



# 0.2% ADENINE DIET-INDUCED MOUSE MODEL OF CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is a global health challenge and is defined as a persistent decline in kidney function and/or identifiable structural damage.

ChemPartner has developed and validated several models of renal disease, offering robust and cost-effective platforms for screening therapies targeting the various stages of disease progression:

MODEL	DESCRIPTION	PATHOLOGY	COMMENTS AND OBSERVATIONS
UUO	The left ureter of anesthetized mice is ligated, leading to complete obstruction	<ul style="list-style-type: none"> <li>Primary feature is tubular injury as a result of obstructed urine flow</li> <li>Renal inflammation</li> <li>Severe tubulointerstitial fibrosis</li> </ul>	<ul style="list-style-type: none"> <li>Surgery-induced model of renal fibrosis</li> <li>Short lead-in and study duration</li> <li>Deviates from clinical CKD pathology in that there is no decrease in renal function</li> <li>Suitable for fast screening of drug candidates</li> <li>Only modest changes observed in serum creatinine and urea concentrations</li> </ul>
Calcium-free oxalate diet-induced CKD	Consumption of the diet leads to the deposition of calcium oxalate crystals in the kidneys	<ul style="list-style-type: none"> <li>Decline in glomerular filtration rate</li> <li>Renal inflammation</li> <li>Tubular atrophy</li> <li>Tubulointerstitial fibrosis</li> <li>Progressive nephrocalcinosis</li> </ul>	<ul style="list-style-type: none"> <li>Evidence in the literature that the model is characterized by profound arterial hypertension and cardiac fibrosis</li> </ul>
0.2% adenine diet-induced CKD	Kidney disease stems from the formation of 2,8-dihydroxyadenine, an adenine metabolite that crystallizes within renal tubules	<ul style="list-style-type: none"> <li>Decline in glomerular filtration rate</li> <li>Renal tubule injury</li> <li>Renal inflammation</li> <li>Tubular atrophy</li> <li>Tubulointerstitial fibrosis</li> <li>Fibrosis of the renal parenchyma</li> </ul>	<ul style="list-style-type: none"> <li>Animals can develop cachexia, which is attributed to lack of palatability of the 0.2% adenine diet</li> <li>Ideal model for profiling drug effects on glomerular filtration rate</li> </ul>

## STUDY OUTLINE

### 0.2% ADENINE DIET-INDUCED PRECLINICAL *IN VIVO* MOUSE MODEL



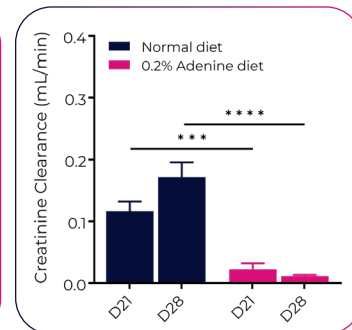
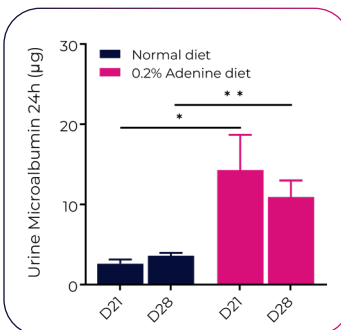
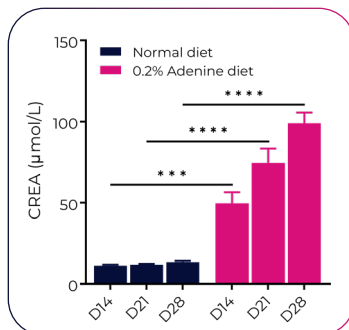
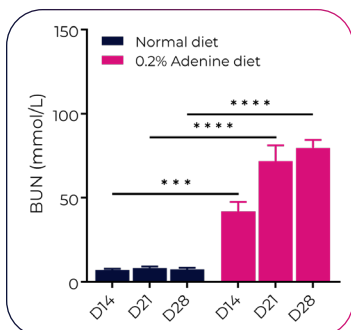
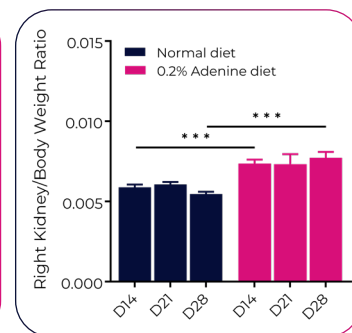
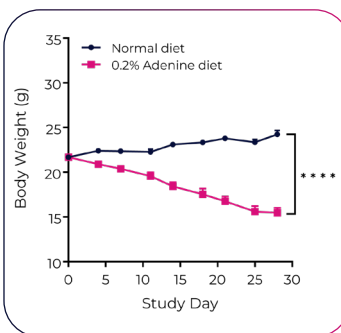
- Strain
  - Male C57BL/6 mice, 7 weeks on arrival
- Model
  - 0.2% adenine diet to model disease induction
  - Standard rodent chow for control mice

#### 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
- Macrophage-specific (F4/80) immunostaining of the kidney

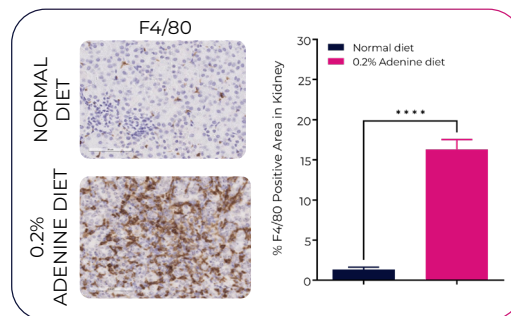
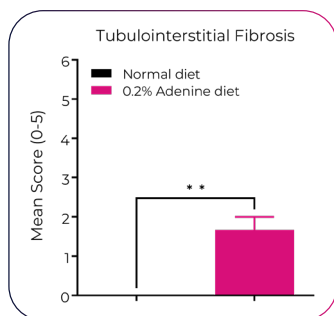
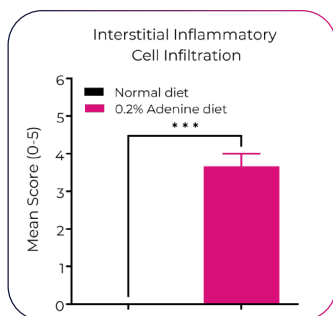
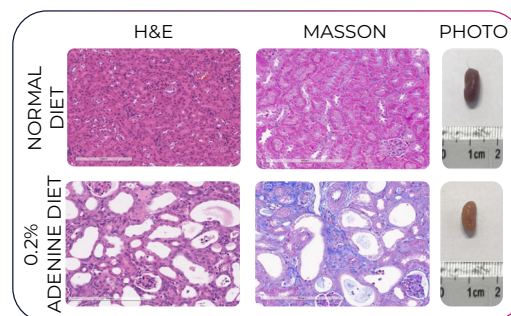
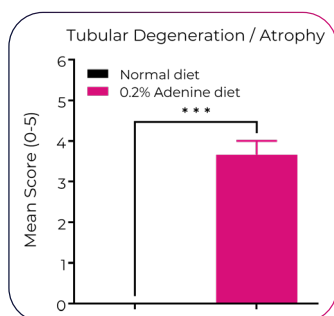
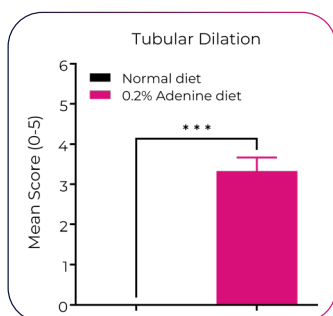
## KEY MODEL CHARACTERISTICS:

- ✓ Mice fed continuously on a 0.2% adenine diet
- ✓ 28-day model
- ✓ Increased right kidney/body weight ratio on study days 14 and 28
- ✓ Elevated blood urea nitrogen (BUN) from study day 14
- ✓ Elevated blood creatinine levels from study day 14
- ✓ Elevated urine microalbumin levels from study day 21
- ✓ Decreased creatinine clearance from study day 21



## HISTOPATHOLOGICAL FEATURES

- ✓ Pale kidneys
- ✓ Significant tubular dilation, tubular degeneration / atrophy, interstitial inflammatory cell infiltration and tubulointerstitial fibrosis from study day 14
- ✓ Increased macrophage infiltration into the kidney



## SUMMARY

The 0.2% adenine diet-induced mouse model is a well validated model of CKD, which is a simple, reproducible, and technically undemanding *in vivo* tool.

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