
Interorgan communication networks in the kidney–lung axis

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Table 1: Synopsis of ICN mediators of AKI-induced remote lung inflammation.

ICN Mediator kidney:lung	Baseline Serum levels	Ischemia reperfusion AKI Serum levels	Bilateral Nephrectomy Serum levels	Onset	Peak or Nadir	Duration	Cellular source	Receptors/ Target cells	Mechanisms of action			Notes
									Lung Endothelial leakage	Lung Neutrophil accumulation	Lung interstitial macrophage accumulation	
Osteopontin	Low	↑	N.D.	0-2 hours	12-24 hours	> 5 days	Kidney only; distal and proximal tubule; later stages other kidney cell types	CD44 expressing circulating or lung immune cells	+++	+++	+++	
αKlotho	High	↓	N.D.	0-3 hours	N.D.	7-10 days	Kidney	FGF23/FGFR1 expressing cells?	+	+	N.D.	
Indoxyl sulfate (uremic toxin)	Low	↑	↑	0-2 hours	Depends on degree of proximal tubule loss	Until renal failure is resolved	Gut-liver-derived: Indole is produced by intestinal bacteria as a degradation product of tryptophan, and is subsequently metabolized in the liver to indoxyl sulfate	Endothelial cells, vascular smooth muscle cells, epithelial cells, monocytes?	N.D.	N.D.	N.D.	Induces IL-6 expression
HMBG1	Low	↑	↑	0-6 hours	N.D.	> 1 day	Broadly expressed in kidney	Acts in part via TLR4 expressing immune cells	+	+	N.D.	
mtDAMPs	Very low	↑	N.D.	0-2 hours	N.D.	> 2days	Present in all kidney cells	Acts via TLR9	N.D.	N.D.	N.D.	
IL-6	Very low	↑	↑	1-2 hours	2 hours	6-12 hours	Kidney, lung, liver, spleen, intestine	IL-6R/gp130 expressing cells	+	+++	N.D.	
KC/CXCL1 (IL-8 in humans)	Very low	↑	↑	1-2 hours	2 hours	1 day	Lung endothelial cells ?	CXCR2 expressing cells	+	+++	N.D.	Induced by IL-6 together with other unknown AKI/nephrectomy- Induced co-factors
TNF	Very low	↑	↑	1-2 hours	2 hours	1-2 days	Immune cells, macrophages	TNFR1 expressing lung endothelial cells; other cell types?	+	+++	N.D.	
IL-10	Very low	↑	↑	4 hours	8-24 hours	> 1 day	Liver, splenic CD4 T cells	Immune cells ?	Decrease by anti-inflammatory action	Decrease by anti-inflammatory action	N.D.	Induced by IL-6; Anti-inflammatory interleukin
NETs	Very low	↑	N.D.	15-20 hours	N.D.	N.D.	Neutrophils	Unknown	N.D.	N.D.	N.D.	