Renal-associated TLR2 mediates ischemia/reperfusion injury in the kidney.

Abstract:

TLRs are conserved pattern recognition receptors that detect motifs of pathogens and host material released during injury. For unknown reasons, renal TLR2 mRNA is mainly expressed by tubular cells and is enhanced upon renal ischemia/reperfusion (I/R) injury. We evaluated the role of TLR2 in I/R injury using TLR2-/- and TLR2+/+ mice, TLR2 antisense oligonucleotides, and chimeric mice deficient in leukocyte or renal TLR2. Tubular cells needed TLR2 to produce significant cytokine and chemokine amounts upon ischemia in vitro. TLR2 played a proinflammatory and detrimental role in vivo after I/R injury, as reflected by a reduction in the amount of local cytokines and chemokines, leukocytes, and the level of renal injury and dysfunction in TLR2-/- mice compared with controls. Analysis of chimeric mice suggested that TLR2 expressed on renal parenchyma plays a crucial role in the induction of inflammation and injury. TLR2-antisense treatment protected mice from renal dysfunction, neutrophil influx, and tubular apoptosis after I/R injury compared with nonsense treatment. In summary, we identified renal-associated TLR2 as an important initiator of inflammatory responses leading to renal injury and dysfunction in I/R injury. These data imply that TLR2 blockade could provide a basis for therapeutic strategies to treat or prevent renal
ischemic injury.

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