Table 1. The value of [TIMP-2] ● [IGFBP7] in AKI patients

Outcome	AKI stage 2 and 3	LOS (median days)	AKI days/ICU days (%)	CRRT initiation (%)	In-ICU mortality, n	Combination of outcomes
NC(+)/AKI(+) vs. NC(-)/AKI(+)	47 (29.7%) vs 16 (19.8%), P=0.097	4.5 vs 7, P=0.017	0.63 vs 0.50, P=0.000	OR 1.965 (95% 0.834-4.633), P=0.109	OR 2.087 (95% 1.241-3.510), P=0.003	OR 2.290 (95% 1.401-3.744), P=0.000

Table 2. Adjusted HRs for death or dialysis within ICU from a multivariate Cox proportional hazards model

Variable	Adjusted HR(95% CI)	P Value
Nephrocheck positivity	2.038(1.285-3.234)	0.003
CKD	1.776(1.060-2.974)	0.029
SOFA score	1.109(1.045-1.176)	0.001
Lactate on admission	1.070(1.014-1.130)	0.014
Creatinine on admission	1.175(1.017-1.356)	0.028
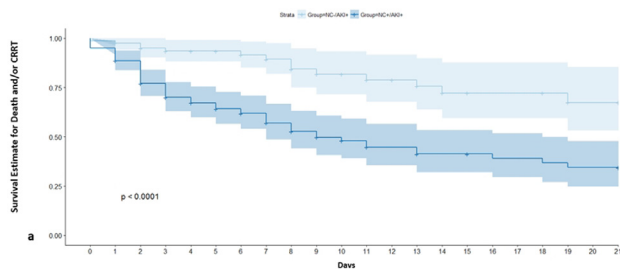
Conclusions: The [TIMP-2]●[IGFBP7] product offers an excellent tool for early recognition of AKI risk where intervention can still alter outcomes. It has been validated in previous cohorts, over-performing other biomarkers in the detection of AKI. Our vision was to expand further on other potential uses of [TIMP-2]●[IGFBP7]. To our knowledge, this is the first study that combines [TIMP-2]●[IGFBP7] values with the clinical diagnosis of AKI to investigate the risk of developing worse outcomes in critically-ill patients. Our study shows that the [TIMP-2]●[IGFBP7] values not only predict AKI risk, but also can serve to identify AKI patients at increased risk for adverse outcomes in ICU.

SAT-129

GROUP 2 INNATE LYMPHOID CELLS ARE REDUNDANT IN EXPERIMENTAL RENAL ISCHEMIA-REPERFUSION INJURY

CAMERON, G*[1], Loering, S[1], Deshpande, A[1,2], Jiang, S[3], Molofsky, A[4], McKenzie, A[5], Hansbro, P[6], Starkey, M[1]

[1]The University of Newcastle and Hunter Medical Research Institute, Priority Research Centre GrowUpWell- School of Biomedical Sciences and Pharmacy, New Lambton Heights, Australia, [2]The John Hunter Children's Hospital, Paediatric Urology, New Lambton Heights, Australia; [3]National University- Department of Renal Medicine- The Canberra Hospital, Department of Immunology and Infectious Disease- John Curtin School of Medical Research, Canberra, Australia, [4]University of California, Department of Laboratory Medicine, San Francisco, Australia, [5]Francis Crick Avenue- Cambridge Biomedical Campus, MRC Laboratory of Molecular Biology, Cambridge, United Kingdom, [6]Centenary Institute and School of Life Sciences- University of Technology, Centre for inflammation, Sydney, Australia

Introduction: Acute kidney injury (AKI) is a well-defined risk factor for the development of chronic kidney disease. Group 2 innate lymphoid cells (ILC2s) are critical regulators of tissue homeostasis and are resident in the kidney. Recent evidence suggests that experimentally increasing the numbers of ILC2s with systemic recombinant mouse interleukin (IL)-25 or IL-33 administration prior to, or following, experimental AKI is protective against early features of renal injury. Whilst these cells can be induced to proliferate and protect against the deleterious consequences of ischemic or chemically-induced AKI, the impact of ILC2 deficiency on the severity of renal injury is unknown.

Methods: ILC2s were identified in kidney homogenates from wild-type (WT) C57BL/6JAusB and IL-5 reporter ($Il5^{venus/+}$) mice using flow cytometry, which was confirmed using immunofluorescence in kidney sections from IL-5 reporter ($Rosa^{td-tomato/+}Il5^{cre/+}$) mice. To assess the role of ILC2s in renal injury, we used an experimental model of AKI induced by 29-minute ischemia-reperfusion injury (IRI) following a contralateral nephrectomy in male WT, ILC2-deficient ($Rora^{fl/fl}Il7r^{cre/+}$) and diphtheria toxoid (DTx)-mediated ILC2-depleted (DTx treated $Icos^{dtr/+}Cd4^{cre/+}$) mice. Heterozygote ($Rora^{fl/+}Il7r^{cre/+}$) and vehicle controls (saline treated $Icos^{dtr/+}Cd4^{cre/+}$) were examined alongside the experimental injury. Sham controls for each genotype received a contralateral nephrectomy only.

Results: An extracellular matrix and adhesion molecules PCR array revealed that mRNA expression of 26/84 targets were increased greater than two-fold, 7-days post-IRI, compared to sham surgery. Histopathological features of acute tubular necrosis occurred 7 days after IRI in the form of dilated tubules, apoptotic tubules with loss of bush border and cast formation, which were not present following sham surgery. Remodelling was assessed with mason's trichrome staining. At 7 days post-IRI there was increased collagen content between the tubules scattered throughout the medulla and cortex of the kidney, which was not present in the sham controls. Since injury and remodelling were present at day 7 in WT mice, this time point was used to assess the role of ILC2-deficiency and -depletion. There were no differences in histopathological score (H&E and PAS kidney sections), collagen deposition (masons trichrome stained sections) or mRNA expression of injury-associated factors (*Lcn2* and *Tnf*); inflammatory chemokines (*Ccl5*, *Ccl20*, *Cxcl1*, *Cxcl2* and *Cxcl10*); tissue remodelling and fibrotic factors (*Col1a1*, *Fn1* and *Tgfb1*); and an ILC2-related growth factor (*Areg*) in kidney homogenate relative to *Hprt* in ILC2-deficient or -depleted mice compared to their appropriate ILC2-sufficient controls. There was 100% survival, irrespective of genotype.

Conclusions: These data demonstrate that the absence of ILC2s does not alter the severity of AKI. The existing literature suggests that activation of ILC2s and production of local type 2 immunity is protective against AKI. ILC2s are likely contributors, but other mechanisms of type 2-mediated immune activation may compensate in the absence of ILC2s. A loss of ILC2s is unlikely to increase susceptibility to, or severity of AKI, but they remain an attractive target for cellular therapies.

SAT-130

RENAL MEDULLARY HYPOXIA DURING EXPERIMENTAL CARDIOPULMONARY BYPASS: EFFECTS OF ALTERED PUMP FLOW AND ARTERIAL PRESSURE

Lankadeva, YR[1], Cochrane, AD[2,3], Marino, B[4], Iguchi, N[1], Hood, SG[1], Bellomo, R[5], May, CN[6], Evans, R*[7]

[1]Florey Institute of Neuroscience and Mental Health- University of Melbourne, Preclinical Critical Care Unit, Melbourne, Australia, [2]Monash Health, Department of Cardiothoracic Surgery, Melbourne, Australia; [3]Monash University, Department of Surgery, Melbourne, Australia; [4]Cell-saving and Perfusion Resources, Clinical Perfusion, Melbourne, Australia, [5]Austin Hospital, Department of Intensive Care, Heidelberg, Australia, [6]Florey Institute of Neuroscience and Mental Health, Preclinical Critical Care Unit, Melbourne, Australia, [7]Monash University, Cardiovascular Disease Program- Biomedicine Discovery Institute and Department of Physiology, Melbourne, Australia

Introduction: Renal medullary hypoxia may be a pathophysiological factor in cardiac surgery-associated acute kidney injury. However, the effects of cardiopulmonary bypass (CPB) on oxygenation of the renal medulla remain poorly understood. Furthermore, whether increased pump flow or arterial pressure can improve renal medullary oxygenation has not been determined. Therefore, in the current study we tested whether CPB causes medullary hypoxia and whether medullary oxygenation during CPB varies with pump flow and mean arterial pressure.

Methods: Twelve sheep were instrumented to allow measurement of whole kidney, medullary and cortical blood flow and oxygenation. The experiment was performed five days later, under isoflurane anesthesia. Sheep were first placed on CPB at a pump flow of 80 mL/kg/min and a target mean arterial pressure of 70 mmHg. Pump flow was then set at 60 and 100 mL/kg/min while mean arterial pressure was maintained at ~70 mmHg. Mean arterial pressure was then increased by infusion of metaraminol (0.2 mg/min) at a set pump flow of 80 mL/kg/min.

Results: Transition to CPB at a pump flow of 80 ml/kg/min was associated with reduced total renal blood flow (RBF, -61% less than the conscious state), along with reduced perfusion in the cortex (-44%) and medulla