# GONADECTOMY PREVENTS THE INCREASE IN BLOOD PRESSURE AND SERUM ACE ACTIVITY IN ACE2 KNOCKOUT DIABETIC MALE MICE

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## INTRODUCTION & AIM

- Whereas ACE2 deletion or inhibition worsens kidney injury[1,2], its amplification ameliorates diabetic nephropathy[3].
- We previously showed that circulating ACE2 activity is increased in male diabetic mice[4].
- The effect of gonadectomy in diabetic ACE2 knockout (ace2KO) male mice has not been previously studied.

## METHODS

c57bl/6 mice

**GONADECTOMY (GDX) at 9wks**

**19wks follow-up**

**30-31wks**

**Age**

**STZ DIABETES INDUCTION at 10-11wks**

**Blood glucose (BG)**

**Body weight (BW) and Kidney weight (KW)**

**Sistolic Blood Pressure(SBP)**

**Serum and Kidney ACE enzymatic activity determination**

**Study groups:**

- Wild-type control (WT-cont); n=12
- Wild-type diabetic (WT-STZ); n=8
- ace2KO control (ace2KO-cont); n=11
- ace2KO diabetic (ace2KO-STZ);n=8
- Gonadectomised ace2KO before diabetes induction (preGDX-ace2KO-STZ); n=10

## RESULTS

| | BG (mg/dl) | KW/BW (%) | UAE (µgAlb/mgCr) |
|---|---|---|---|
| WT-cont | 211.33±6.38 | 0.97±0.03 | 18.47±2.46 |
| WT-STZ | 537.10±29.54* | 1.30±0.06* | 220.73±37.43* |
| ace2KO-cont | 196.54±8.48 | 1.12±0,04* | 14.44±2.38 |
| ace2KO-STZ | 518.75±34.39# | 1.39±0.05# | 394.28±252.86# |
| preGDX-ace2KO-STZ | 245.18±12.83#† | 0.81±0.03*$#† | 14.56±3.13$† |

**Table 1. Physiological parameters observed in the experimental groups at the end of the study.** Hyperglycemia was observed in all groups given STZ. KW/BW and UAE were increased in both diabetic wild-type and ace2KO mice. UAE was increased 12-fold in WT-STZ mice and 27-fold in ace2KO-STZ mice compared with their non diabetic controls. Gonadectomised diabetic ace2KO showed significantly lower values of blood glucose, KW/BW and UAE compared to non-gonadectomised diabetic ACE2KO

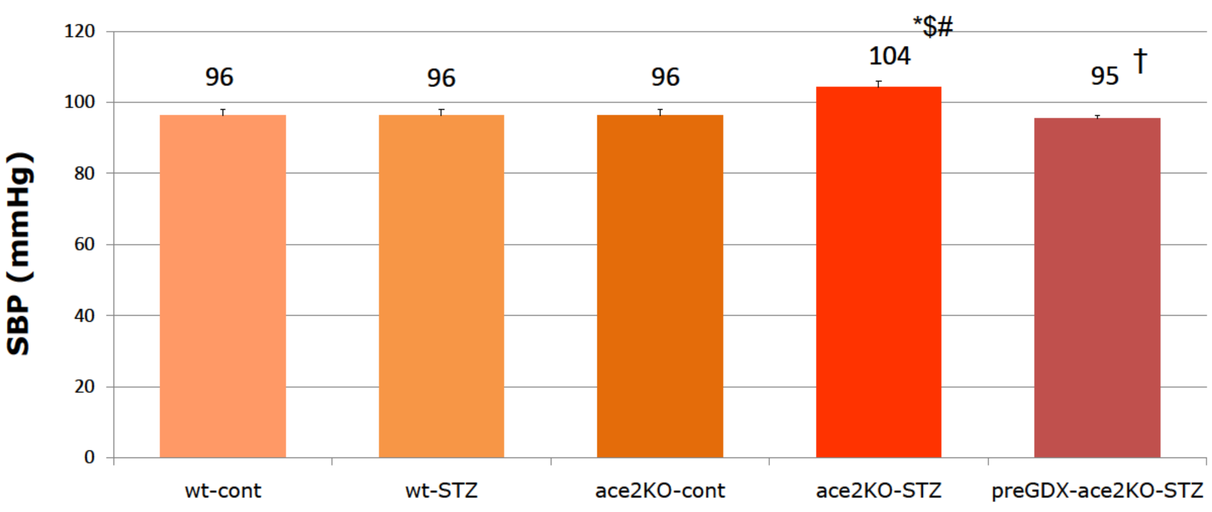
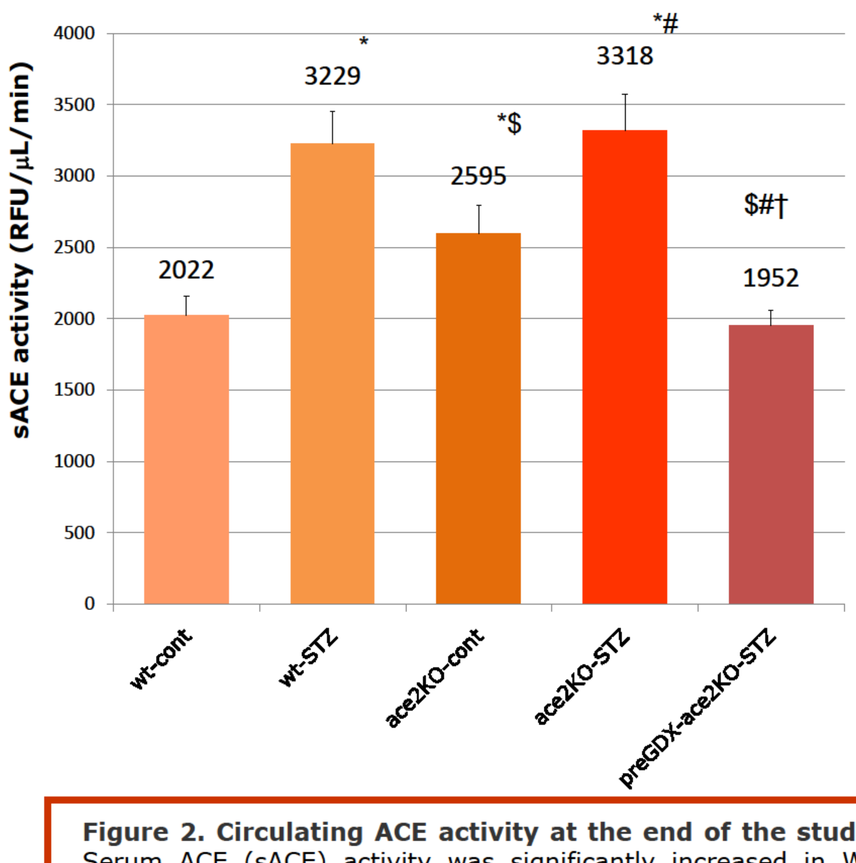
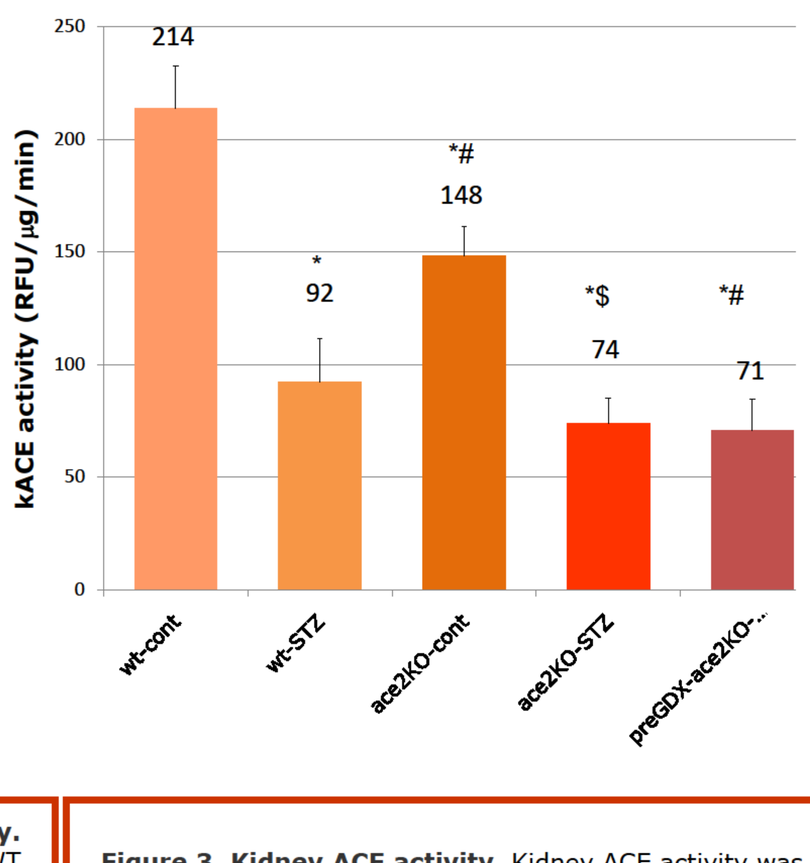



**Figure 1. Systolic Blood Pressure at the end of the study.** Ace2KO diabetic mice had increased SBP as compared to diabetic WT. In addition, gonadectomised diabetic ace2KO showed significantly lower values of SBP compared to non-gonadectomised diabetic ace2KO.

**p<0.05 vs. wt-cont; $ p<0.05 vs. wt-STZ; # p<0.05 vs. ace2ko-cont; † p<0.05 vs. ace2ko-STZ**



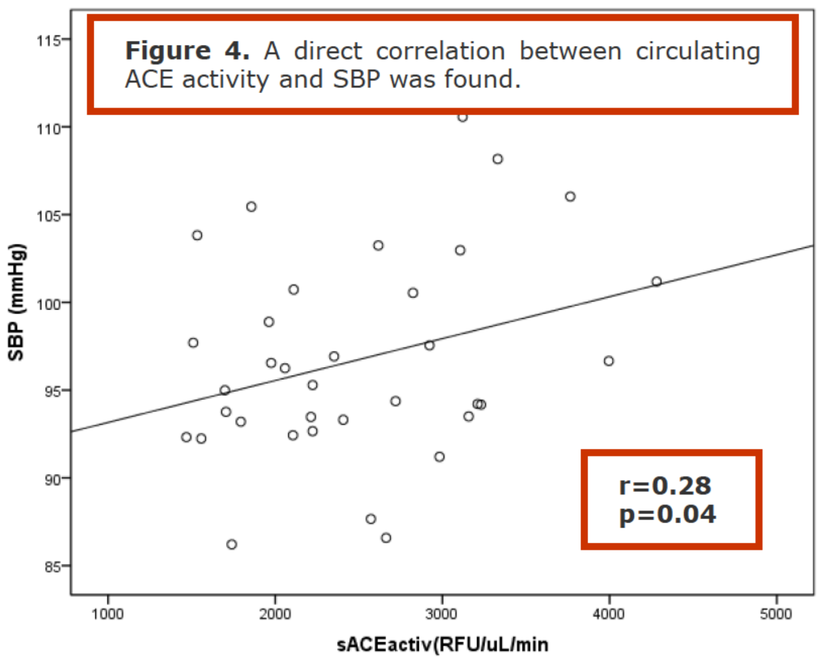




**Figure 4.** A direct correlation between circulating ACE activity and SBP was found.

**Figure 2. Circulating ACE activity at the end of the study.** Serum ACE (sACE) activity was significantly increased in WT diabetic mice as compared to WT-cont. sACE activity was increased in ace2KO control mice as compared to WT-cont mice. Gonadectomy significantly decreased circulating ACE activity in diabetic ace2KO mice.

**Figure 3. Kidney ACE activity.** Kidney ACE activity was significantly reduced in diabetic animals. Furthermore, Kidney ACE activity showed significantly lower values in ace2KO control mice compared to the WT controls

## CONCLUSIONS

- In ACE2KO mice circulating ACE activity was increased as compared to WT mice.
- In addition, in diabetic ACE2KO mice SBP was increased compared to diabetic WT mice.
- Gonadectomy reduced blood glucose, UAE, renal hypertrophy, blood pressure and circulating ACE activity.

## REFERENCES

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