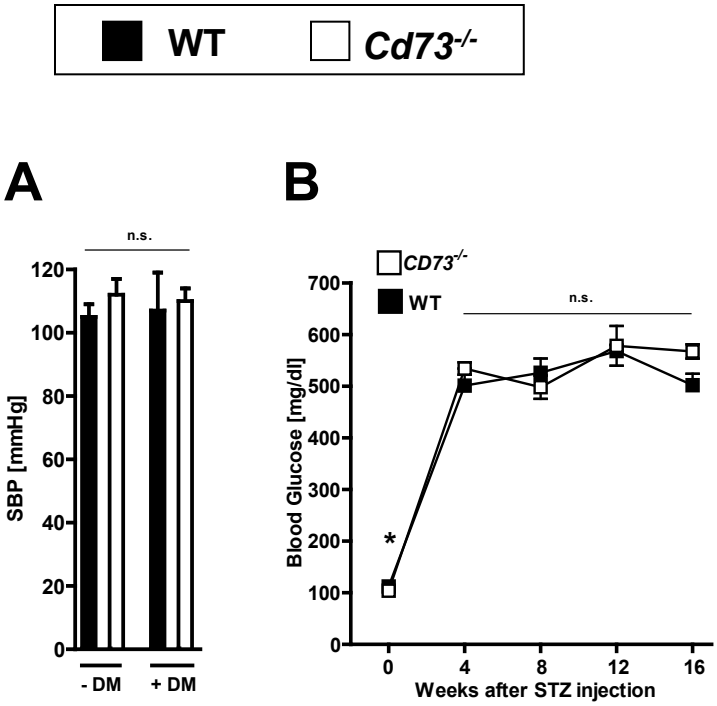
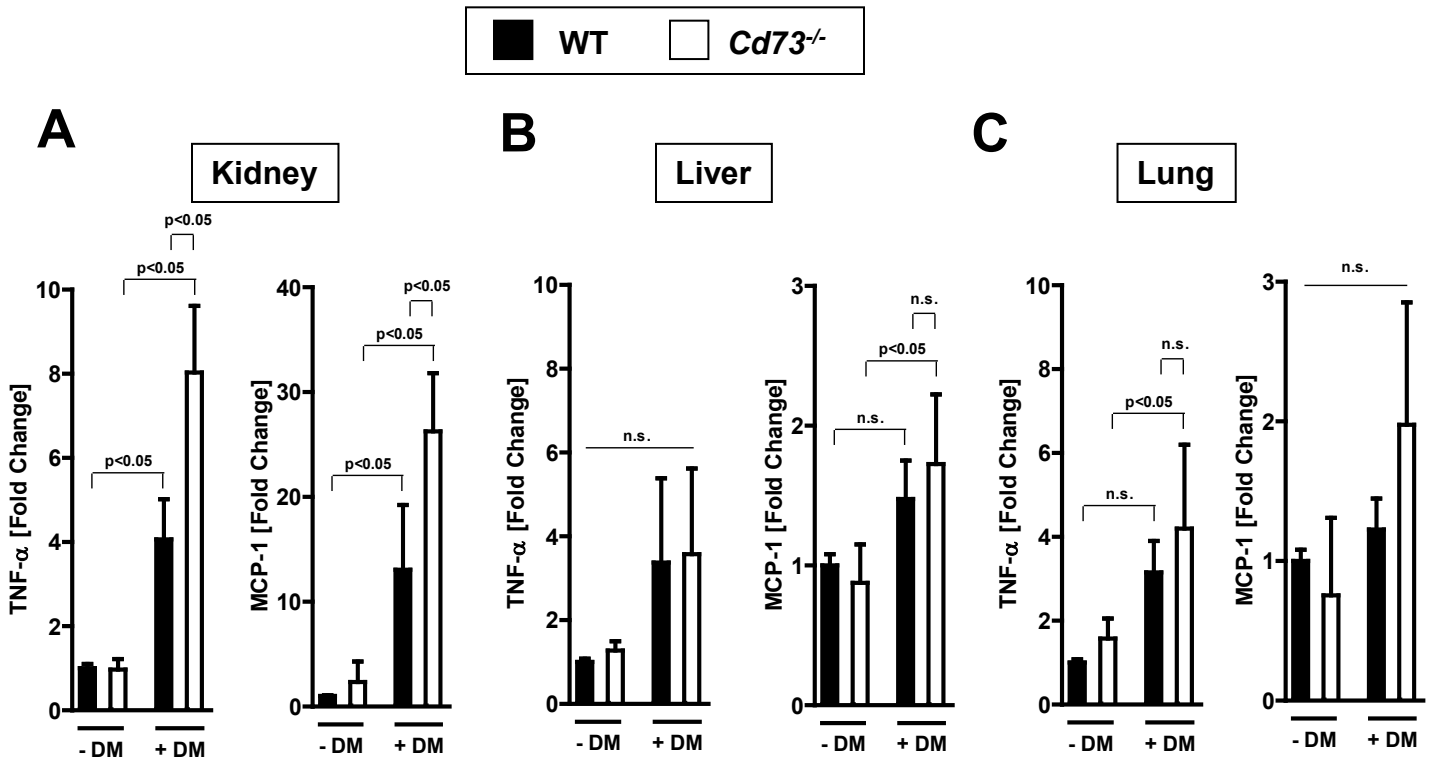
Supplementary Figure 1



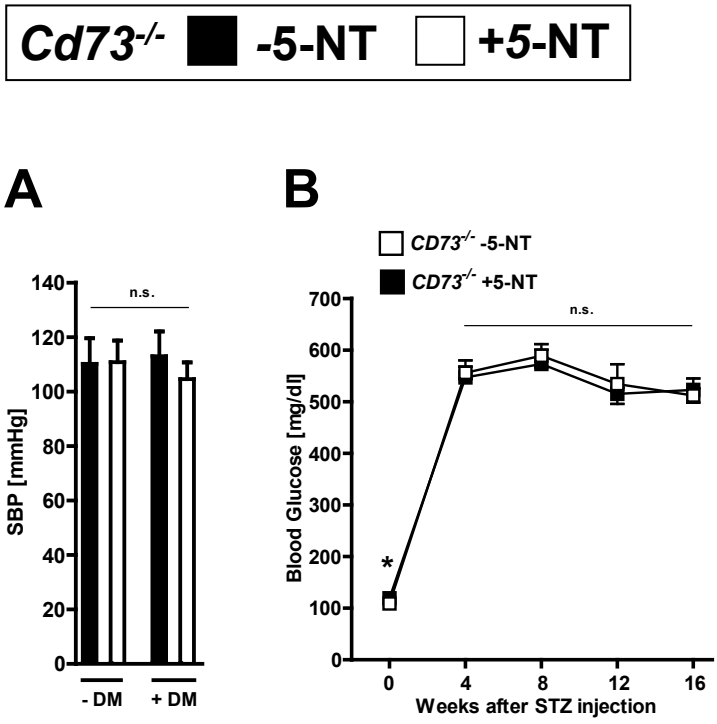
Supple. Fig. 2 Systolic blood pressure (SBP) and blood glucose in *Cd73*$^{-/-}$ mice.
Cd73$^{-/-}$ mice and age-, weight-, and gender-matched wild type mice were subjected to streptozotocin (STZ)-induced diabetes for 16 weeks until measurement of (a) systolic blood pressure and (b) blood glucose (n=6 in each group).

Supplementary Figure 2



Supple. Fig. 3 Organ inflammation during diabetes in *Cd73*$^{-/-}$ mice.
Cd73$^{-/-}$ mice and age-, weight-, and gender-matched wildtype mice were subjected to streptozotocin (STZ)-induced diabetes for 16 weeks until measurement of TNF-α and MCP-1 in (a) kidneys, (b) livers and (c) lungs (n=6 in each group).

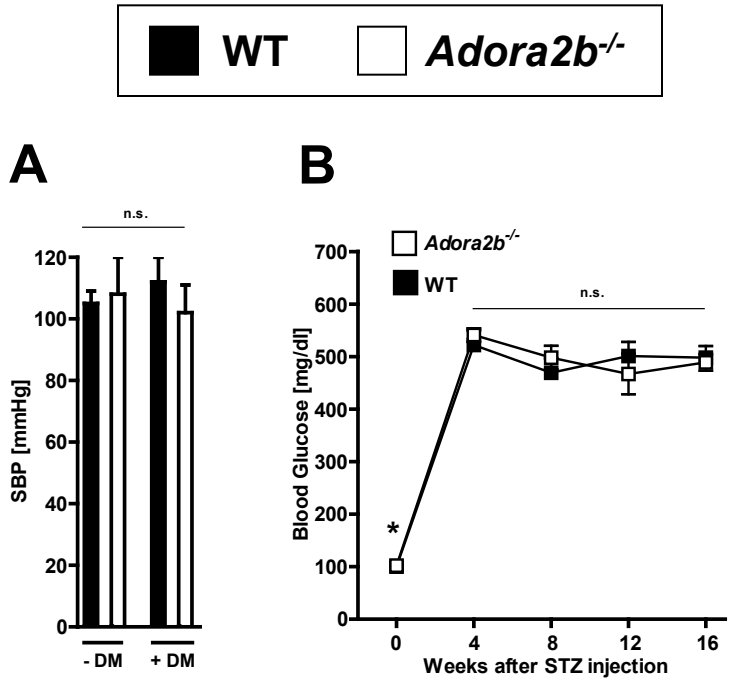
Supplementary Figure 3

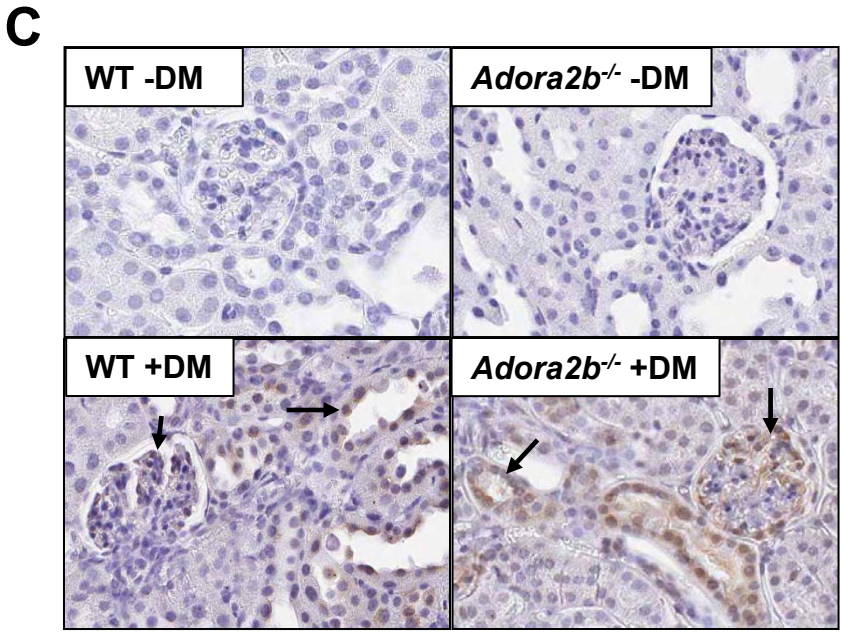


Supple. Fig. 4 Systolic blood pressure (SBP) and blood glucose in 5'ecto-nucleotidase (5-NT) treated *Cd73*$^{-/-}$ mice.

Cd73$^{-/-}$ mice and age-, weight-, and gender-matched wild type mice with and without 5'ecto-nucleotidase treatment were subjected to streptozotocin (STZ)-induced diabetes for 16 weeks until measurement of (a) systolic blood pressure and (b) blood glucose (n=6 in each group).

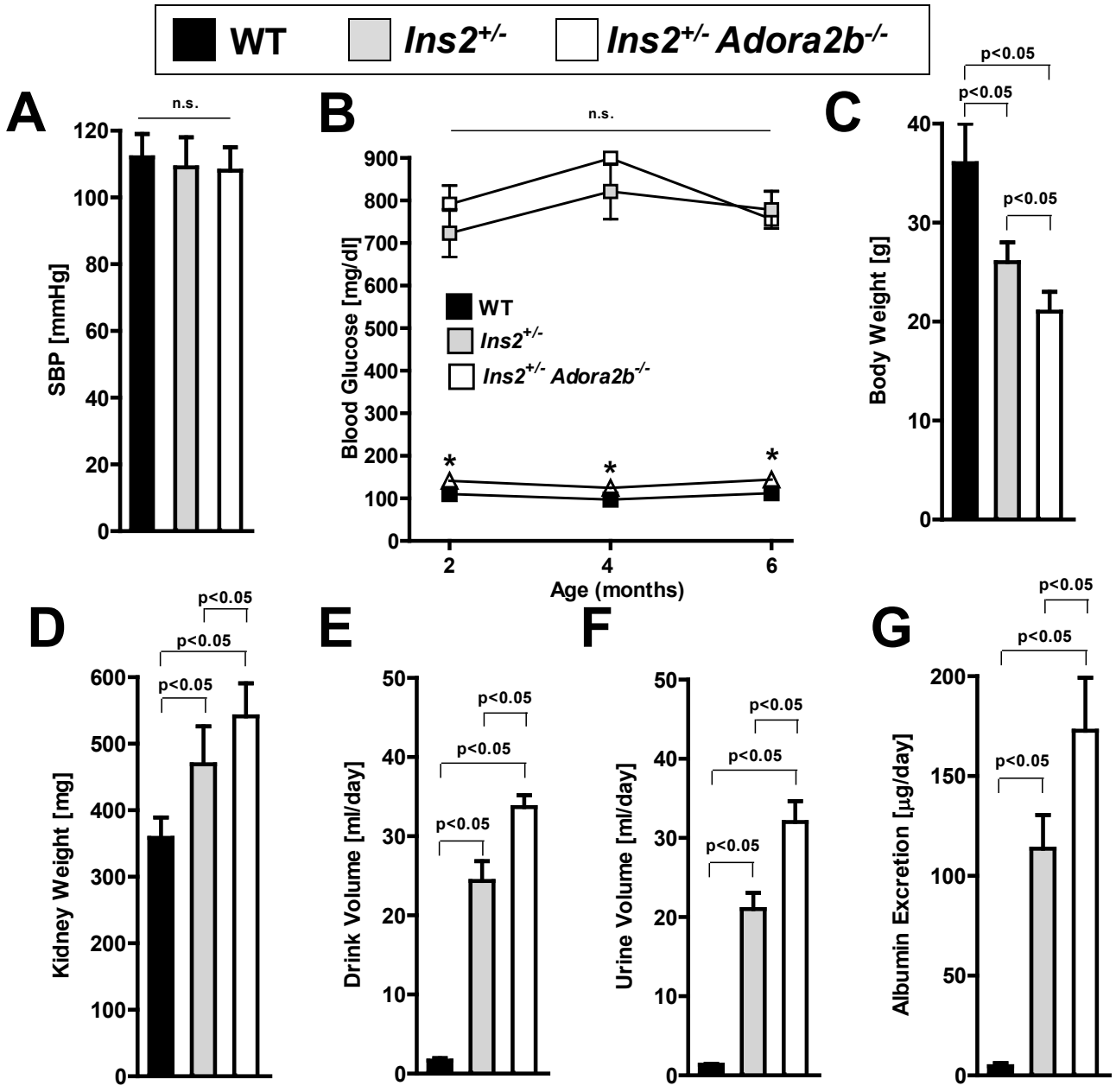
Supplementary Figure 4





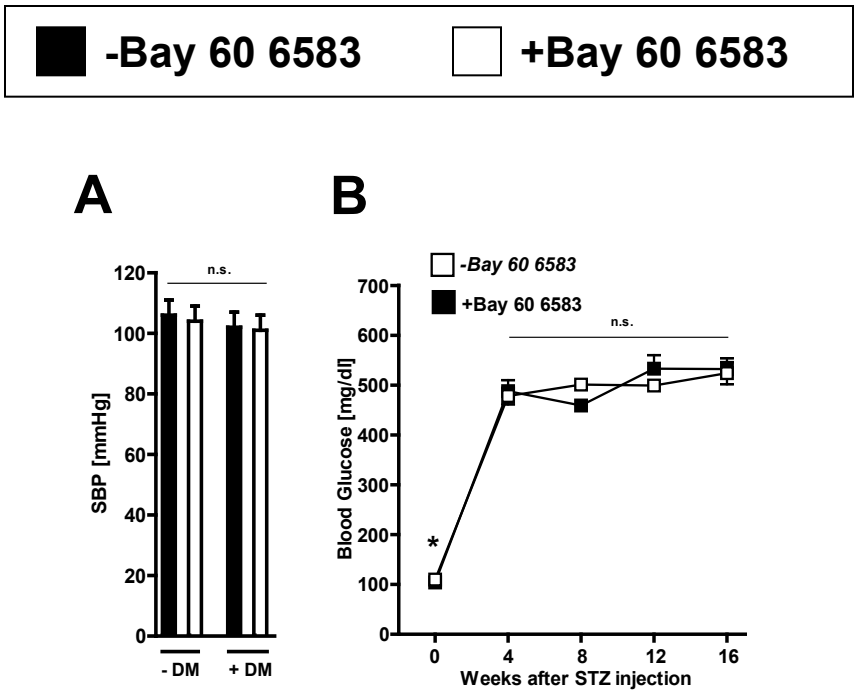
Supple. Fig. 5 Systolic blood pressure (SBP) and blood glucose in *Adora2b*$^{-/-}$ mice.
Adora2b$^{-/-}$ mice and age-, weight-, and gender-matched wild type mice were subjected to streptozotocin (STZ)-induced diabetes for 16 weeks until measurement of (a) systolic blood pressure and (b) blood glucose (n=6 in each group). (c) VEGF expression (arrows) in glomerular epithelia and tubular cells.

Supplementary Figure 5



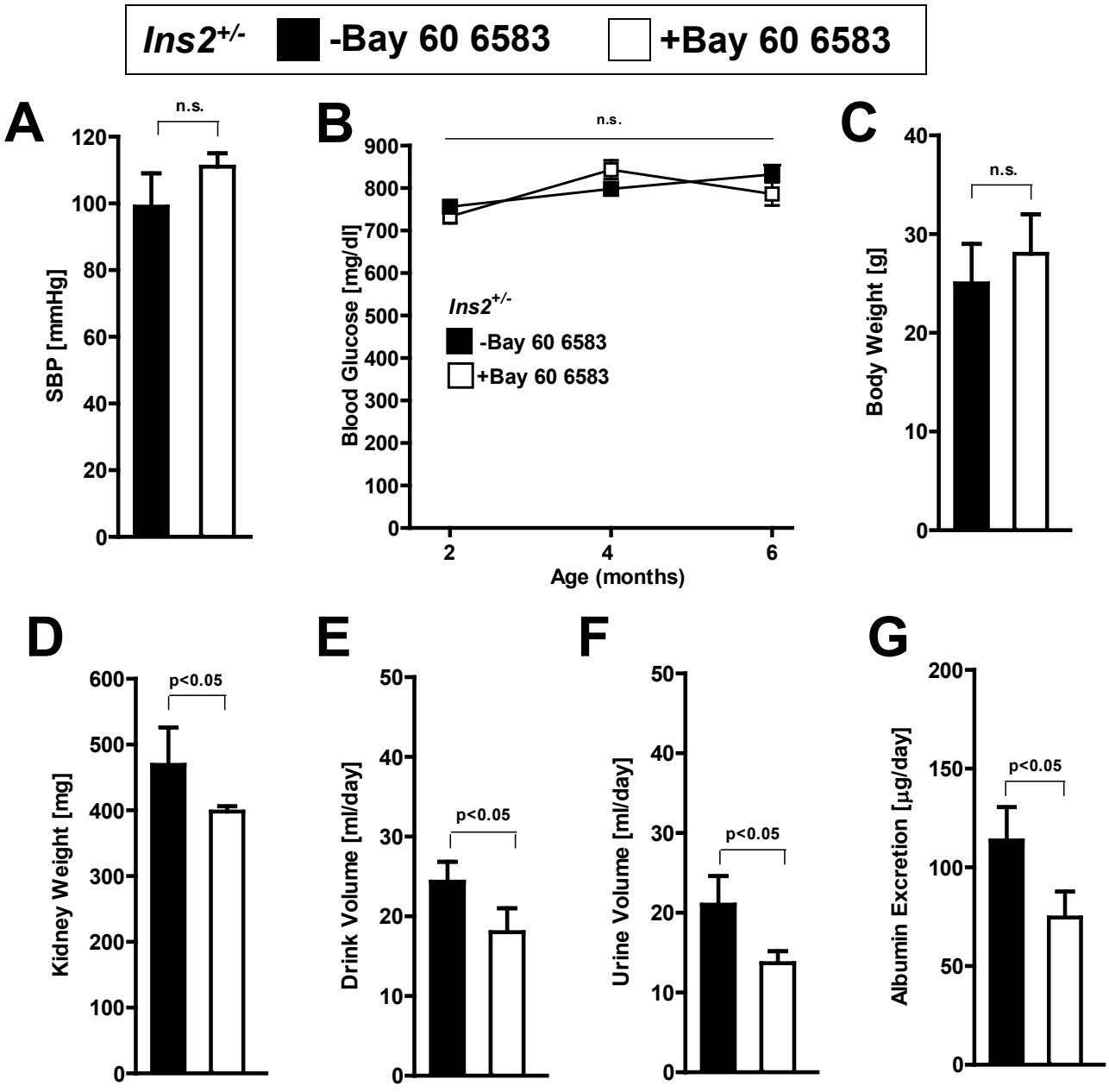
Supple. Fig. 6 Akita mice crossed with Adora2b$^{-/-}$ have a severe phenotype of diabetic nephropathy. Male Akita (*Ins2*$^{+/-}$) mice were crossed with female *Adora2b*$^{-/-}$ mice and at the age of 6 months measurements were performed and organs were removed for (**a**) systolic blood pressure, (**b**) blood glucose levels, (**c**) body weight, (**d**) kidney weight, (**e**) drink volume, (**f**) urine volume and (**g**) albumine excretion, (n=4-6 in each group).

Supplementary Figure 6



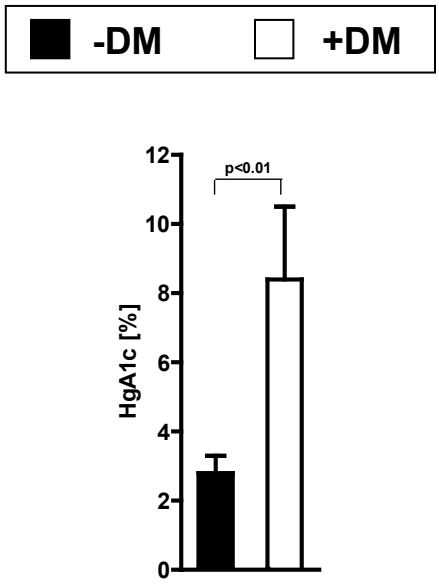
Supple. Fig. 7 Systolic blood pressure (SBP) and blood glucose in C57Bl6 mice with and without BAY 60-6583 treatment. C57Bl6 mice with or without BAY60-6583 treatment were subjected to streptozotocin (STZ)-induced diabetes for 16 weeks until measurement of (a) systolic blood pressure and (b) blood glucose (n=6 in each group).

Supplementary Figure 7



Supple. Fig 8 Improvement of diabetic nephropathy in Akita mice with Adora2b agonist treatment. Male Akita (*Ins2*$^{+/-}$) mice were treated with BAY 60-6583 or vehicle via Alzet pump (0.3µg/mouse/per h). Delivery time of the Alzet pumps was six weeks. First placement of the Alzet pump was at the age of seven weeks. Alzet pumps were replaced at week 13 and 19. After 6 months of diabetes with or without BAY 60-6583 treatment blood and organs were taken for (**a**) systolic blood pressure, (**b**) blood glucose (**c**) body weight, (**d**) kidney weight, (**e**) drink volume, (**f**) urine volume and (**g**) albumin excretion, (n=4-6 in each group).

Supplementary Figure 8



Supple. Fig. 1: Glycolysated hemoglobin levels in streptozotocin-induced diabetic C57Bl6 mice.
HgA1c levels were evelated in wild type mice 16 weeks following STZ-induced diabetes (n=7).