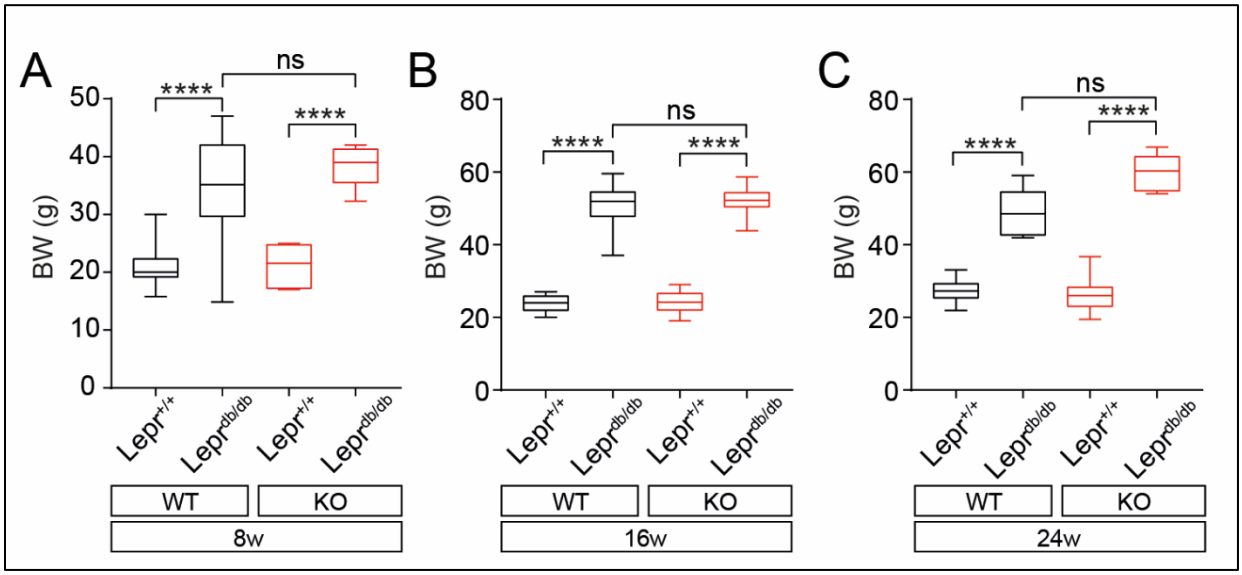
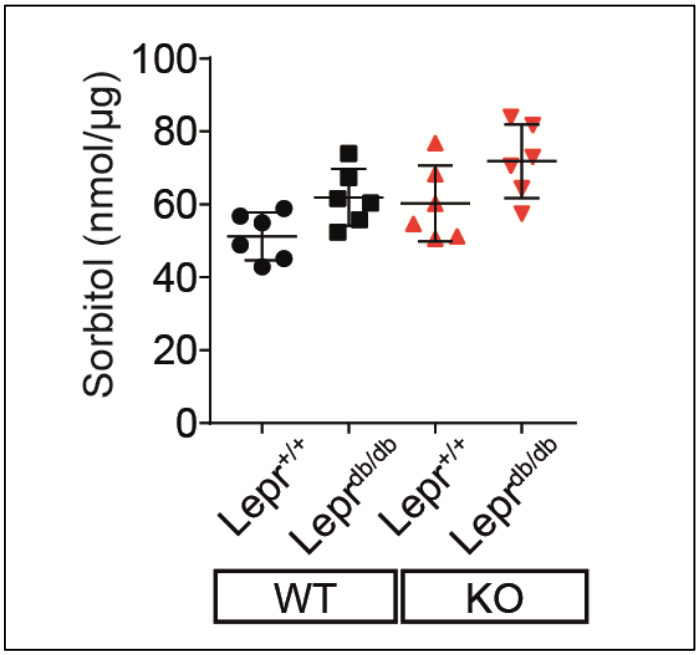
Supplementary data

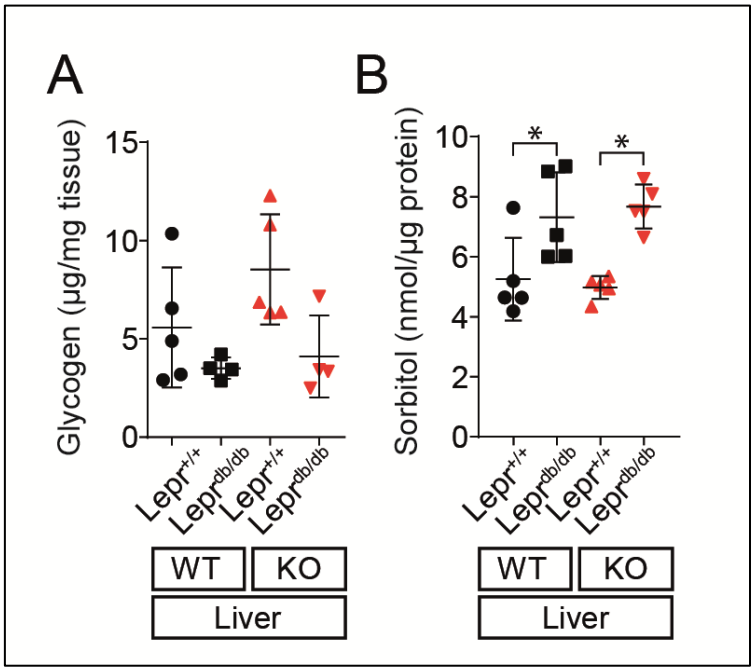
Supplementary Figure S1: (A-C) Box and whisker plots showing bodyweights of $Lepr^{+/+}$ (WT/KO) and $Lepr^{db/db}$ (WT/KO) mice at age of 8, 16 and 24 weeks respectively. Numbers of animals investigated are n≥8. Values are expressed as mean and min to max. ****p <0.0001, ns=not significant.



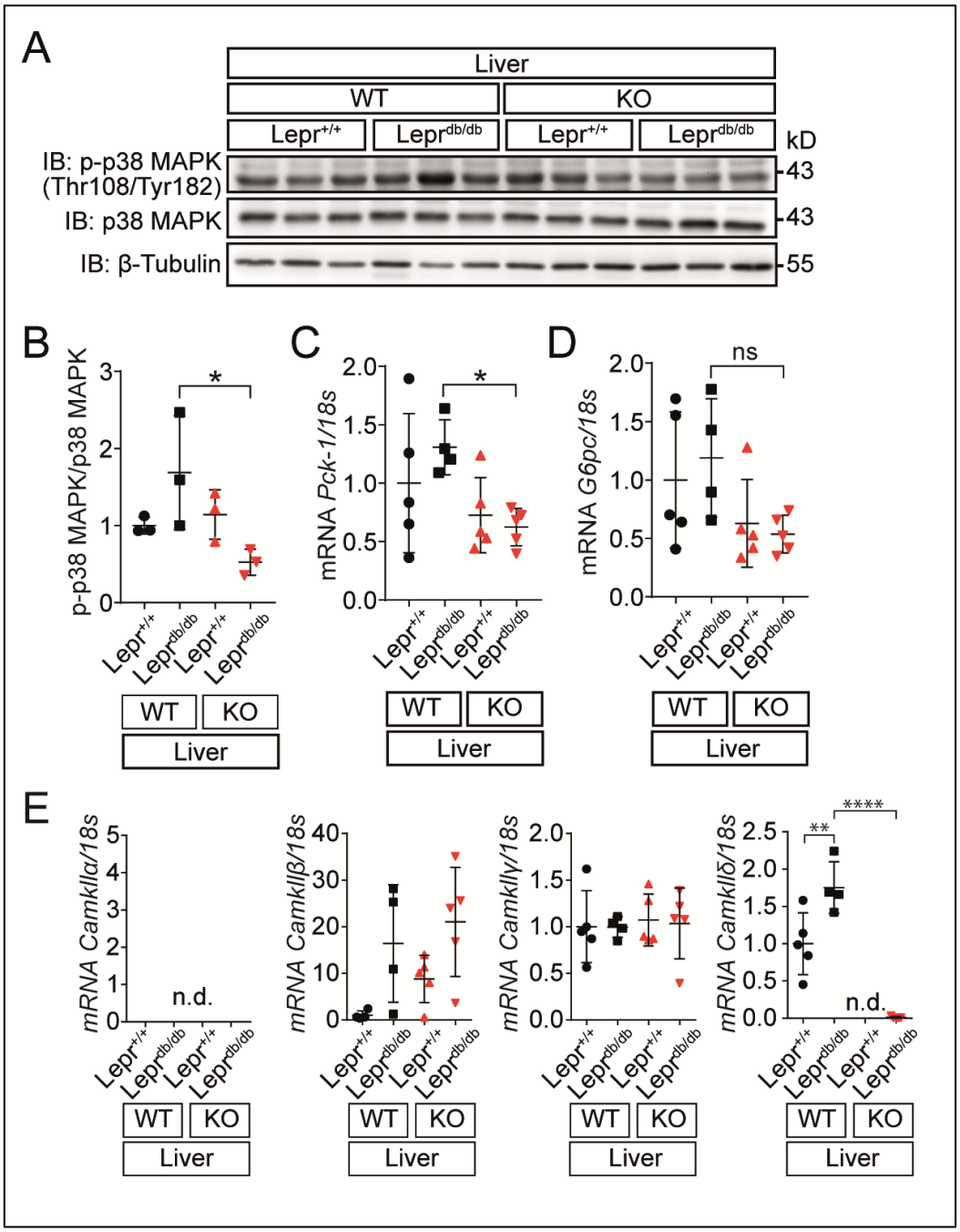
Supplementary Figure S2: Levels of sorbitol in skeletal muscle are equal in $Lepr^{+/+}$ and $Lepr^{db/db}$ conditions in WT and KO animals. Numbers of investigated animals are indicated as dots. All values are expressed as mean and SD.



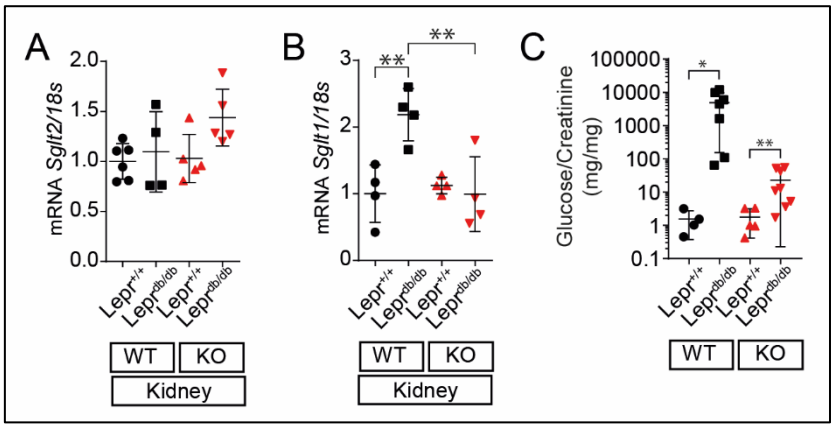
Supplementary Figure S3: (A) Glycogen and **(B)** Sorbitol content in liver tissue of indicated mice. Numbers of investigated animals are indicated as dots. All values are expressed as mean and SD. *p <0.05.



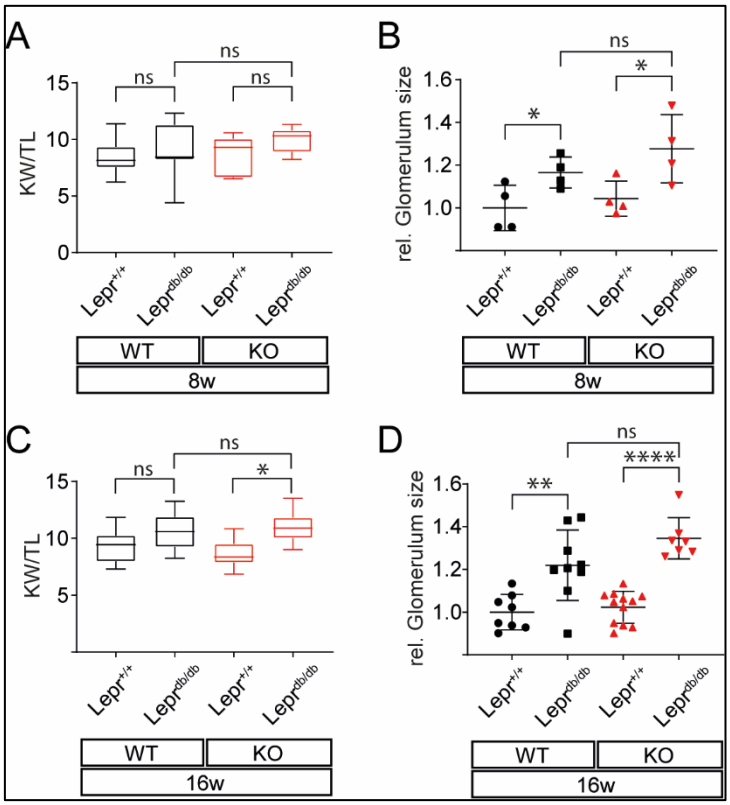
Supplementary Figure S4: (A) Immunoblot showing phosphorylated and total p-38 MAPK levels in livers of indicated mice, β-tubulin was used as loading control. **(B)** Graph showing reduced phosphorylation of p-38 MAPK in Lepr$^{db/db}$/KO animals. mRNA expression of *Pck-1* **(C)** and *G6pc* **(D)** is reduced in Lepr$^{db/db}$/KO compared to Lepr$^{db/db}$/WT mice. **(E)** mRNA expression of CaMKII-α, -β, -γ and -δ isoforms in liver. Numbers of animals investigated are indicated as dots. All values are expressed as mean and SD. *p <0.05, **p<0.01, ****p <0.0001, ns=not significant, n.d.=not detectable.



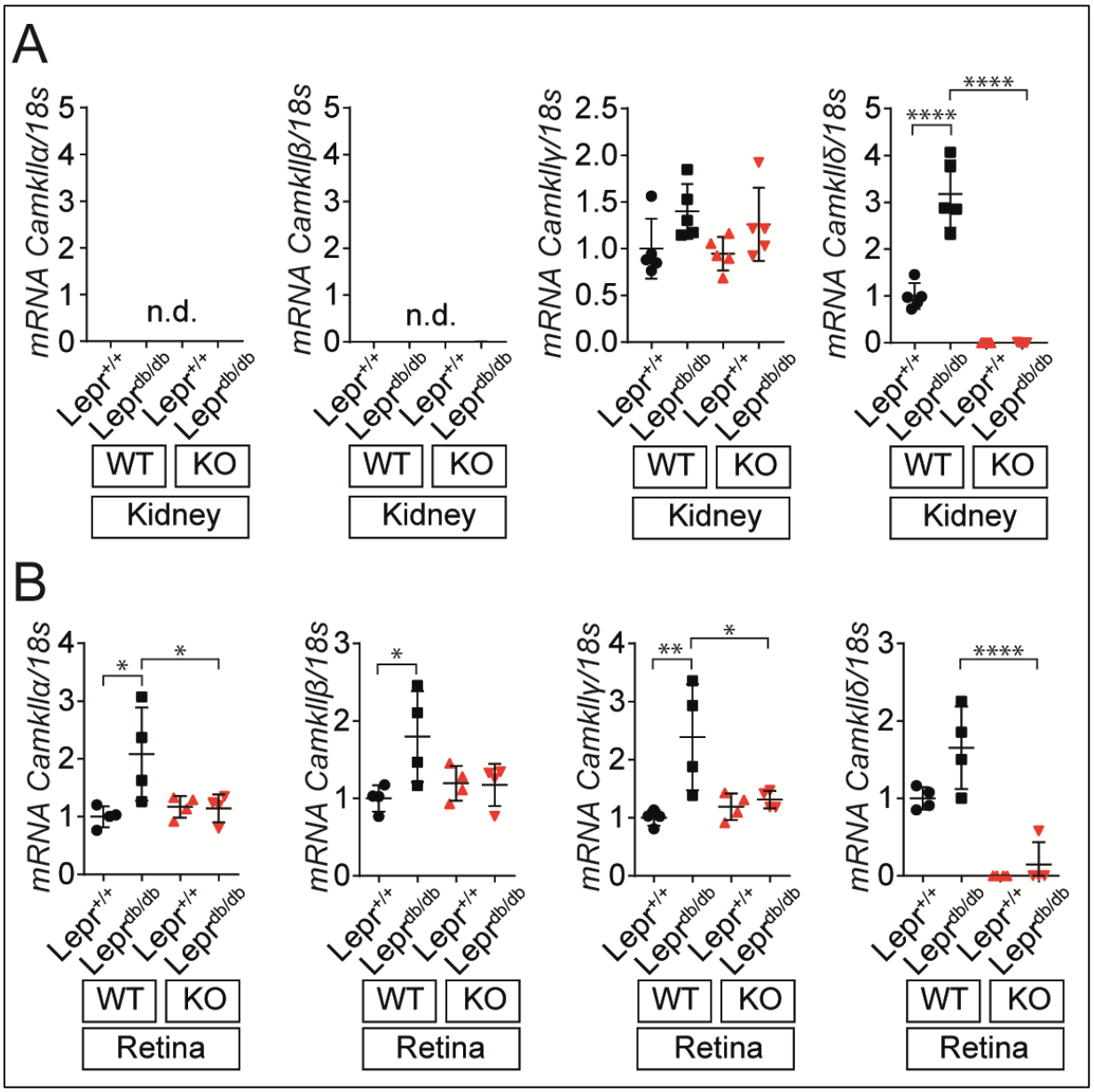
Supplementary Figure S5: (A/B) mRNA expression of renal *Sglt2* and *Sglt1* normalized to 18s mRNA respectively. **(C)** Urinary glucose concentrations of indicated mice normalized to creatinine. Numbers of animals investigated are indicated as dots. All values are expressed as mean and SD. *p <0.05, **p<0.01, ns=not significant.



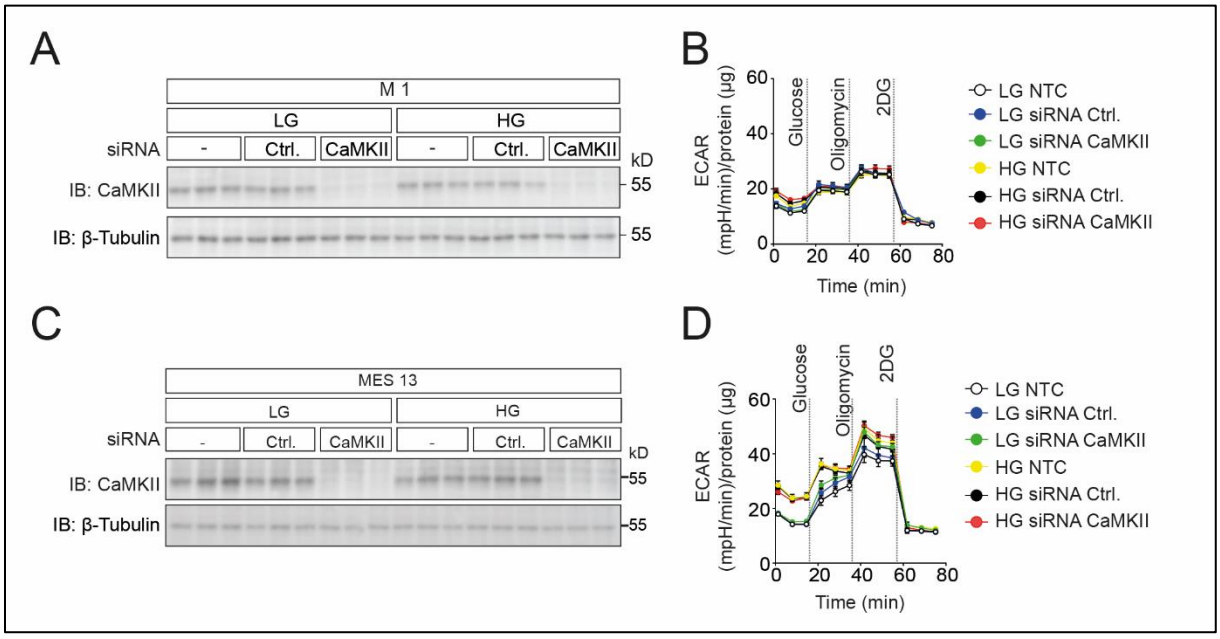
Supplementary Figure S6: (A/B) Kidney weight and relative glomerulum size of 8- and **(C/D)** 16 week old mice showing glomerular hypertrophy in both $Lepr^{db/db}$ (WT and KO) groups. Numbers of animals investigated are indicated as dots or n≥8 in box and whisker plots. Values are expressed as mean and SD in scatter plots and as mean and min to max in box and whisker plots. *p <0.05, *p<0.01, ****p <0.0001, ns=not significant.



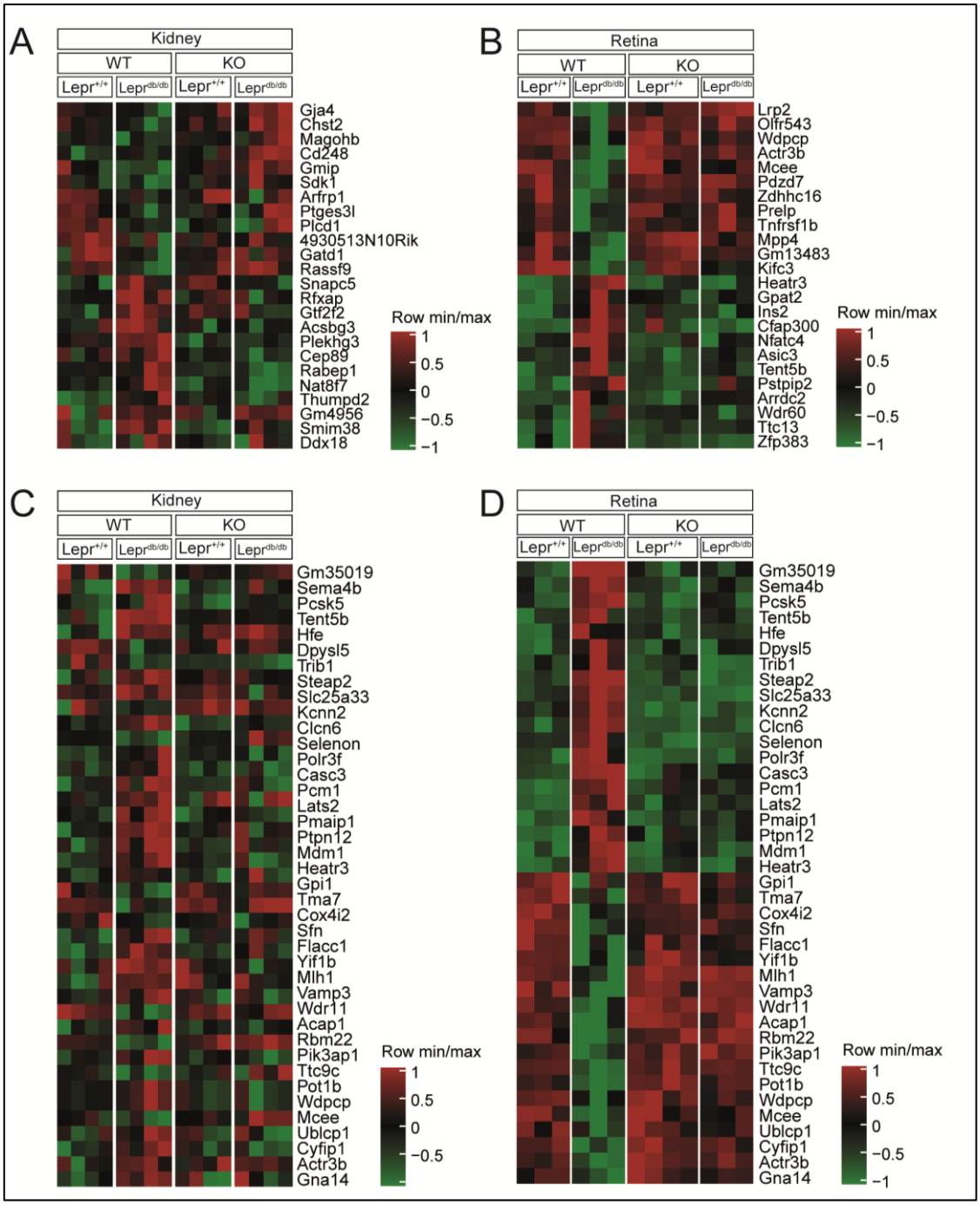
Supplementary Figure S7: (A) mRNA expression of *CaMKII-α, -β, -γ* and *-δ* isoforms in kidney and **(B)** in retina. Numbers of animals investigated are indicated as dots. All values are expressed as mean and SD. *p <0.05, **p<0.01, ****p <0.0001, n.d.=not detectable.



Supplementary Figure S8: (A/C) Immunoblot demonstrating successful siRNA mediated knockdown of CaMKII in M1 and MES13 cells. **(B/D)** Glycolysis stress test performed with a seahorse analyser in M1 and MES13 cells.



Supplementary Figure S9: (A/B) Heatmaps of top regulated genes in WT kidney *or* WT retina compared to KO in retina or kidney. **(C/D)** Heatmaps of genes differentially regulated in retina *and* kidney of WT mice but not in retina of KO mice. Numbers of animals investigated are n=4 in A and C and n≥3 in B and D.



Supplementary Figure S10: (A) Heatmap of differentially regulated genes involved in lipid metabolism in retina and **(B)** kidney. **(C)** Heatmap of lipid classes represents only minor changes of lipidome in serum, kidney and retina between the indicated groups. (D) PCA plots of lipidome changes in serum, kidney and retina Lepr$^{+/+}$/WT vs. Lepr$^{db/db}$/WT (left diagrams) and Lepr$^{+/+}$/KO vs. Lepr$^{db/db}$/KO. **(E)** Bar graph showing levels of Phosphatidyl ethanolamine (PE) and Cholesterol (Chol) in Retina. Numbers of animals investigated are n≥3 in A and B and n≥4 in C-E.