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**Abstract**

Renal ischemia-reperfusion injury (I/R) remains a critical clinical situation. Several evidence revealed the potential reno-protective effects of Vitamin D and/or pioglitazone, on renal I/R. This study addresses the possible involvement of the Wnt4/ $\beta$ -catenin signaling, *p*-S536NF- $\kappa$ Bp65, PPAR $\gamma$ , Ang II/TGF- $\beta$ , and ACE2 as potential effectors to vitamin D and pioglitazone-mediated renoprotective effects. Two sets of Sprague-Dawley rats (n=30 rat each), were randomized into sham, I/R, Vit D "alfacalcidol" (5 ng/kg/day), pioglitazone (5 mg/kg/day), and Vit D + pioglitazone groups. In all groups renal biochemical parameters, as well as inflammatory and structural profiles were assessed, besides the expression/contents of Wnt4/ $\beta$ -catenin and *p*S536-NF- $\kappa$ Bp65. All

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