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MOUSE MODEL OF ACUTE KIDNEY INJURY (AKI)

- AKI is a sudden, and often reversible, decline in the ability of the kidneys to work and perform their normal functions
- In patients admitted to hospital, AKI is reported in 10-15% of cases
  - The incidence in intensive care units has been reported to be in excess of 50% of patients
  - One of the most common causes of AKI in hospitalized patients is nephrotoxicity, or the use of medications with a nephrotoxic effect
- The risks and pathogenesis of AKI are summarized below:

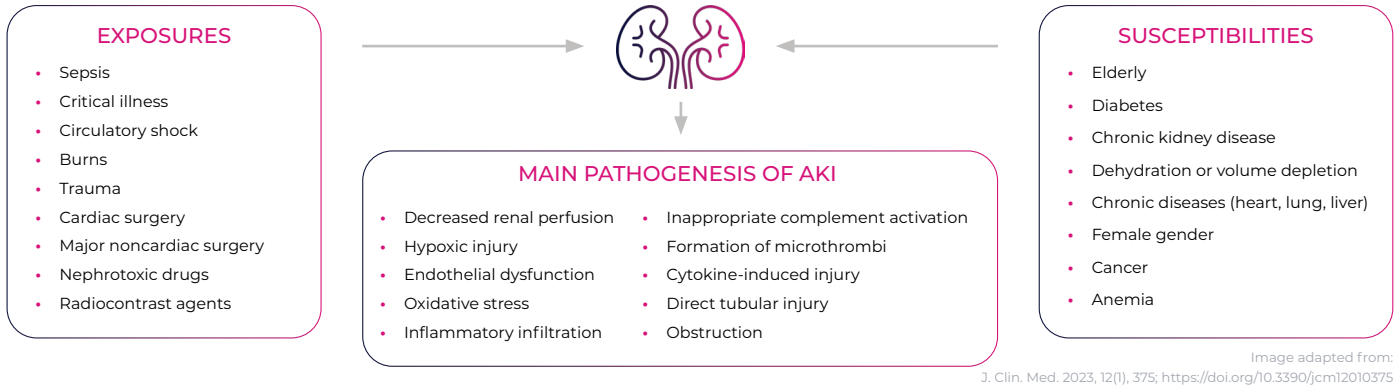
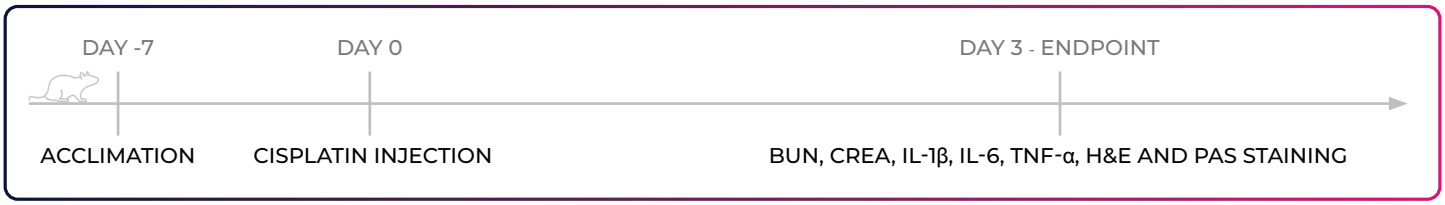


Image adapted from:
J. Clin. Med. 2023, 12(1), 375; https://doi.org/10.3390/jcm12010375

Currently, there are no targeted pharmacotherapies approved for the treatment of AKI and the optimal timing of renal replacement therapy in critically ill patients is unclear, and is an area of active investigation. ChemPartner offers a robust, AKI mouse model for your metabolic research, providing an efficient platform for the fast screening of drug candidates targeting acute kidney injury.

STUDY OUTLINE

CISPLATIN-INDUCED PRECLINICAL *IN VIVO* MOUSE MODEL OF AKI



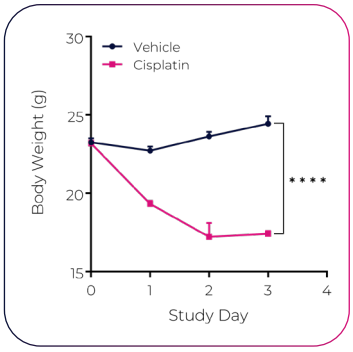
- Strain
  - Male BALB/c mice, 7 weeks on arrival
- Model
  - Cisplatin, 15mg/kg, *i.p.*, single dose

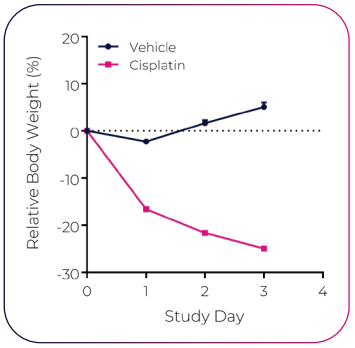
MAJOR READOUTS

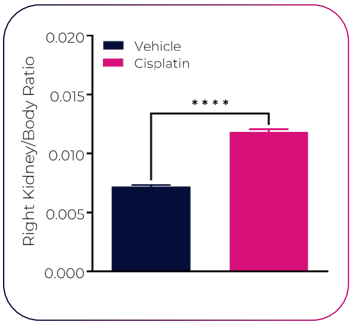
- Daily body weight measurements
- BUN, CREA and right kidney/body weight ratio
- Serum: IL-1β, IL-6, and TNF-α, measurements
- H&E and PAS staining to assess tubular injury
- Survival

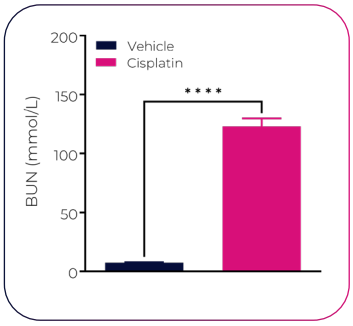
KEY MODEL CHARACTERISTICS:

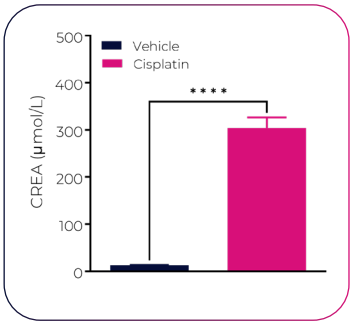
- AKI induced following single dose cisplatin
- Significantly increased right kidney/body weight ratio on study day 3
- Significantly elevated blood urea nitrogen (BUN) and creatinine (CREA) on study day 3
- Significantly decreased survival probability of cisplatin treated mice on study day 3

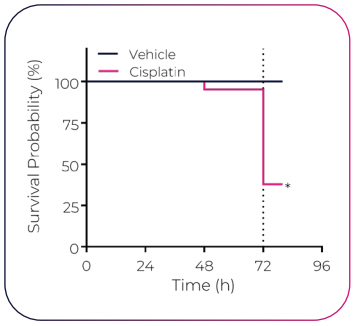






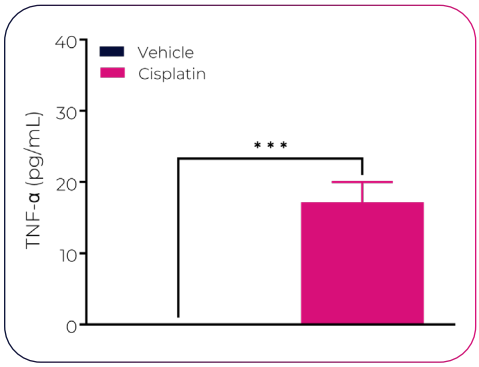


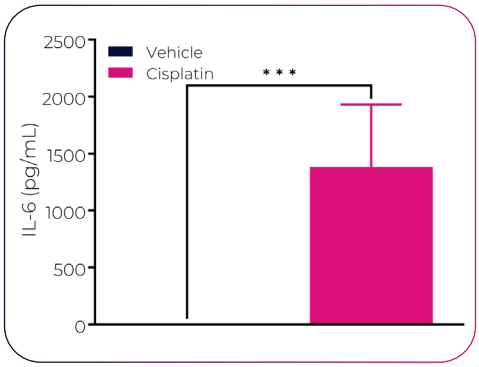


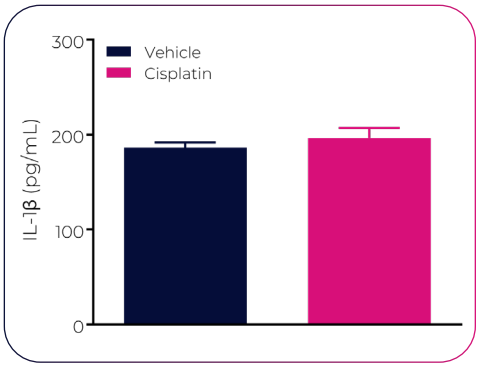


CYTOKINE PROFILE

- Significantly elevated serum TNF-α and IL-6 levels on study day 3

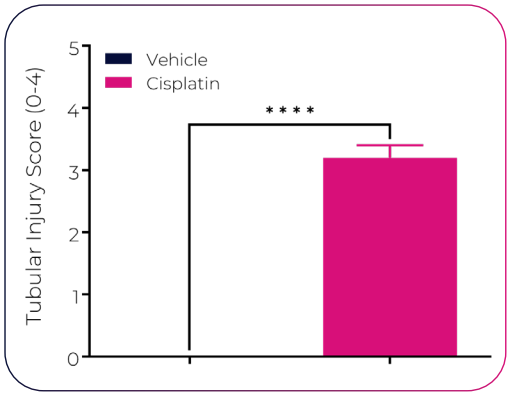


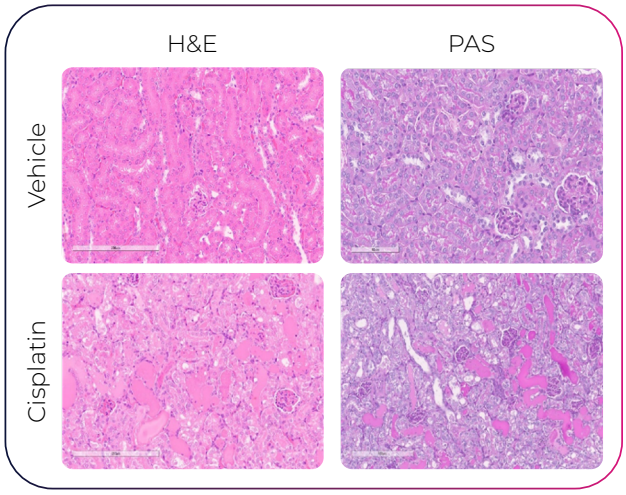




HISTOPATHOLOGICAL FEATURES

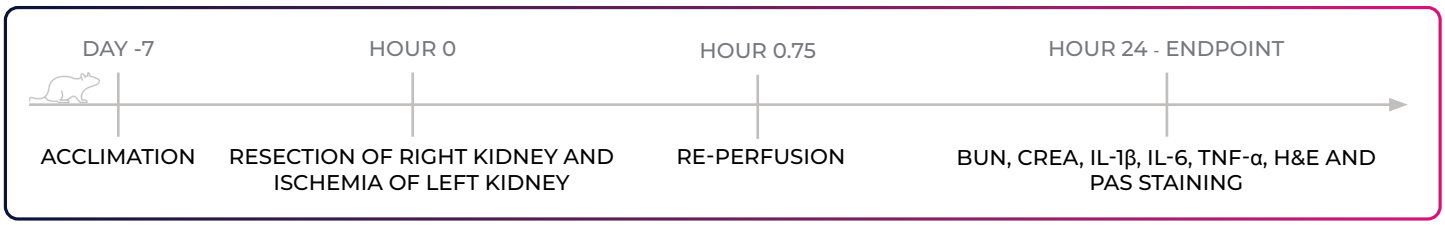
- Cisplatin-treated mice had significant tubular injury (26-75% of the kidney area injured) on study day 3





STUDY OUTLINE

uIRI/UNx PRECLINICAL *IN VIVO* MOUSE MODEL OF AKI



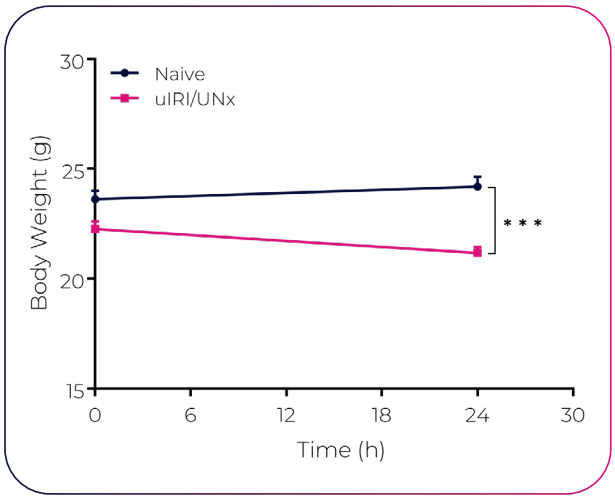
- Strain
  - Male C57BL/6 mice, 7 weeks on arrival
- Model
  - Obstruction of blood flow to the left kidney for 45 min and surgical resection of the right kidney
  - Naïve mice did not undergo sham-surgical procedures

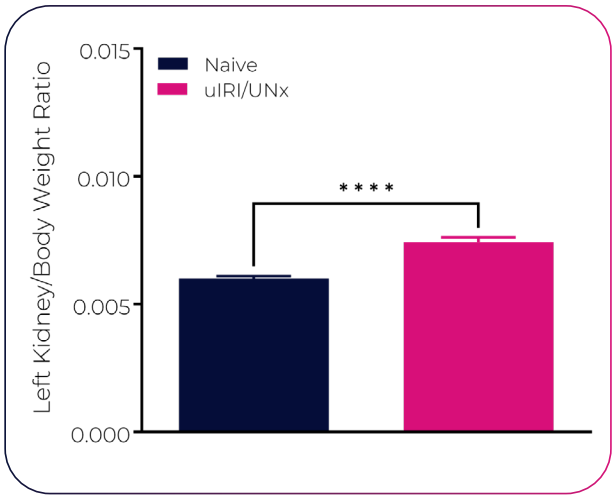
MAJOR READOUTS

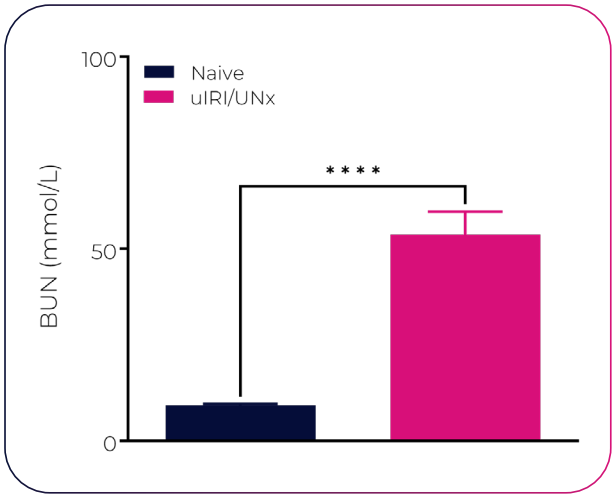
- Daily body weight measurements
- BUN, CREA and left kidney/body weight ratio
- Serum: IL-1β, IL-6 , and TNF-α measurements
- H&E and PAS staining to assess tubular injury

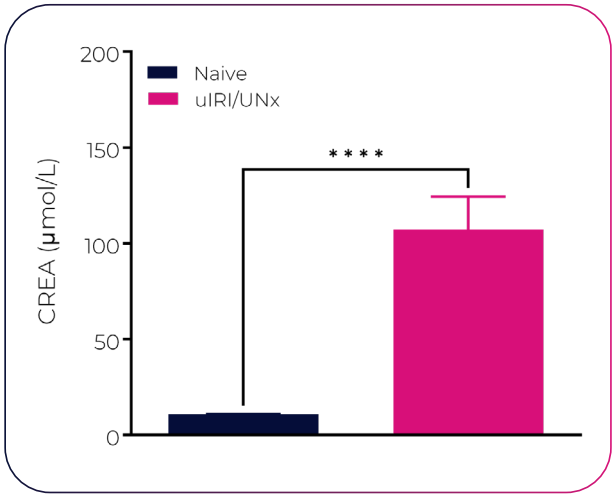
KEY MODEL CHARACTERISTICS:

- AKI rapidly induced (24 h) following ischaemic injury (45 min obstruction) to the left kidney and surgical resection of the right kidney
- Significantly increased left kidney/body weight ratio in uIRI/UNx surgically-prepared mice
- Significantly elevated blood urea nitrogen (BUN) and creatinine (CREA) levels were detectable in the sera of mice 24 h post uIRI/UNx surgery



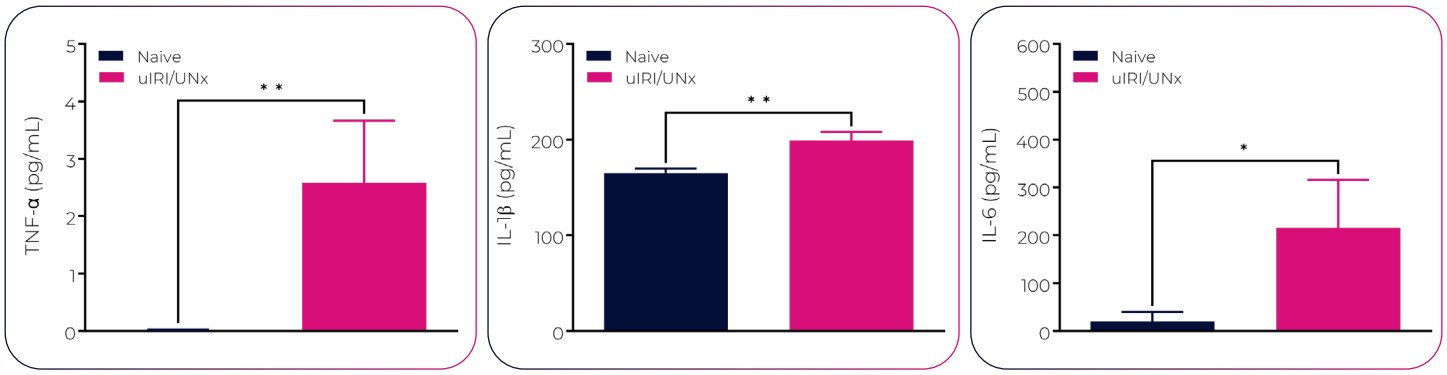






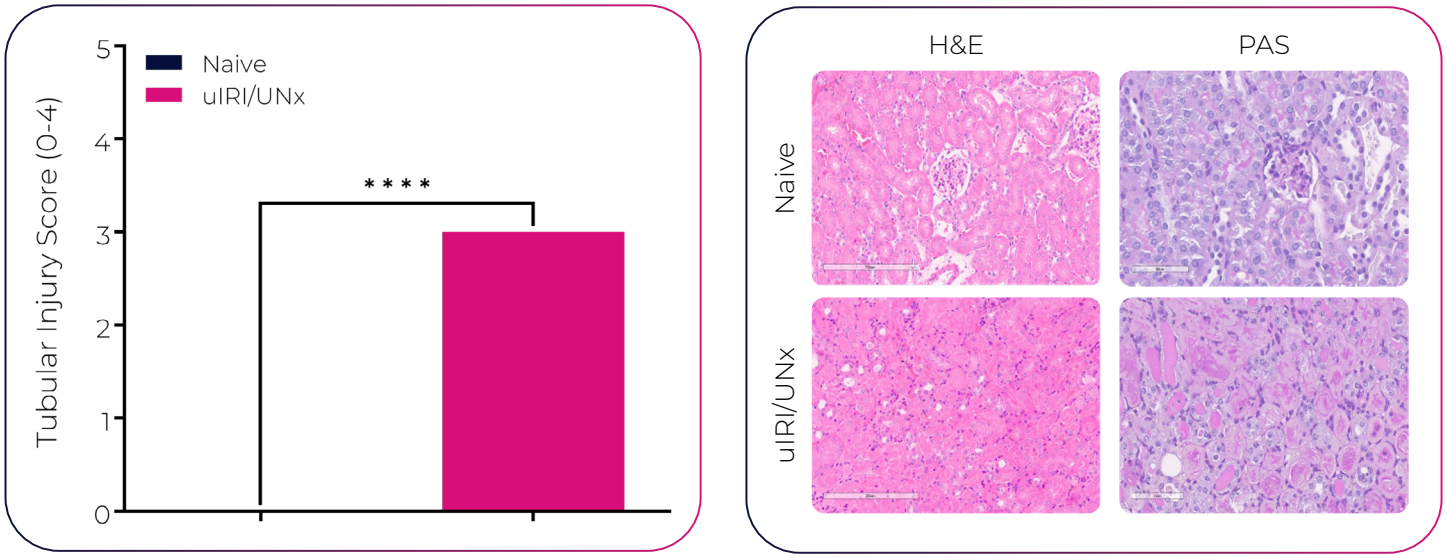
CYTOKINE PROFILE

- Significantly elevated serum TNF-α, IL-1β and IL-6 levels in uIRI/UNx surgically-prepared mice



HISTOPATHOLOGICAL FEATURES

- Significant tubular injury (26-75% of the kidney area injured) observed 24 h post uIRI/UNx surgery



SUMMARY

The utilization of cost-effective, clinically relevant *in vivo* models for studying kidney tubular injury will allow the rapid assessment of drug candidates and drug efficacy testing. The cisplatin-induced mouse model and the uIRI/UNx surgically-prepared mouse model are useful preclinical *in vivo* tools for evaluating anti-nephrotoxic drugs for kidney tubular injury and mimic many of the biochemical and histopathological features of acute kidney injury.

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