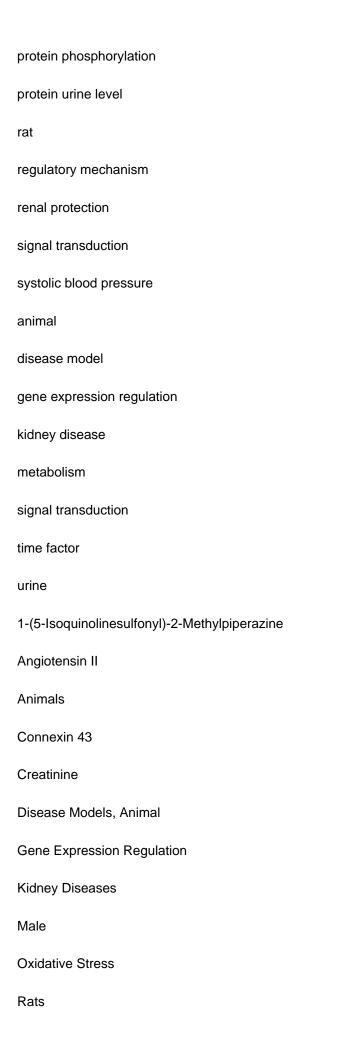
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In various models of chronic kidney disease, the amount and localization of Cx43 in the nephron is known to increase, but the intracellular pathways that regulate these changes have not been identified. Therefore, we proposed that: ?In the model of renal damage induced by infusion of angiotensin II (AngII), a RhoA/ROCK-dependent pathway, is activated and regulates the abundance of renal Cx43". In rats, we evaluated: 1) the time-point where the renal damage induced by AnglI is no longer reversible; and 2) the involvement of a RhoA/ROCK-dependent pathway and its relationship with the amount of Cx43 in this irreversible stage. Systolic blood pressure (SBP) and renal function (urinary protein/urinary creatinine: Uprot/UCrea) were evaluated as systemic and organ outcomes, respectively. In kidney tissue, we also evaluated: 1) oxidative stress (amount of thiobarbituric acid reactive species), 2) inflammation (immunoperoxidase detection of the inflammatory markers ED-1 and IL-1?), 3) fibrosis (immune detection of type III collagen; Col III) and 4) activity of RhoA/ROCK (amount of phosphorylated MYPT1; p-MYPT1). The ratio Uprot/UCrea, SBP, oxidative stress, inflammation, amount of Cx43 and p-MYPT1 remained high 2 weeks after suspending AnglI treatment in rats treated for 4 weeks with AnglI. These responses were not observed in rats treated with AnglI for less than 4 weeks, in which all measurements returned spontaneously close to the control values after suspending AnglI treatment. Rats treated with AnglI for 6 weeks and co-treated for the last 4 weeks with Fasudil, an inhibitor of ROCK, showed high SBP but did not present renal damage or increased amount of renal Cx43. Therefore, renal damage induced by AngII correlates with the activation of RhoA/ROCK and the increase in Cx43 amounts and can be prevented by inhibitors of this pathway. © 2019 by the authors. Licensee MDPI, Basel, Switzerland.

Cx43
Fasudil
Fibrosis
Hypertensive nephropathy
Inflammation
Oxidative stress
alpha tubulin
angiotensin II
CD68 antigen
collagen type 3
collagen type 4
connexin 43
creatinine
fasudil
interleukin 1beta
mypt1 protein
peptides and proteins
protein
Rho kinase
RhoA guanine nucleotide binding protein
thiobarbituric acid reactive substance
unclassified drug
1 (5 isoquinolinesulfonyl) 2 methylpiperazine
angiotensin II
connexin 43
creatinine

fasudil
GJA1 protein, mouse
Rho kinase
RhoA guanine nucleotide binding protein
RhoA protein, mouse
animal experiment
animal model
animal tissue
Article
clinical evaluation
clinical outcome
controlled study
correlation function
creatinine urine level
enzyme activation
enzyme activity
histopathology
immunoperoxidase staining
inflammation
kidney fibrosis
kidney function
kidney injury
kidney tissue
male
nonhuman
oxidative stress



rho-Associated Kinases

rhoA GTP-Binding Protein

Signal Transduction

Time Factors