INTRODUCTION AND AIM

Diabetic nephropathy (DN) is a serious long-term complication of diabetes. There is no curative treatment of DN, and the lack of knowledge about the mechanisms leading to DN hampers the development of efficient therapies.

In order to develop a more precise assessment of translatable nephrotic changes, we used novel and refined image analyses and stereological methods to estimate key histopathological features of DN in a DN mouse model combining genetic diabetes (db/db mouse) with uninephrectomy (UNx). The data are considered of high value for future preclinical drug development efforts.

RESULTS

UNx does not affect body weight or blood glucose in diabetic mice

Figure 2a | Weekly body weight (BW, g) and blood glucose (BG, mmol/L). Green dashed lines indicate termination of the first group of mice (11 weeks).

**‡‡‡ p<0.001 vs sham db/db. *** p<0.001 vs UNx db/db.

Increased glomerulosclerosis in diabetic UNx mice

Figure 5a | Representative PAS stained images from sham db/db, sham db/db, and UNx db/db mice. Scale bar = 100µm.

UNx increases total collagen III in the kidney

Figure 5b | Total glomerular volume was quantified stereologically (mm³) on PAS stained sections in the right kidney after 11 and 16 weeks.

CONCLUSION

UNx does not affect body weight or blood glucose in female db/db mice. The UNx db/db mouse model displays key features of diabetic nephropathy, incl. progressive albuminuria, kidney hypertrophy, kidney fibrosis, increased glomerular volume, and increased glomerulosclerosis. Stereological quantification refines the use of the db/db UNx model in diabetic nephropathy research.

Figure 7a | Podocin (green, podocytes), Collagen IV (yellow, fibrosis) double stainings were used to identify glomerulosclerosis (red overlay).

Figure 7b | Total collagen IV was quantified stereologically (mm³) on podocin/Collagen IV double stained sections in the right kidney after 11 and 16 weeks.