ReninAAV UNx db/db model of DKD



Advanced mouse model of diabetic kidney disease (DKD) with type 2 diabetes and hypertension

Gubra ReninAAV UNx db/db mouse model of DKD

The Gubra advanced mouse model of DKD – the ReninAAV UNx db/db model – exhibits key features of late stage DKD and progressive albuminuria along with histopathological features such as severe glomerulosclerosis.

Key model traits

- Genetically-induced obesity and diabetes.
- Induction of hypertension using a renin-encoding adeno-associated virus in uninephrectomized db/db mice.
- Progressive albuminuria.
- Advanced glomerulosclerosis and tubular injury.
- Therapeutic evaluation of drug efficacy

Model induction	Renin-encoding adeno-associated viral induction of hypertension and unilateral nephrectomy in db/db mice.
Strain	Female BKS.Cg-Dock7m +/+ Leprdb/J mouse

Study outline



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Metabolic and biochemical characteristics

ReninAAV UNx db/db mice develop insulin resistance, type 2 diabetes and hypertension. In parallel severe albuminuria is observed.

	db/m	ReninAAV UNx db/db
Body weight (g)	23.8 ± 0.4	47.6 ± 1.6
Kidney weight (mg)	158 ± 5	337 ± 19
Heart weight (mg)	126 ± 3	284 ± 17
Blood glucose (mmol/L)	6.4 ± 0.1	20.0 ± 2.7
Blood pressure (mmHg)	-	164 ± 7
Urine ACR (µg/mg)	111 ± 9	13,153 ± 3,896

Plasma and urine biomarkers

Plasma and urine biomarkers for assesment of kidney function and injury.



Effects of 12 weeks treatment with standard of care (SOC) on plasma and urine markers in female ReninAAV UNx db/db mice.

Histomorphometric evaluation of fibrosis and inflammation

Effects of 12 weeks of treatment with standard of care (SOC) in female ReninAAV UNx db/db mice as assessed by immunohistochemistry and morphometric analyses.

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ReninAAV UNx db/db Vehicle

ReninAAV UNx db/db Lisinopril + Empagliflozin



AI-assisted glomerulosclerosis scoring

Glomerulosclerosis is assessed using our in-house developed deep learning based APP (GHOST - Gubra Histopathological Objective Scoring Technology).





Periodic Acid-Schiff stained kidney section from Renin AAV UNx db/ db mice after 12 weeks of treatment with vehicle or standard-of-care. AI-assisted identification of glomeruli and scoring of glomerulosclerosis according to a standardized preclinical score is indicated.

Tubular injury quantified by histomorphometric evaluation

Kidney injury molecule-1 (KIM-1) is elevated in the kidney of ReninAAV UNx db/db mice as assessed by immunohistochemistry and morphometric quantification. Treatment with standard of care for 12 weeks reduced KIM-1.



ReninAAV UNx db/db



KIM-1 stained kidney sections from ReninAAV UNx db/db treated for 12 weeks with vehicle (top) or standard-of-care combo (bottom)



Light sheet fluorescence microscopy and 3D imaging

Gubra's LSFM and 3D imaging platform enable automized analyses of the intact mouse kidney.



according to volume in the intact mouse



Automized image analyses of the intact mouse kidney

Structural endpoints such as glomerular volume and total number are analysed using inhoused developed algorithms.

Data demonstrates changes in glomerular volume (left) and number per kidney as associated with hypertension in the ReninAAV UNx db/db mouse model.

Mean glomeruli size

kidney.



3D image analyses of albuminuria

ReninAAV UNx db/db mice exhibit increased albuminuria as assessed by urine albuminto-creatinine ratio and as visualized here by 3D imaging of fluorescently labelled lectin and albumin.



Wild type



UNx db/db



ReninAAV UNx db/db

