EFFECT OF MALE GENDER AND DIABETES ON CIRCULATING ACE2 ACTIVITY IN STREPTOZOTOCIN (STZ)-INDUCED MICE

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INTRODUCTION & AIM

- Male gender predisposes to chronic kidney disease[1].
- We previously showed that circulating ACE2 activity is increased in male and diabetic NOD mice.
- We proposed to study gender and the effect of diabetes in the stretptozotocin (STZ) mice on circulating ACE2. In addition, we also studied the effect of gonadectomy in diabetic and control mice.

METHODS

c57bl/6 mice

GONADECTOMY (GDX) at 12-13wks

Age

19wks follow-up
(Blood glucose every 2 weeks)

30-31wks

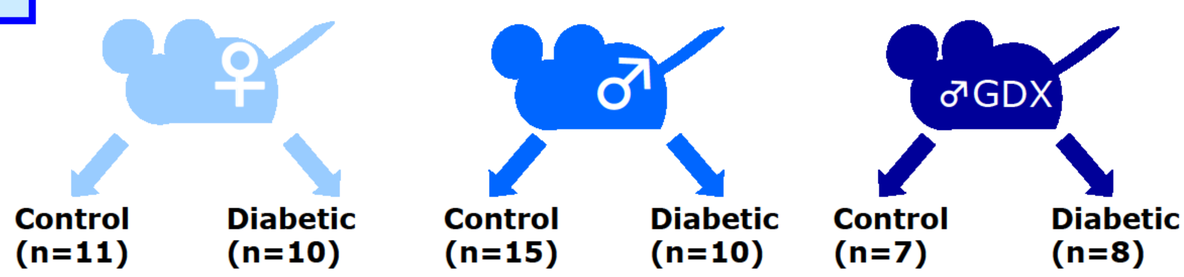
STZ DIABETES INDUCTION
at 10-11wks

Body weight (BW) and Kidney weight (KW)

Sistolic Blood Pressure(SBP)

Serum ACE2 enzymatic activity determination[2,3]

Study groups:



Control (n=11) | Diabetic (n=10) | Control (n=15) | Diabetic (n=10) | Control (n=7) | Diabetic (n=8)

RESULTS

	Age (wks)	Body weight (gr)	%KW/BW	SBP (mmHg)
CONTROL FEMALES	30.78±0.20	26.75±0.95	0.91±0.02	98.22±2.11
CONTROL MALES	30.31±0.12	36.61±1.00*	0.97±0.03*	96.37±1.63
CONTROL GDX	30.06±0.30	30.32±0.94*$	0.79±0.03*$	100.14±2.11
DIABETIC FEMALES	30.64±0.24	21.56±0.56&	1.44±0.08&	106±3.81
DIABETIC MALES	30.30±0.23	26.89±0.74*&	1.30±0.06&	96.42±1.46*
DIABETIC GDX	30.05±0.22	24.96±0.58*$&	0.89±0.02*$&	97.79±1.68

Table 1. Physiological parameters observed in the experimental groups at the end of the study. All diabetic groups showed significantly lower body weight and higher % of kidney weight respect to body weight (%KW/BW) as compared to their controls. Gonadectomy significantly decreased body weight and %KW/BW in both control and diabetic male mice.

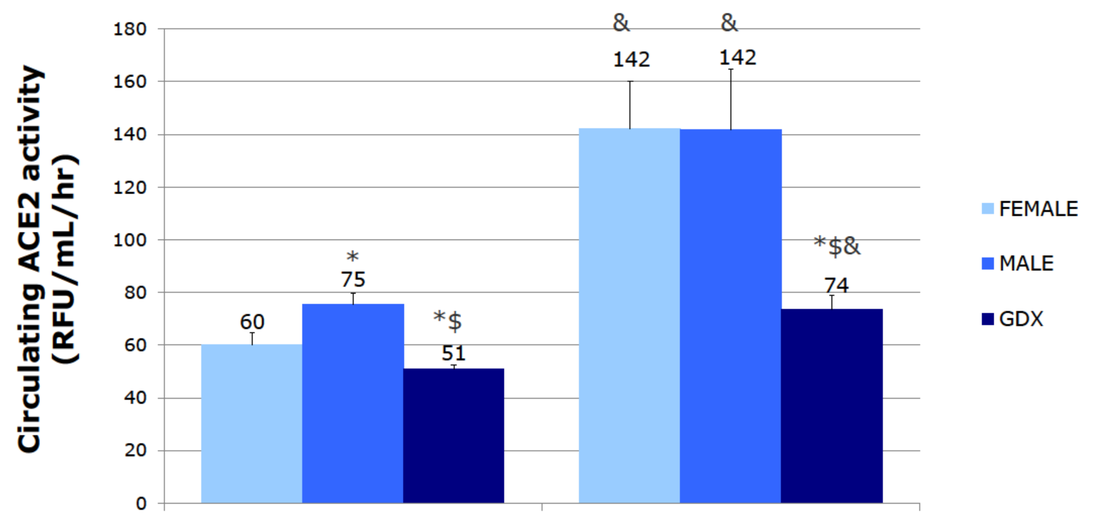
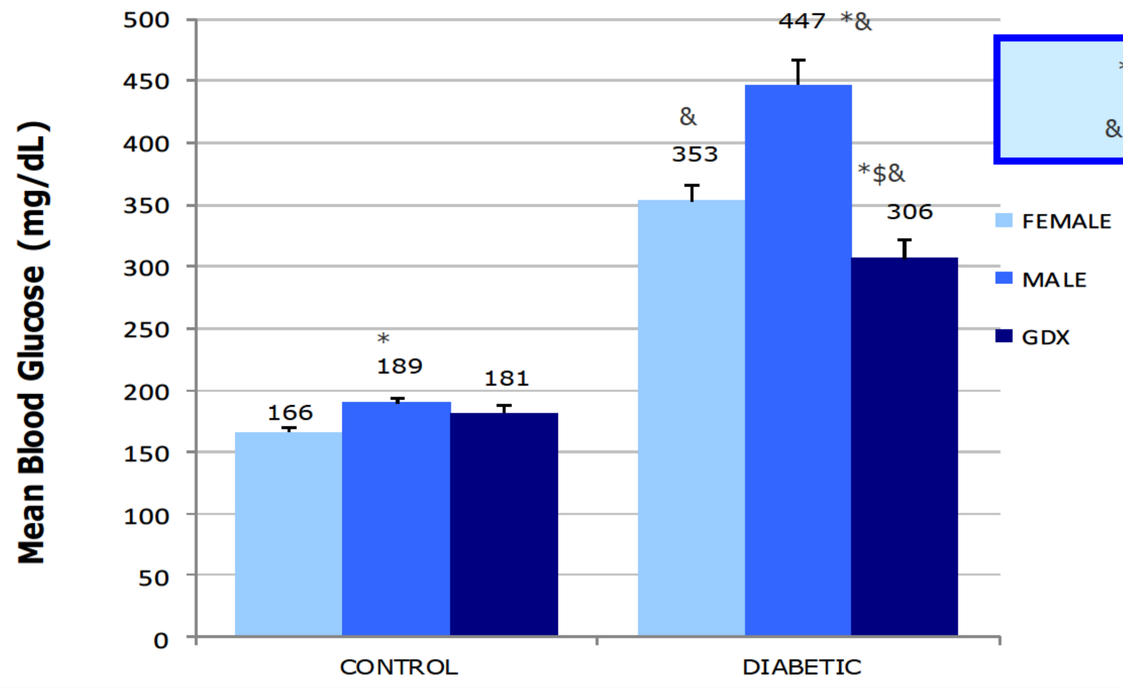


Figure 2. Circulating ACE2 enzimatic activity at the end of the study. Circulating ACE2 activity was increased in both male and female diabetic mice compared to their controls. Control male mice showed significantly higher circulating ACE2 activity than females, and castration decreased circulating ACE2 activity in both control and diabetic male mice.



* p<0,05 vs. FEMALE
$ p<0,05 vs. MALE
& p<0,05 vs. CONTROL

Figure 1. Mean Blood Glucose during the follow-up. Hyperglycemia was observed in all STZ groups. Mean Blood Glucose (BG) was significantly higher in males as compared to females for both control and diabetic groups. Furthermore, gonadectomy significantly decreased hyperglycemia in the diabetic mice.

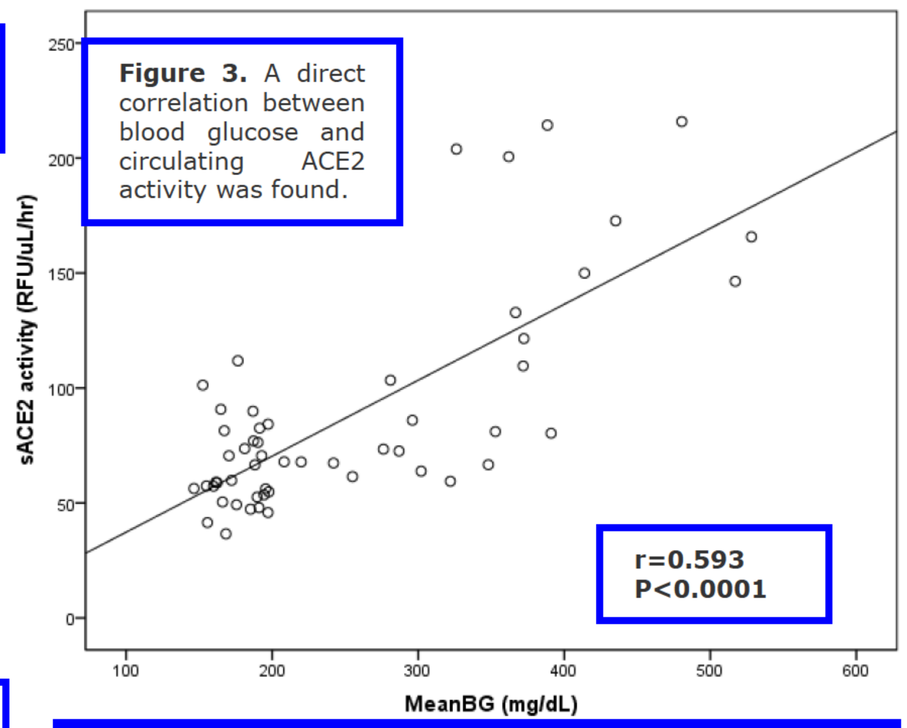


Figure 3. A direct correlation between blood glucose and circulating ACE2 activity was found.

CONCLUSIONS

- Diabetes increase glycemia and circulating ACE2 activity.
- Gonadectomy reduces levels of glycemia in males.
- Gonadectomy also diminishes the increase in circulating ACE2 activity observed in control male mice.
- Thus, the increase in circulating ACE2 activity observed in diabetic male mice may be due, at least in part, to a modulation of circulating male sex hormones.

REFERENCES

[1]Neugarten J, Acharya A, Silbiger SR. Effect of gender on the progression of nondiabetic renal disease: a meta-analysis. J Am Soc Nephrol 2000; 11: 319–329.

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Diabetes - experimental models

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