**B lymphocytes mediate acute kidney injury**

**Introduction:** Acute kidney injury (AKI) affects approximately 10% of hospital inpatients and is the commonest cause of delayed graft function in kidney transplants, but there are currently no specific therapies available. Signals released from damaged cells may trigger immune activation (sterile inflammation), exacerbating tissue damage. Activated B cells secrete antibody, but there is an increasing appreciation of their antibody-independent functions such as cytokine and chemokine production.

**Aims:** We sought to investigate whether B cells contribute to sterile inflammation in AKI, coordinating neutrophil and monocyte recruitment to the injured kidney.

**Results:** In a murine model, we observed a four-fold increase in circulating leucocytes within an hour of AKI induction. One third of these leucocytes were B cells. After 6 to 12 hours, there was a reduction in bone marrow and splenic B cells and a corresponding increase in the number of B cells in the kidney, particularly B1a cells. We found that post-AKI, B cells upregulated CD11b, and entry into the kidney was CD11b-dependent. These kidney B cells produced CCL7 and CXCL2, facilitating neutrophil and monocyte recruitment. Blockade of CCL7 ameliorated the severity of AKI. In human kidneys, we found significantly higher *CCL7* transcript levels in samples obtained from donors with AKI compared to controls, confirming the importance of this pathway in patients.

To further investigate the of role B1a cells in AKI *in vivo*, we took advantage of the sialic-acid-binding immunoglobulin-like lectin G (SIGLEC-G) knockout mice which have increased numbers of B1a cells and lower threshold of B cell activation. SIGLEC-G-/- mice had more severe AKI and conversely, administration to wildtype mice of a Siglec-G agonist, sialic acid (Neu5AC), which inhibits B cell activation, ameliorated AKI and reduced renal neutrophil infiltration.

**Conclusion:** Together our data suggest that B cells may contribute to innate immune responses in sterile inflammation in AKI, revealing a novel potential therapeutic target.