

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

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

This is the author's manuscript

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1563296> since 2017-02-14T18:03:54Z

Published version:

DOI:10.1097/01.shk.0000472033.95062.d0

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

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; Thiernemann, C

Shock (Augusta, Ga.)

Volume:44 Suppl 2

Pages:10

DOI:10.1097/01.shk.0000472033.95062.d0

Published:2015-Oct

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.