








CALCIUM-FREE OXALATE DIET-INDUCED MOUSE MODEL OF CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is a global health challenge that affects approximately 10-15% of the population in developed countries.

- CKD is attributed to a progressive and irreversible loss of kidney function
- Prevalence increases with age; in particular people with hypertension, obesity or diabetes
- The main histological characteristics of CKD include; glomerular sclerosis and glomerular collapse, interstitial fibrosis, tubular fibrosis, tubular atrophy, and interstitial infiltration
- CKD progression can be categorized into the stages outlined below:

STAGE 1	STAGE 2	STAGE 3A/STAGE 3B	STAGE 4	STAGE 5
GFR \geq 90	89 \geq GFR \geq 60	59 \geq GFR \geq 40 / 44 \geq GFR \geq 30	29 \geq GFR \geq 15	GFR<15
				
Normal or high function	Mildly decreased function	Mild to moderately decreased function	Severely decreased function	Kidney Failure

STUDY OUTLINE

CALCIUM-FREE OXALATE DIET-INDUCED PRECLINICAL *IN VIVO* MOUSE MODEL



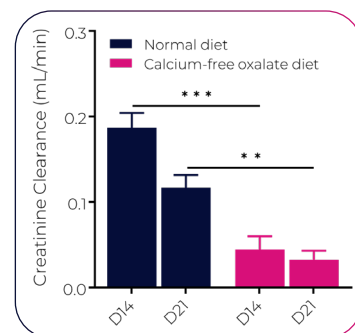
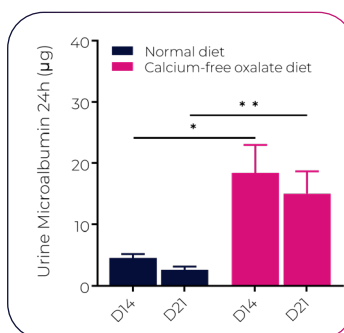
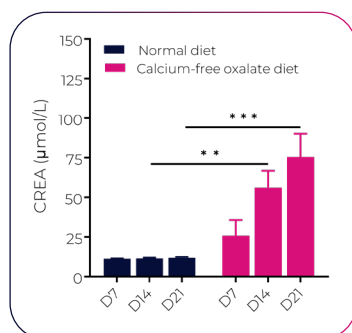
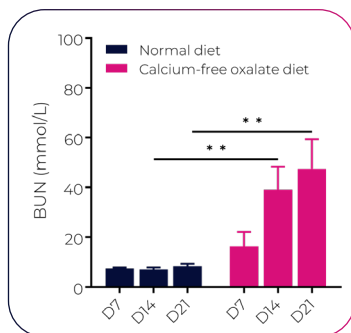
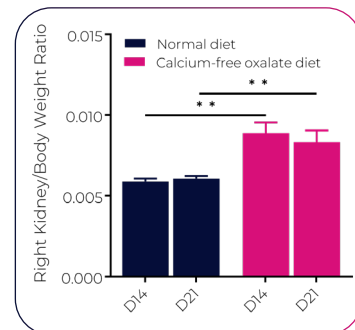
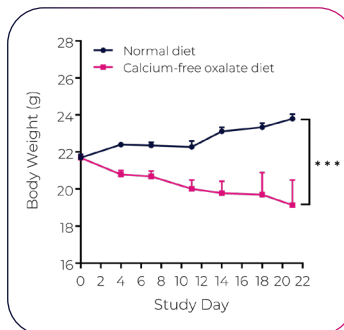
- Strain
 - Male C57BL/6 mice, 7 weeks on arrival
- Model
 - Calcium-free oxalate diet to model disease induction
 - Standard rodent chow for control mice

MAJOR READOUTS

- Body weight
- BUN, CREA, creatinine clearance, urine microalbumin (UMALB), and right kidney/body weight ratio
- H&E and Masson staining for tubular degeneration/atrophy score, tubular dilation score, interstitial inflammatory cell infiltration score and tubulointerstitial fibrosis

KEY MODEL CHARACTERISTICS:

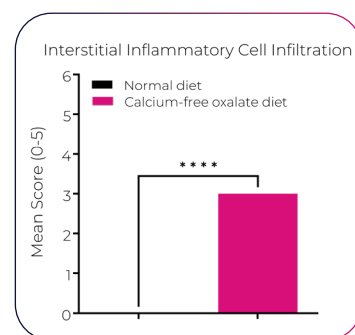
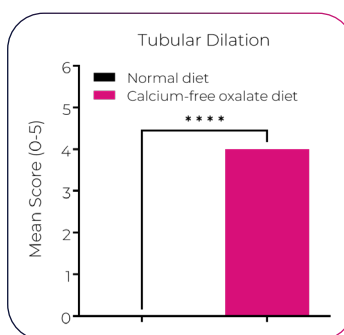
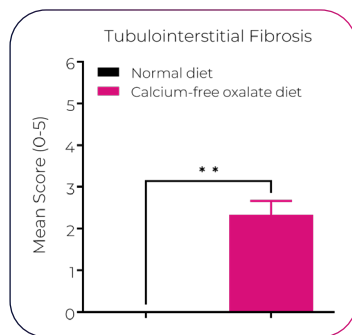
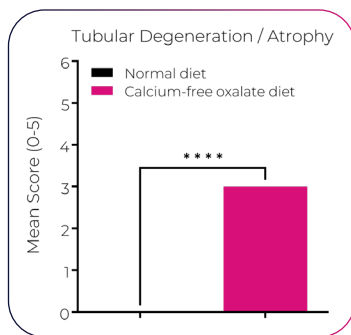
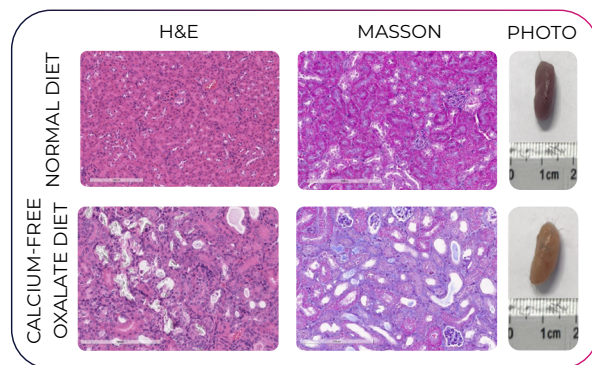
- ✓ Mice fed continuously on a calcium-free oxalate diet
- ✓ Up to 21-day dosing window
- ✓ Increased right kidney/body weight ratio from study day 14
- ✓ Elevated blood urea nitrogen (BUN) from study day 7
- ✓ Elevated blood creatinine levels from study day 7
- ✓ Elevated urine microalbumin levels from study day 14
- ✓ Decreased creatinine clearance from study day 14



HISTOPATHOLOGICAL FEATURES

Mice consuming a calcium-free oxalate diet had the following histopathological features:

- ✓ Kidneys appear pale in appearance
- ✓ Significant tubular dilation of the kidney from study day 14
- ✓ Significant tubular degeneration / atrophy from study day 14
- ✓ Significant interstitial inflammatory cell infiltration from study day 14
- ✓ Significant tubulointerstitial fibrosis from study day 14



SUMMARY

The calcium-free oxalate diet-induced mouse model is a simple, reproducible, and technically undemanding *in vivo* tool, offering novel opportunities for CKD research.

The model is well validated; demonstrating many of the biochemical and histopathological features of chronic kidney disease.

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