Nature Reviews Nephrology **10**, 183 (2014); published online 11 February 2014; doi:10.1038/nrneph.2014.19

ACUTE KIDNEY INJURY

CRITICAL ROLE OF COMPLEMENT IN ENDMT

Complement has a critical role in the induction of endothelial–mesenchymal transition (EndMT) during renal ischaemia–reperfusion injury, according to new findings. "These data shed light on the pathogenic factors that regulate this particular form of endothelial dysfunction, which has an important role in the regulation of renal fibrosis," says researcher Giuseppe Castellano.

Ischaemia–reperfusion injury is a common cause of acute kidney injury (AKI) and is associated with substantial morbidity in kidney transplant recipients. "Endothelial cell damage and renal fibrosis are pivotal in the induction and extension phases of acute graft injury during ischaemia–reperfusion injury," explains Castellano. "However, the factors that contribute to endothelial damage in ischaemia–reperfusion injury are poorly understood."

Castellano and colleagues previously showed that during ischaemia–reperfusion injury, activation of the classical and lectin pathways of the complement system occurs primarily at the endothelial cell level. In the current study, they used a porcine model and recombinant C1 inhibitor to investigate the potential role of complement activation in the induction of EndMT and renal fibrosis during ischaemia–reperfusion injury.

"In our model, vascular rarefaction occuring in renal ischaemia–reperfusion injury was associated with EndMT, as indicated by significant alterations in endothelial cell phenotype accompanied by the development of tubulointerstitial fibrosis," says Castellano. "This process was driven *in vitro* and *in vivo* by activation of the Akt pathway and was hampered by inhibition of the complement system."

He continues: "considering the significant contribution of the vascular compartment to the development of renal injury, we hypothesize that therapeutic inhibition of the complement and Akt systems may be essential to prevent vascular damage and tissue fibrosis, not only in transplanted kidneys, but also in other forms of AKI. Thus, we think that in the near future, patients with various forms of AKI might benefit from new therapies that target the complement system directly at the vascular level."

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Original article Curci, C. *et al*. Endothelial-to-mesenchymal transition and renal fibrosis in ischaemia/reperfusion injury are mediated by complement anaphylatoxins and Akt pathway. *Nephrol. Dial. Transplant*. doi:10.1093/ndt/gft516