Effects of liraglutide in the SDT fatty rat – a type 2 diabetic cardio-renal model

Physiogenex
THE METABOLIC DISEASES EXPERTS

Study design

SDT fatty rat, male 5-week old, n=40

10-week acclimation

15-w of age

20-w of age/5-week treatment: unilateral nephrectomy

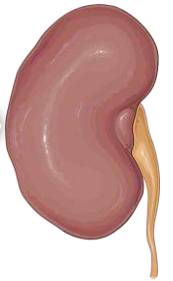
0.3% salt supplemented drinking water for 5 weeks

hyperfiltration phase

GFR decline phase

25-w of age

histology analysis



Control or liraglutide s.c. QD 0.4mg/kg/day

randomization:
-Glomerular Filtration Rate (Medibeacon)
-blood glucose
-body weight

4-week treatment:
-Glomerular Filtration Rate (Medibeacon)
-blood glucose & urine parameters

6-week treatment:
-blood glucose

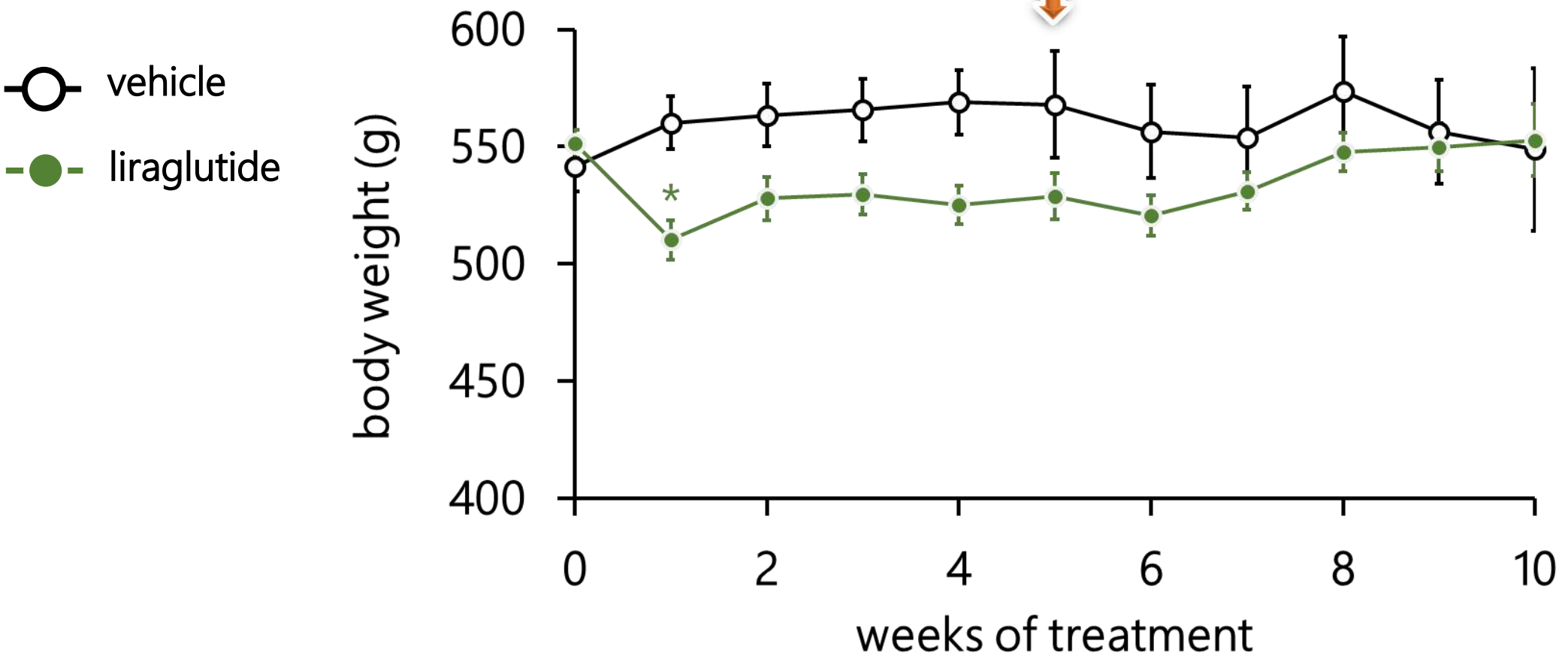
10-week treatment:
-Glomerular Filtration Rate (Medibeacon)
-blood glucose & urine parameters

-echocardiography (systolic/diastolic function)
-systolic/diastolic blood pressure/heart rate

Physiogenex
THE METABOLIC DISEASES EXPERTS

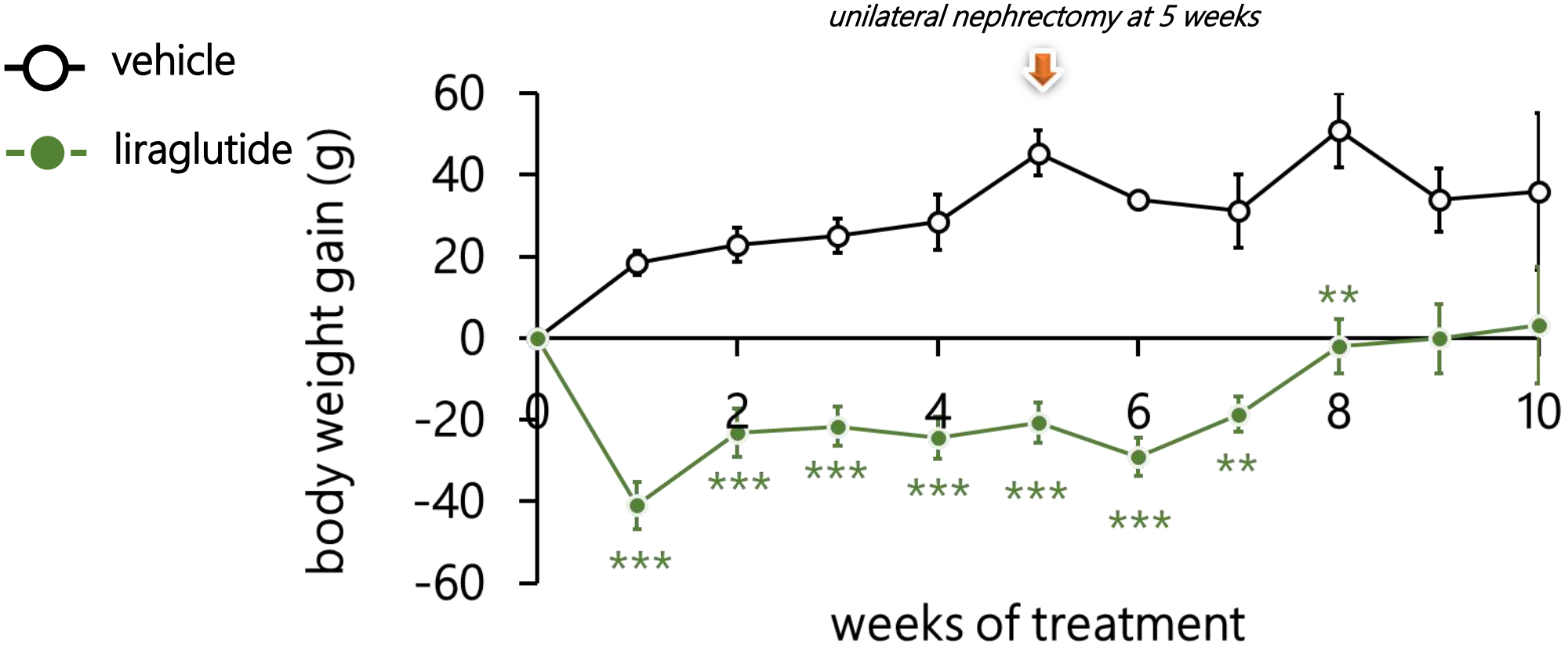
Diabetic nephropathy

Body weight follow-up



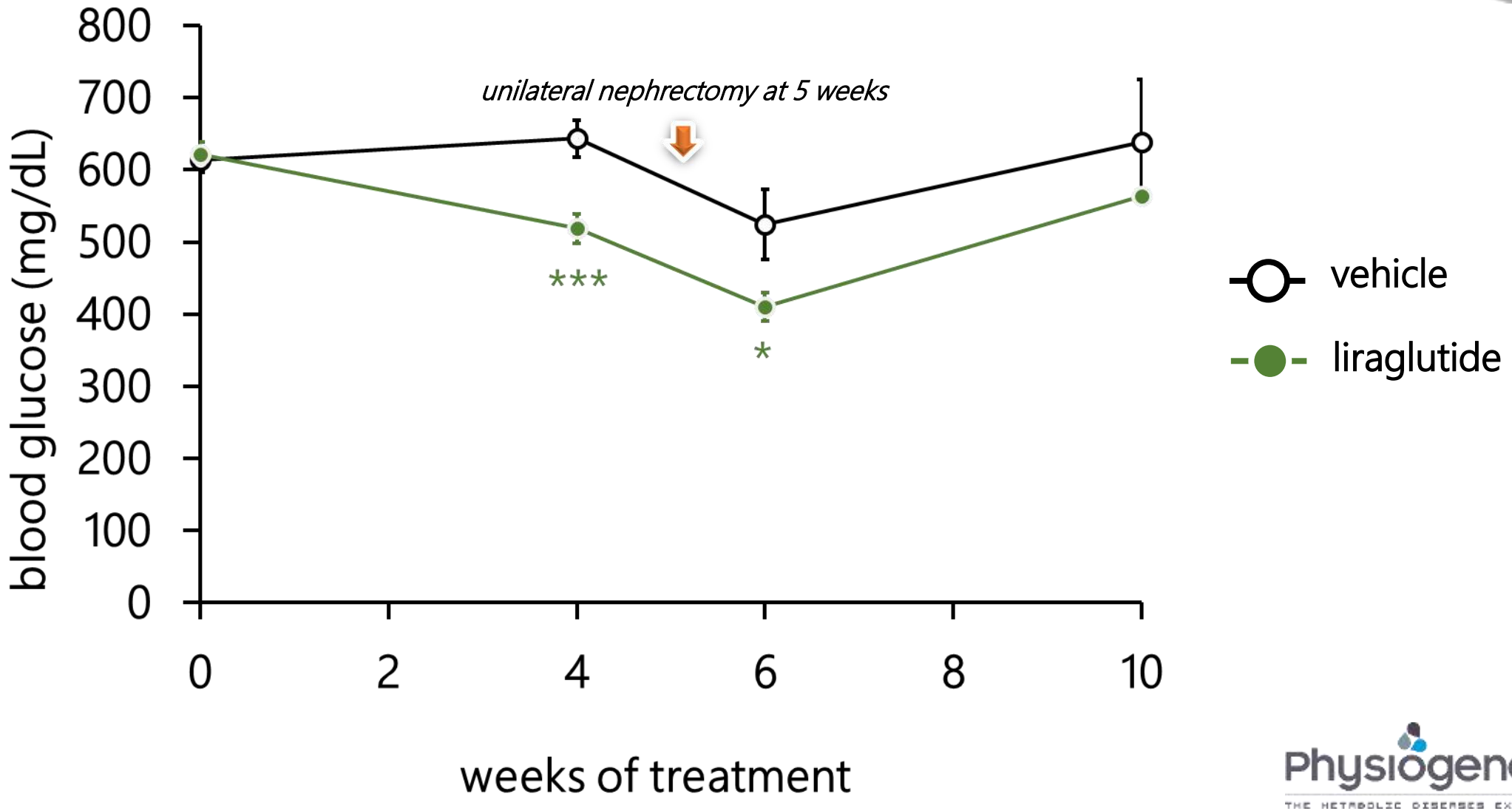
Physiogenex
THE METABOLIC DISEASES EXPERTS

Body weight gain/loss follow-up



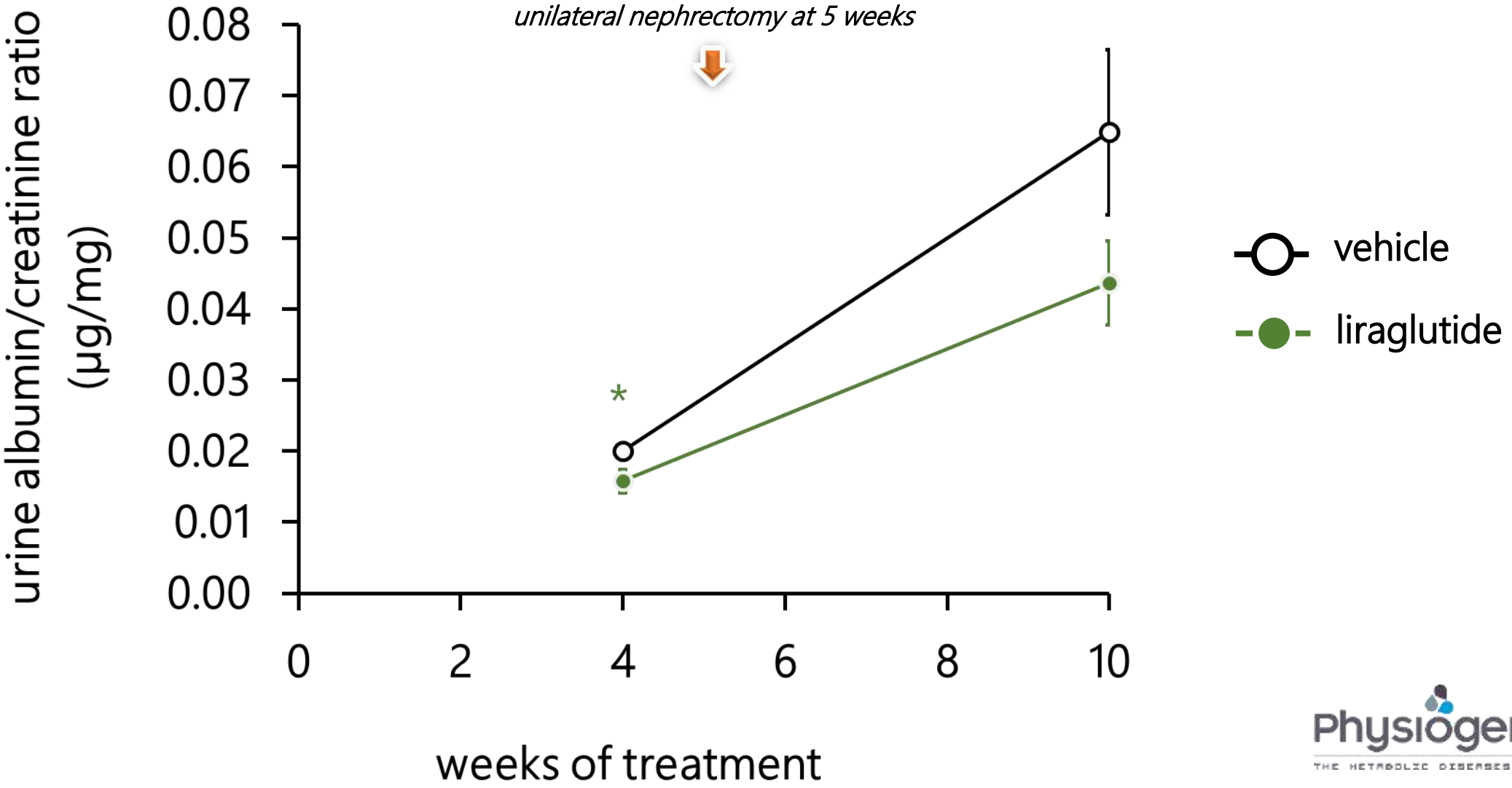
Physiogenex
THE METABOLIC DISEASES EXPERTS

Fed blood glucose follow-up



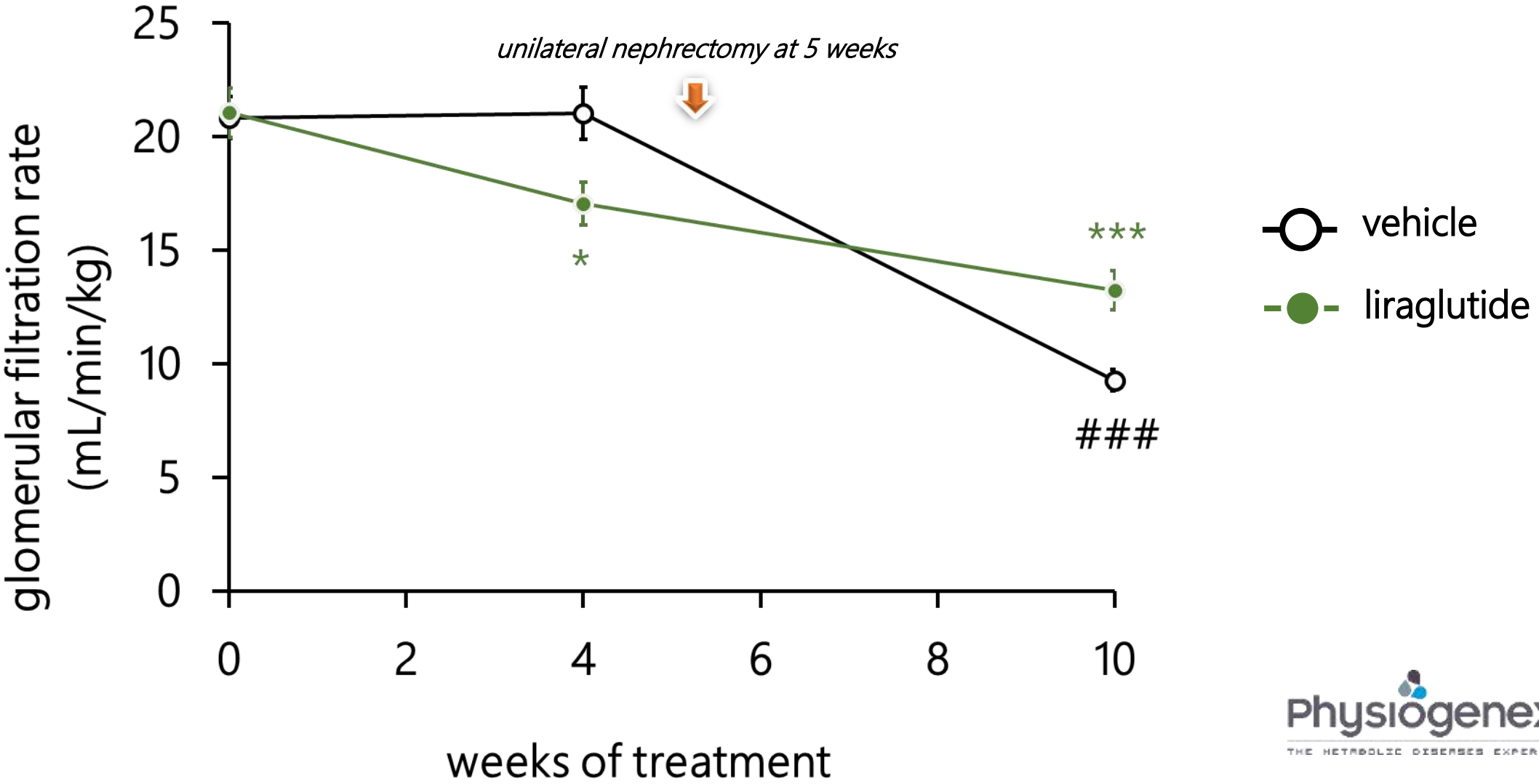
Physiogenex
THE METABOLIC DISEASES EXPERTS

Urine albumin/creatinine ratio follow-up



Physiogenex
THE METABOLIC DISEASES EXPERTS

Glomerular filtration rate follow-up (FITC-sinistrin & Medibeacon transdermal monitor)



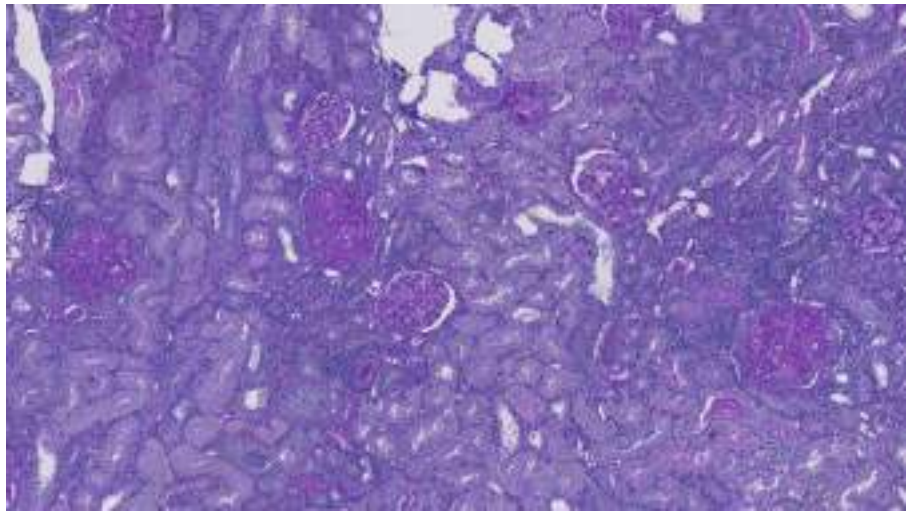
Physiogenex
THE METABOLIC DISEASES EXPERTS

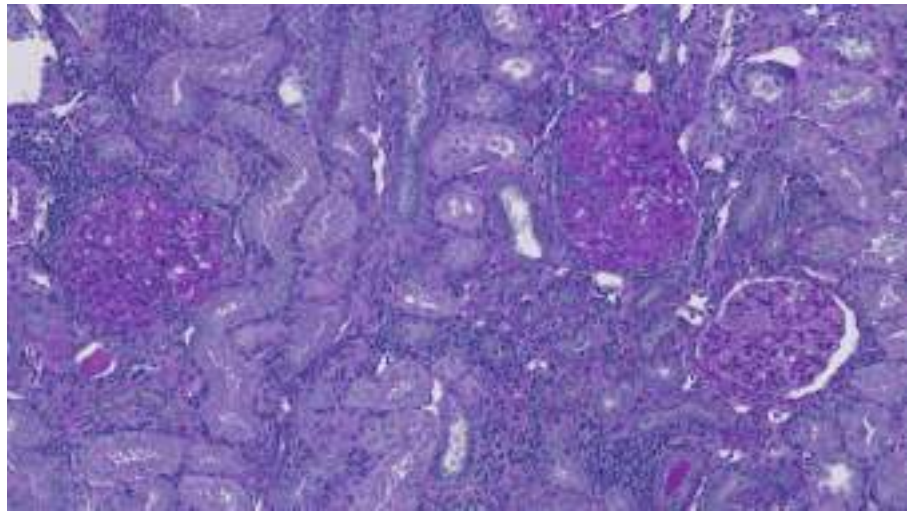
Kidney histopathology (PAS staining - glomerulosclerosis)

x10

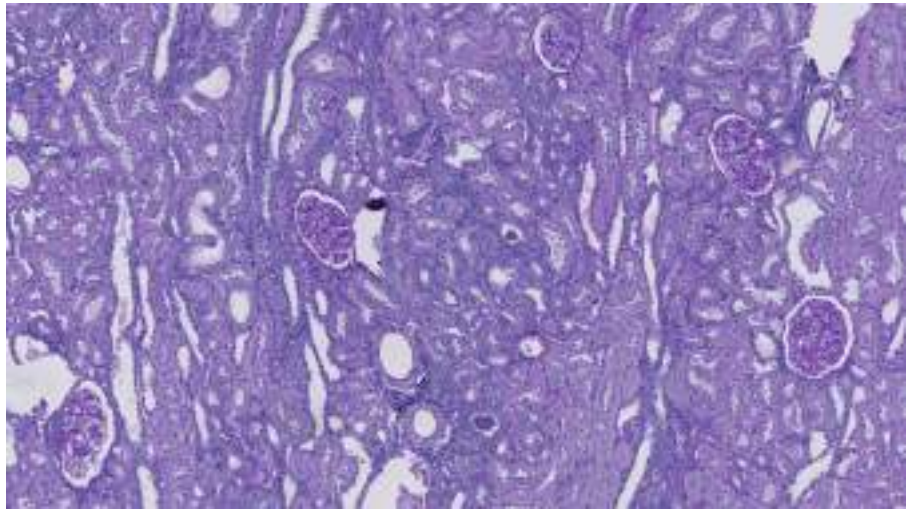
x20

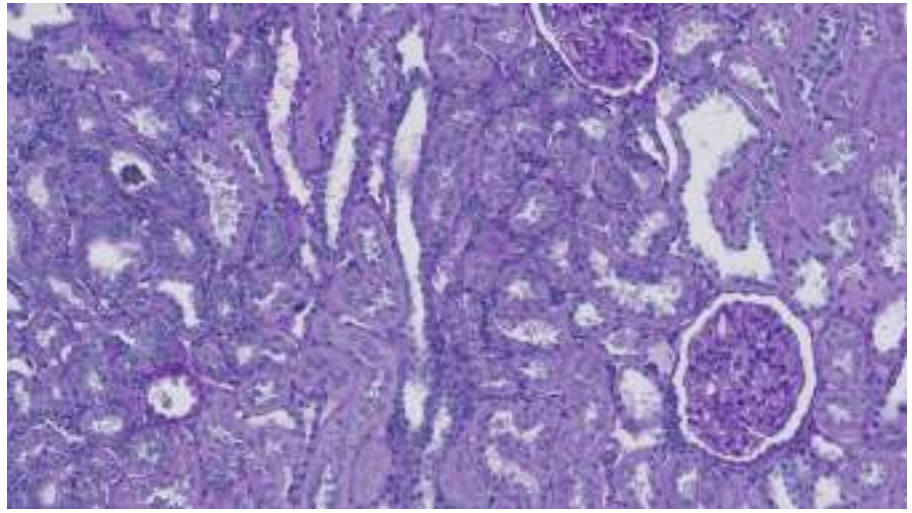
vehicle





LIRA





Physiogenex

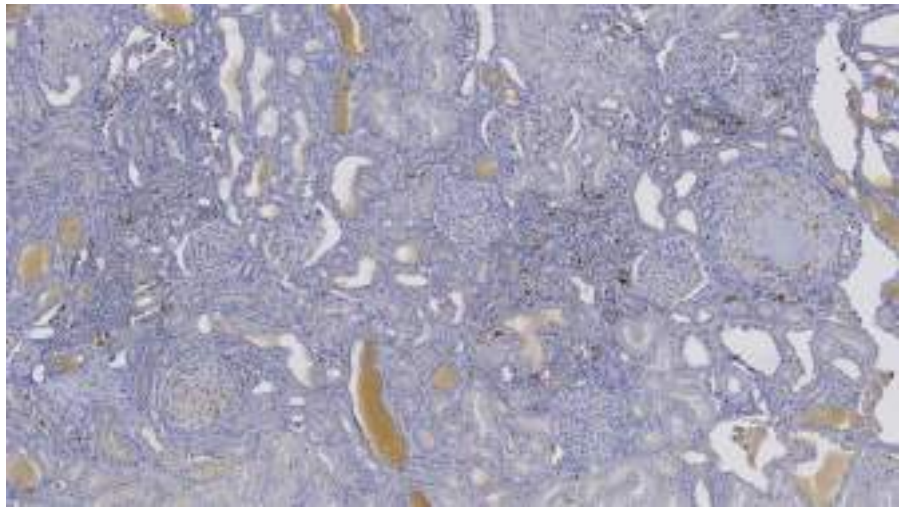
THE METABOLIC DISEASES EXPERTS

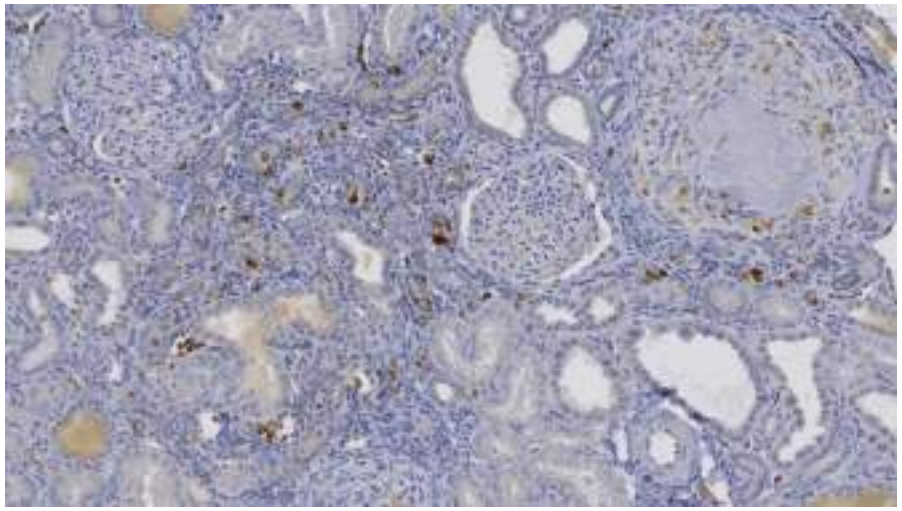
Kidney histopathology (ED1 staining - inflammation)

x10

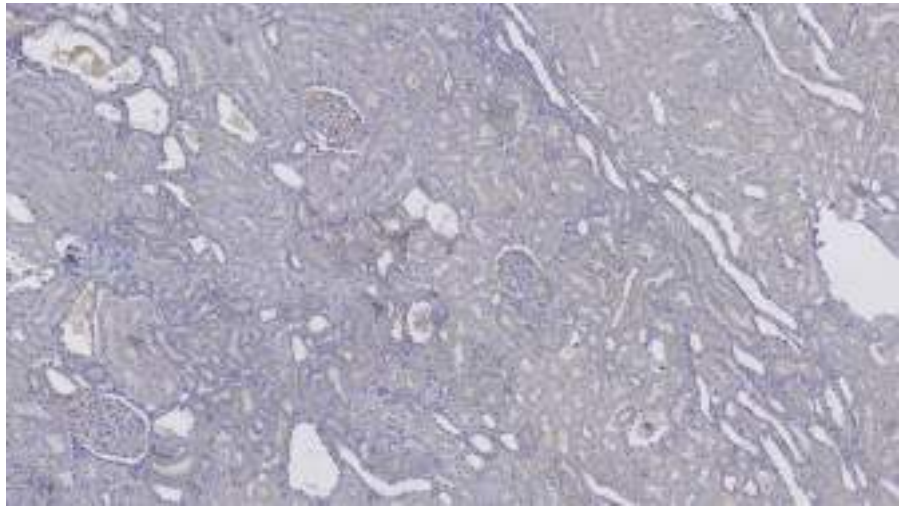
x20

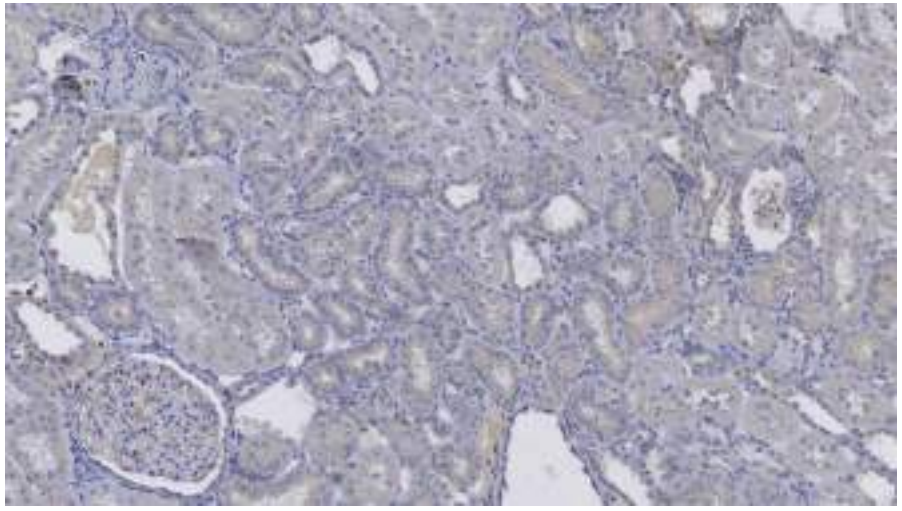
vehicle





LIRA





Physiogenex

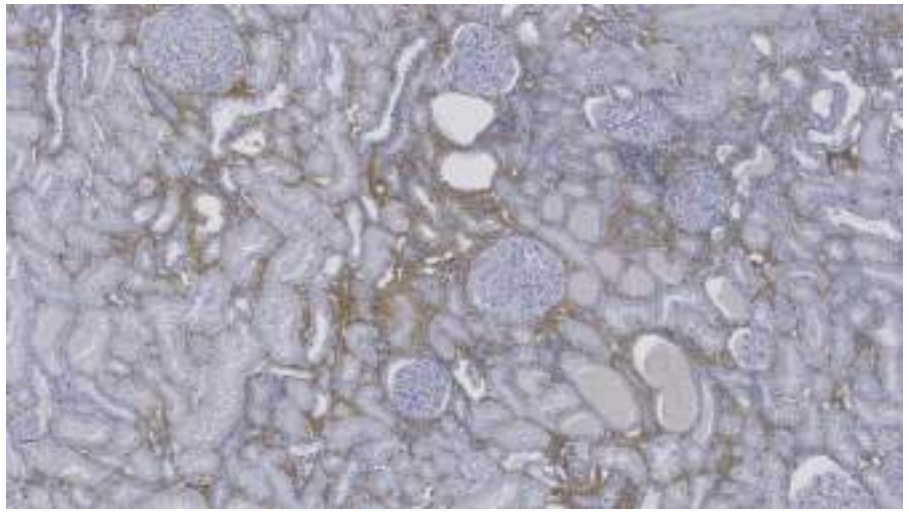
THE METABOLIC DISEASES EXPERTS

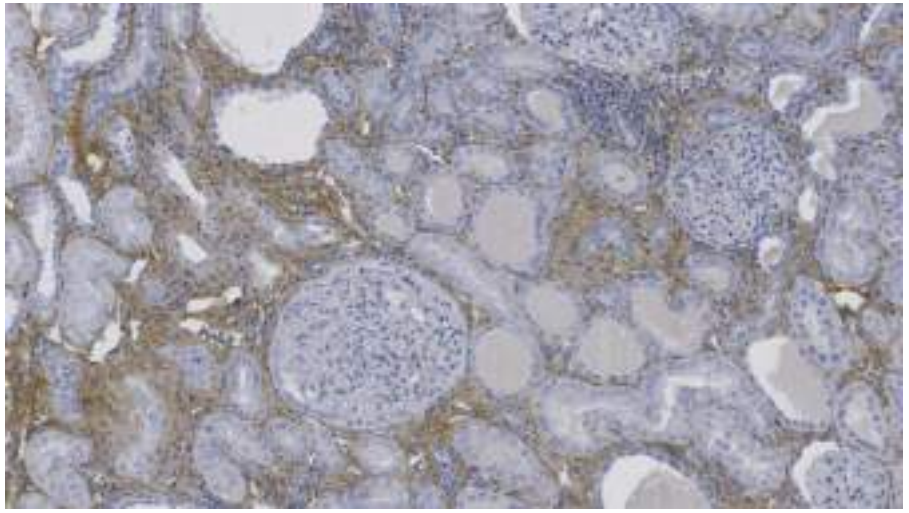
Kidney histopathology (collagen III staining - fibrosis)

x10

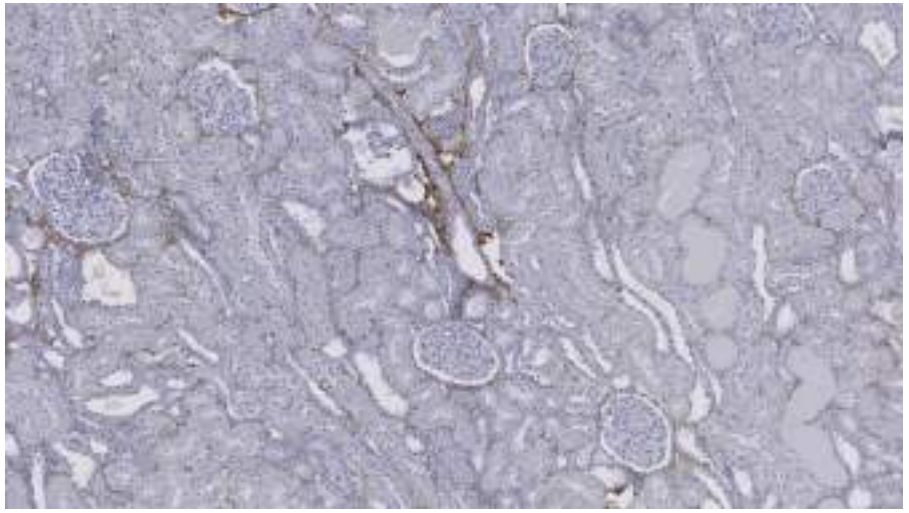
x20

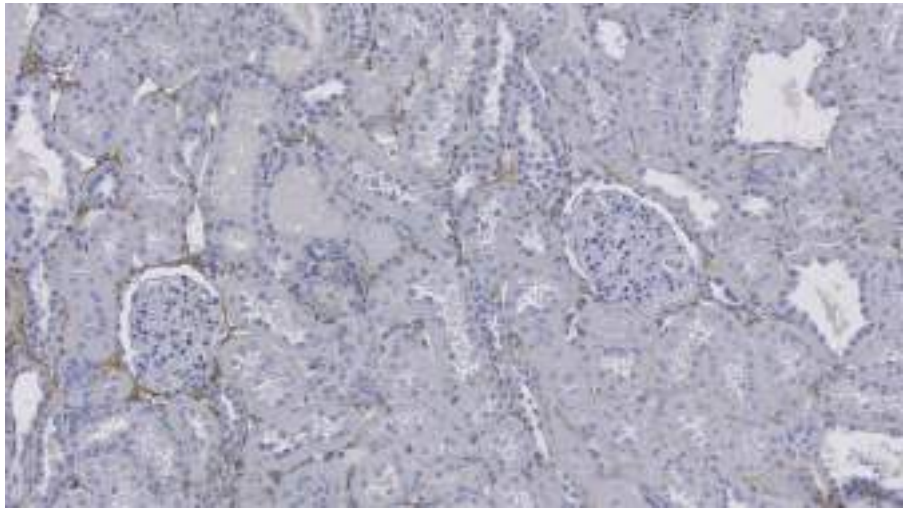
vehicle





LIRA

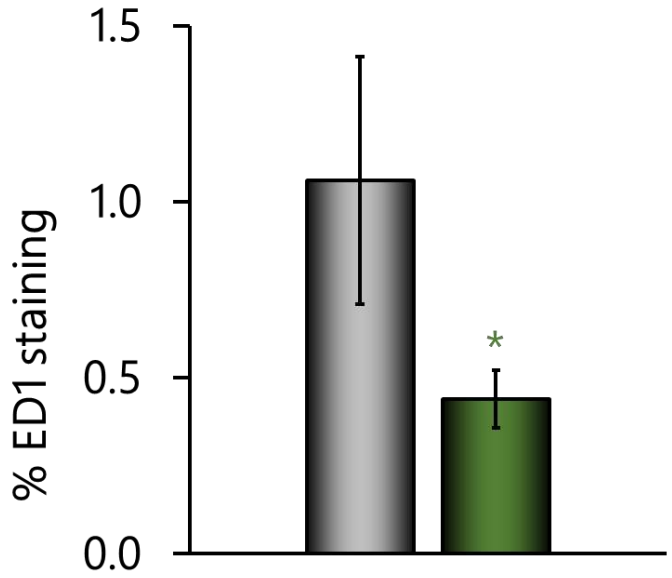


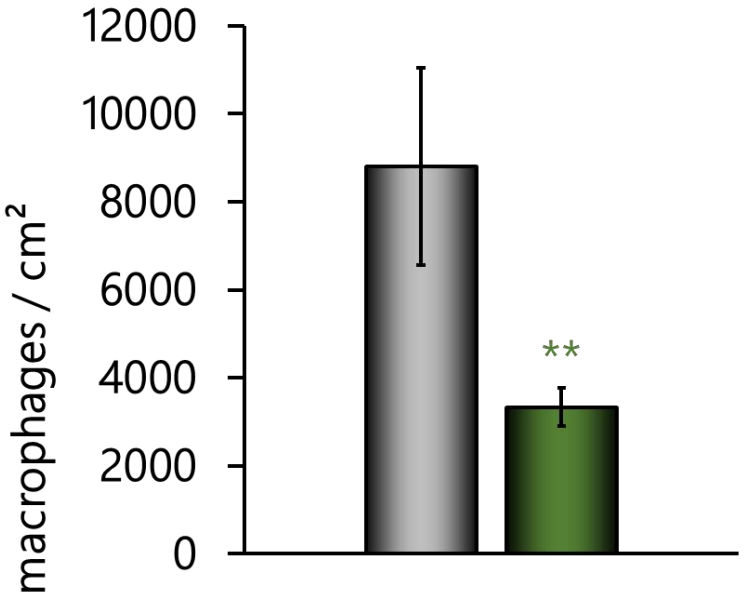


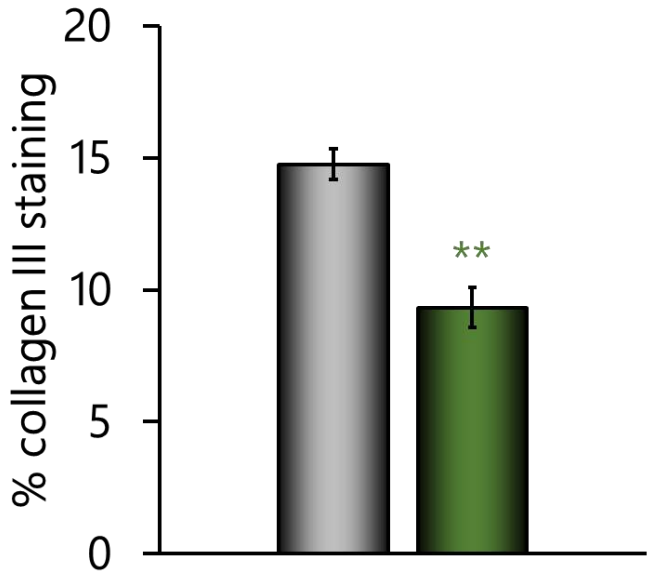
Physiogenex

THE METABOLIC DISEASES EXPERTS

Kidney histopathology







Physiogenex
THE METABOLIC DISEASES EXPERTS

Conclusion (1)

In SDT fatty rats and in the present experimental conditions:

- Liraglutide induces transient body weight loss.
- Liraglutide reduces hyperglycemia.
- Liraglutide reduces hyperfiltration, while it prevents the GFR decline after unilateral nephrectomy.
- Liraglutide reduces kidney inflammation and fibrosis.

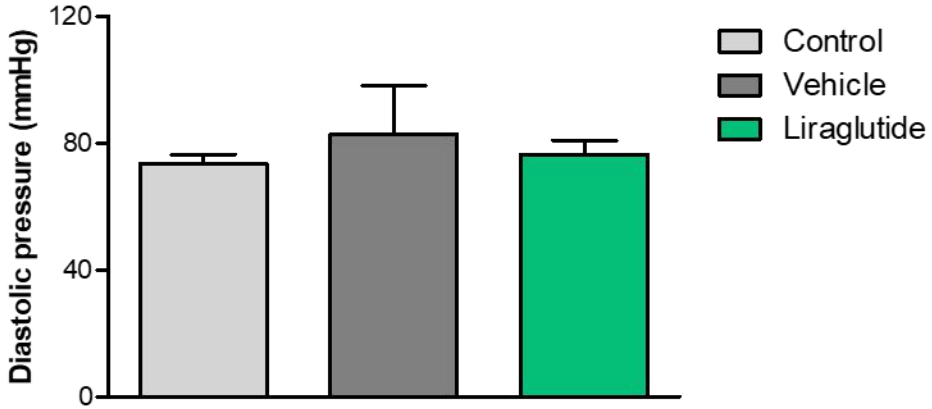
Given the benefits of liraglutide, further cardiovascular characterization was then performed.

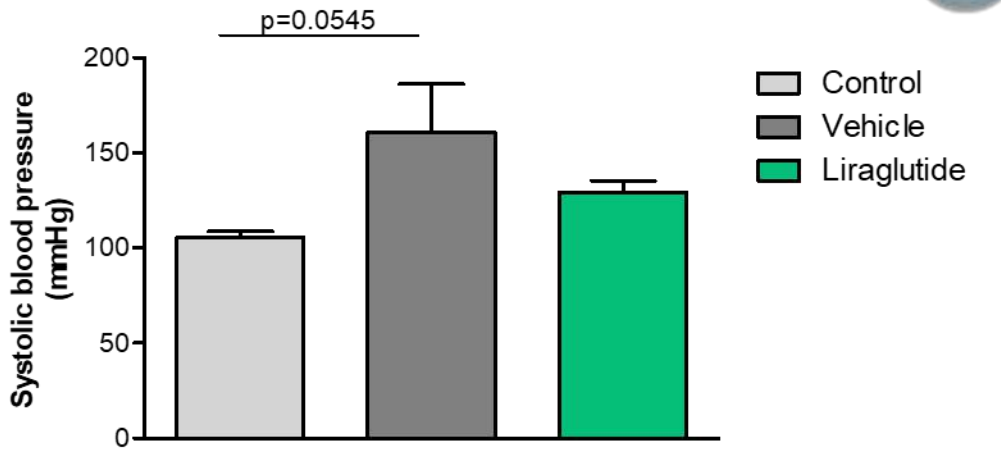
Physiogenex
THE METABOLIC DISEASES EXPERTS

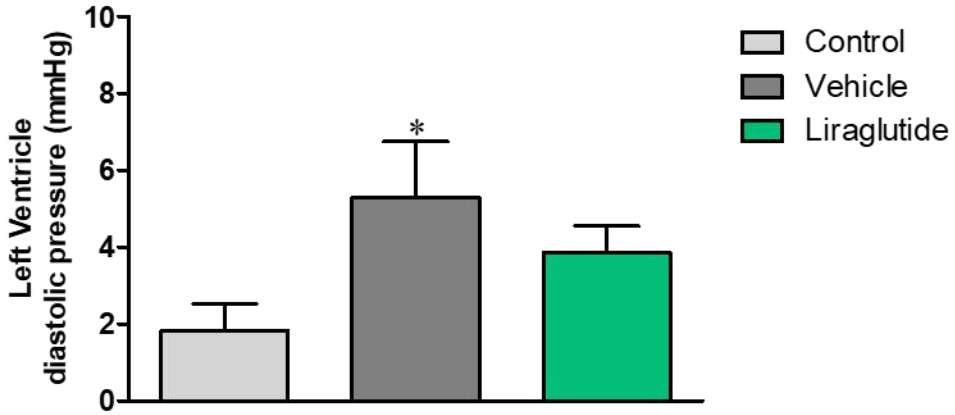
blood/intraventricular pressure and echocardiography measurements at 10 weeks of treatment

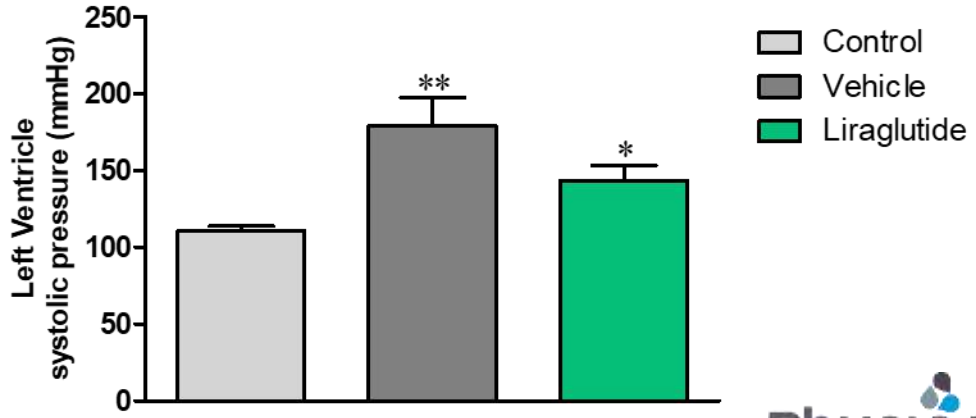
Physiogenex
THE METABOLIC DISEASES EXPERTS

Blood pressure and intraventricular pressure





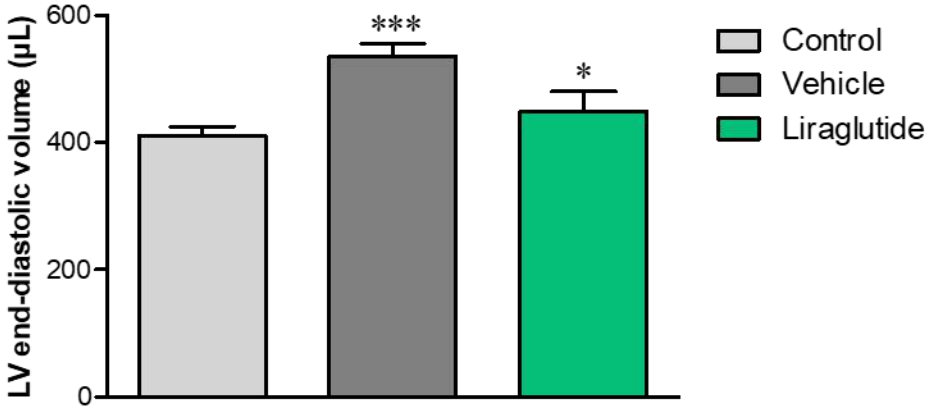


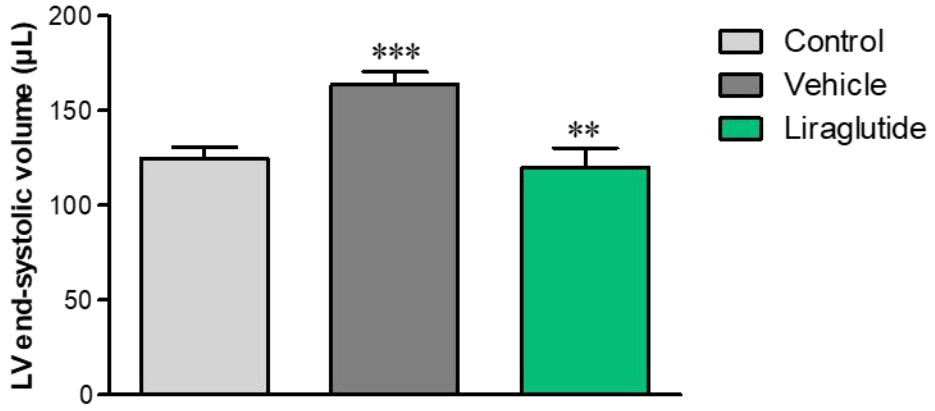


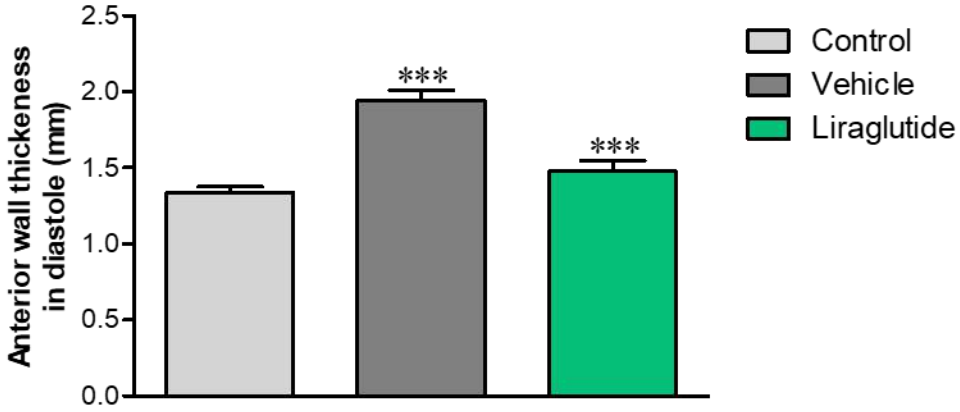
control = chow fed sprague dawley rats (baseline/control values)

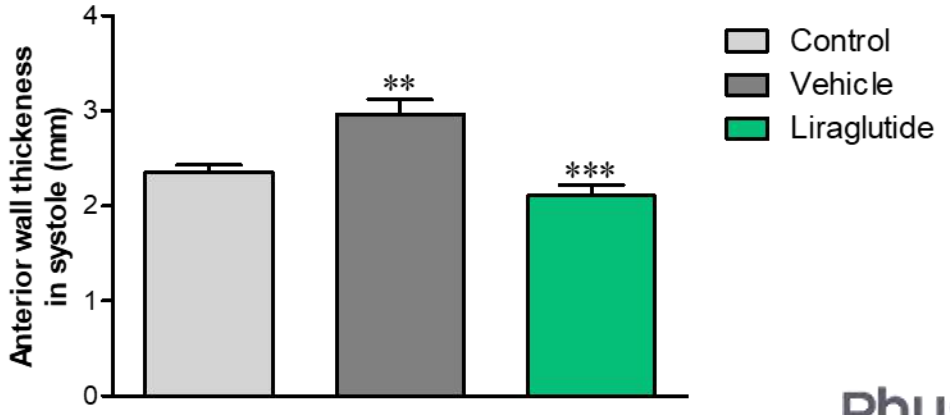
Physiogenex
THE METABOLIC DISEASES EXPERTS

Left ventricular volume and wall thickeness



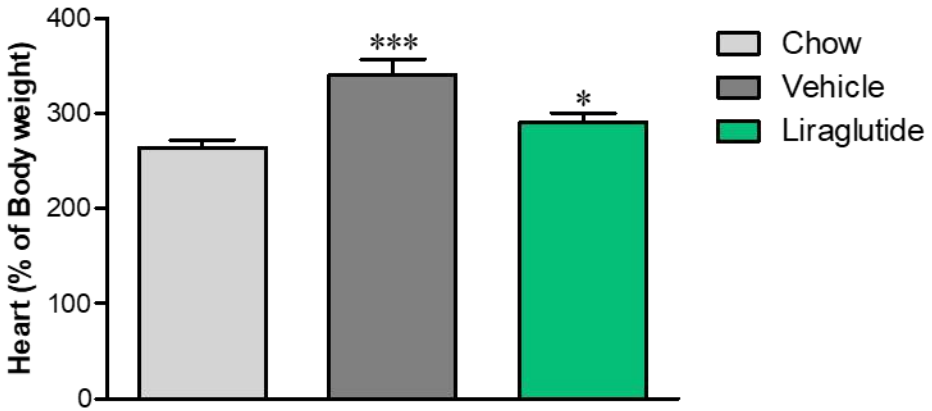


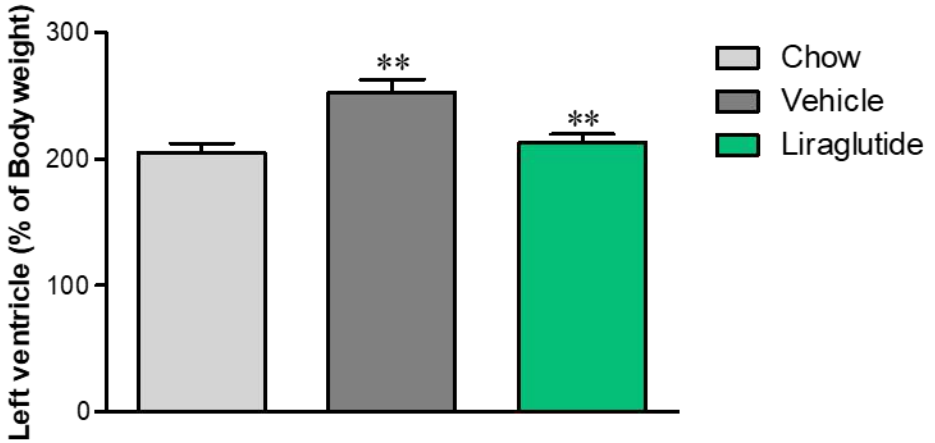




Physiogenex
THE METABOLIC DISEASES EXPERTS

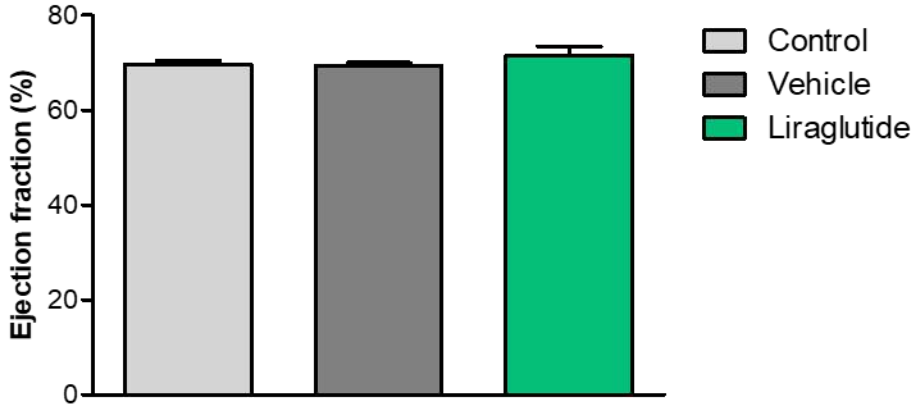
Heart and left ventricle weight

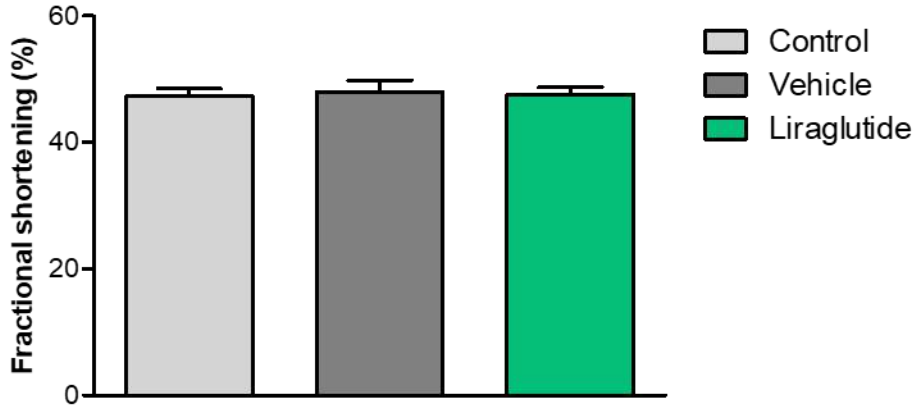


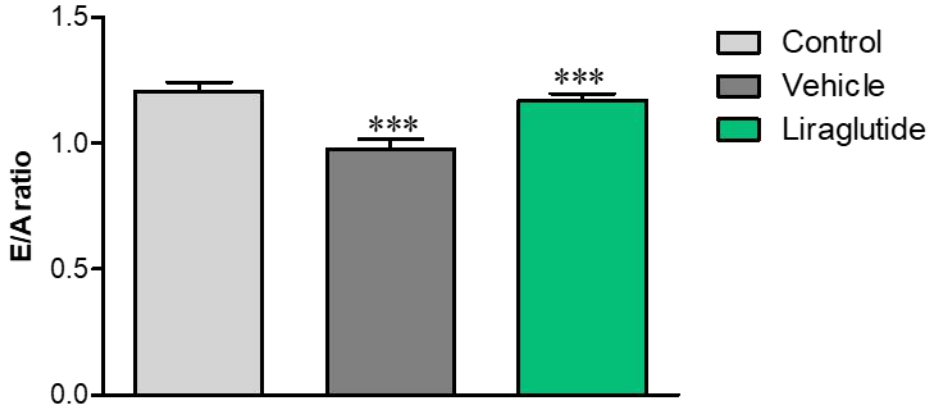


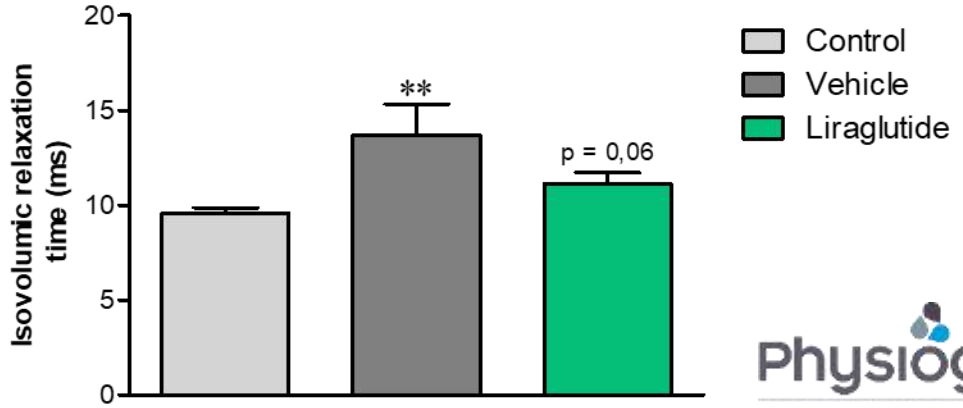
Physiogenex
THE METABOLIC DISEASES EXPERTS

Diastolic and systolic function









Physiogenex
THE METABOLIC DISEASES EXPERTS

Conclusion (2)

In SDT fatty rats and in the present experimental conditions:

- Liraglutide reduced both arterial and left ventricle end-systolic pressures and tended to reduce end-diastolic pressure.
- Liraglutide significantly reduced both left ventricle enlargement and wall thickeness.
- SDT fatty rats showed diastolic dysfunction with preserved systolic function (preserved ejection fraction and fractional shortening). Liraglutide normalized diastolic function.

Physiogenex
THE METABOLIC DISEASES EXPERTS