

Unilateral nephrectomy, ischemia/reperfusion injury and cyclosporine (NIRC) model

AN *IN VIVO* MODEL FOR ACUTE TO CHRONIC ISCHEMIA/REPERFUSION (IR) INJURY

Model

Chronic kidney disease (CKD) after ischemia reperfusion (IR) is associated with tissue damage characterized by interstitial fibrosis and tubular atrophy. Renal fibrosis contributes to the progressive loss of kidney function.

IR and immunosuppressive therapy are a major cause of progressive renal failure after kidney transplantation. Renal toxicity induced by chronic administration of calcineurin inhibitors such as cyclosporin seems to play an important role in the progression of kidney fibrosis.

In this model, CKD is induced by IR injury and cyclosporin treatment in uninephrectomized rats.

Species

Rat

Interest

Rat NIRC mimics the development of chronic kidney disease occurring in clinical conditions after ischemia reperfusion and immunosuppressive therapy.

This model is suitable for testing drugs with anti-fibrotic effects and/or for screening new immunosuppressive drugs having less nephrotoxicity than cyclosporine A.

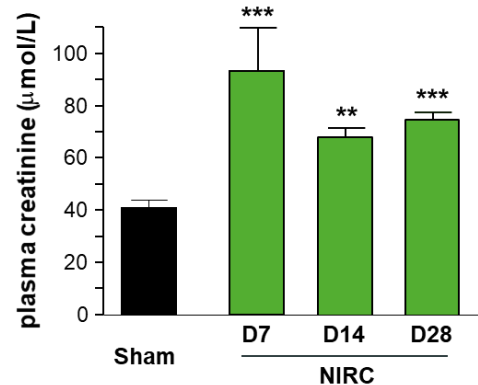
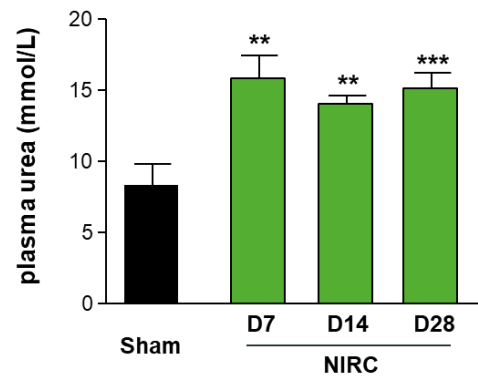
Model Description

- Surgical procedure: unilateral nephrectomy followed by atraumatic clamping of remaining kidney's pedicle (ischemia) and blood flow restoration (reperfusion).
- Treatment: daily cyclosporine treatment for 1 to 4 weeks after IR.
- Standard protocol duration: 5 weeks.
- Pathophysiological features: impaired renal function, renal fibrosis and tubular injury

Evaluated Parameters

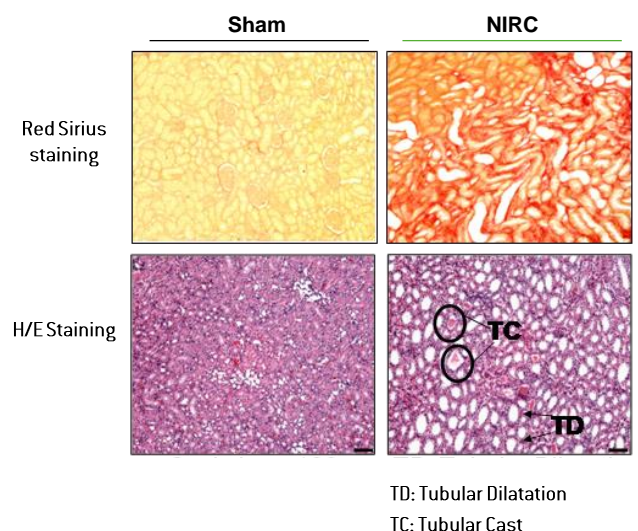
- Body and kidney weight
- Renal function:
 - Biochemical dosage of plasma and urinary creatinine and urea
 - Estimated and transdermal Glomerular Filtration Rate (GFR).
- Tubular injury: tubular dilatation semi-quantification on hematoxylin and eosin (HE)-stained sections
- Renal fibrosis: fibrosis quantification on Red Sirius-stained kidney sections by image analysis (stained surface in %)

Impaired renal function in NIRC rats



***P<0.001 (n=16-18/group, W1-9; n=7-8/group, W10-12)

Renal fibrosis and tubular damage in NIRC rats



NIRC rats showed an increase in kidney collagen accumulation (Red-Sirius staining) and tubular damage (HE staining) compared to Sham.

Scale bar = 100 µm