The late inhibition of inhibitor of IκB kinase attenuates acute kidney injury and the subsequent development of fibrosis in a rat model of ischemia/reperfusion injury.

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INF/IR-11:
THE LATE INHIBITION OF INHIBITOR OF IKB KINASE
ATTENUATES ACUTE KIDNEY INJURY AND THE SUBSEQUENT
DEVELOPMENT OF FIBROSIS IN A RAT MODEL OF ISCHAEMIA
REPERFUSION INJURY.

By: Johnson, F; Patel, N; Collino, M; Bennetti, E; Thiemermann, C
Shock (Augusta, Ga.)
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Abstract
INTRODUCTION: Sepsis is the most common cause of acute kidney injury (AKI), and AKI has now been
described as a major risk factor for chronic kidney disease (CKD). Post-inflammatory renal scarring from the
activation of nuclear factor-kappaB (NF-kappaB) due to AKI may be an important contributor to CKD
development. NF-kappaB is a diverse family of transcription factors activated by inhibitor of kappaB kinase
(IKK).

METHODS: Male Wistar rats underwent a right-hand nephrectomy and unilateral renal ischaemia for 30
minutes or sham operation (no ischemia) (n=8). Two groups of animals subject to ischemia reperfusion
injury (IRI) were administered the IKK inhibitor IKK16 (1 mg/kg i.v. in 10% DMSO) given at 24-h post-
reperfusion. Control animals were allowed to recover and culled at 1 (n=4), 2 (n=4), 3 (n=4), 7 (n=4), 14
(n=4) or 28 (n=7) days, and IKK16 treated animals were culled at 2 (n=4) or 28-days (n=7). 24-h prior to
experiment termination, rats were placed into metabolic cages for urine collection.

RESULTS: When compared to sham-operation rats, rats subjected to unilateral renal IRI (control) developed
AKI. Late administration of IKK16 resulted in a significant improvement in renal function (lower
creatinine/urea) and structural injury at 48-h post reperfusion. When compared to rats subjected to sham-
operation, control rats demonstrated significant increases in Sirius red staining (indicative of fibrosis) at 28-
days post reperfusion, which was markedly reduced by the late administration of IKK16.

CONCLUSION: The late inhibition of IKK may, therefore, have therapeutic potential in the recovery of AKI
and the prevention of subsequent CKD.

Author Information
Address: 1William Harvey Research Institute, Barts and the London, London, UK 2Department of Drug
Science and Technology, University of Turin, Italy.