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

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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

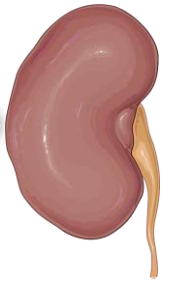
0.3% salt supplemented drinking water for 5 weeks

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

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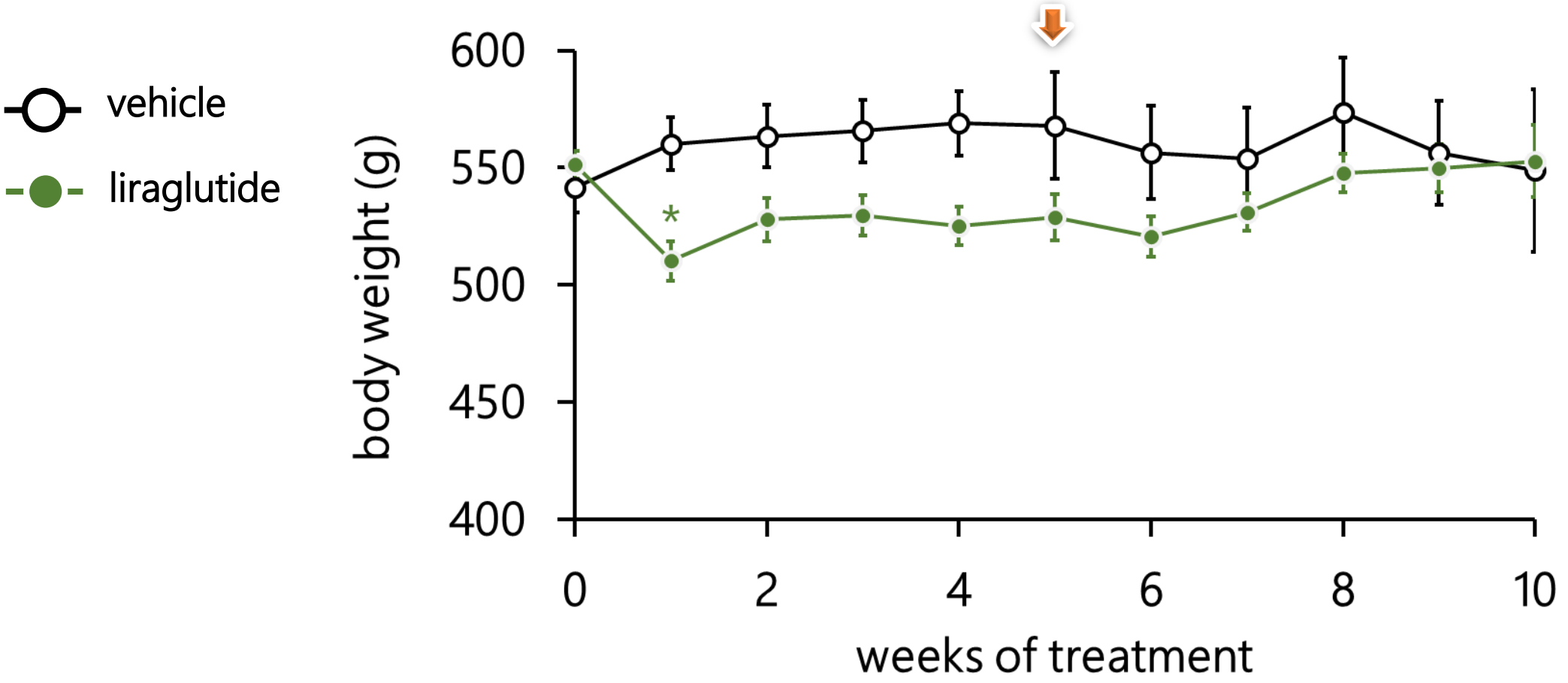
Diabetic nephropathy

Body weight follow-up



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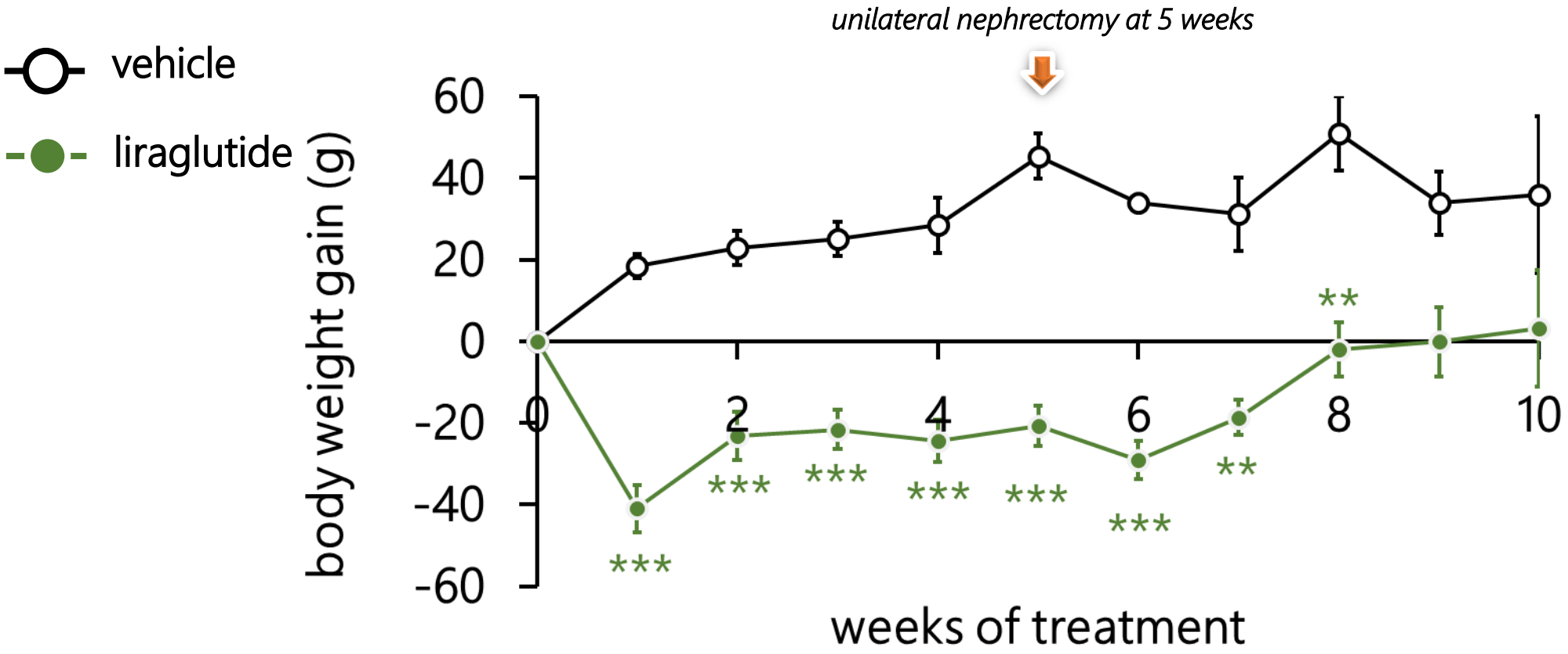
Body weight gain/loss follow-up



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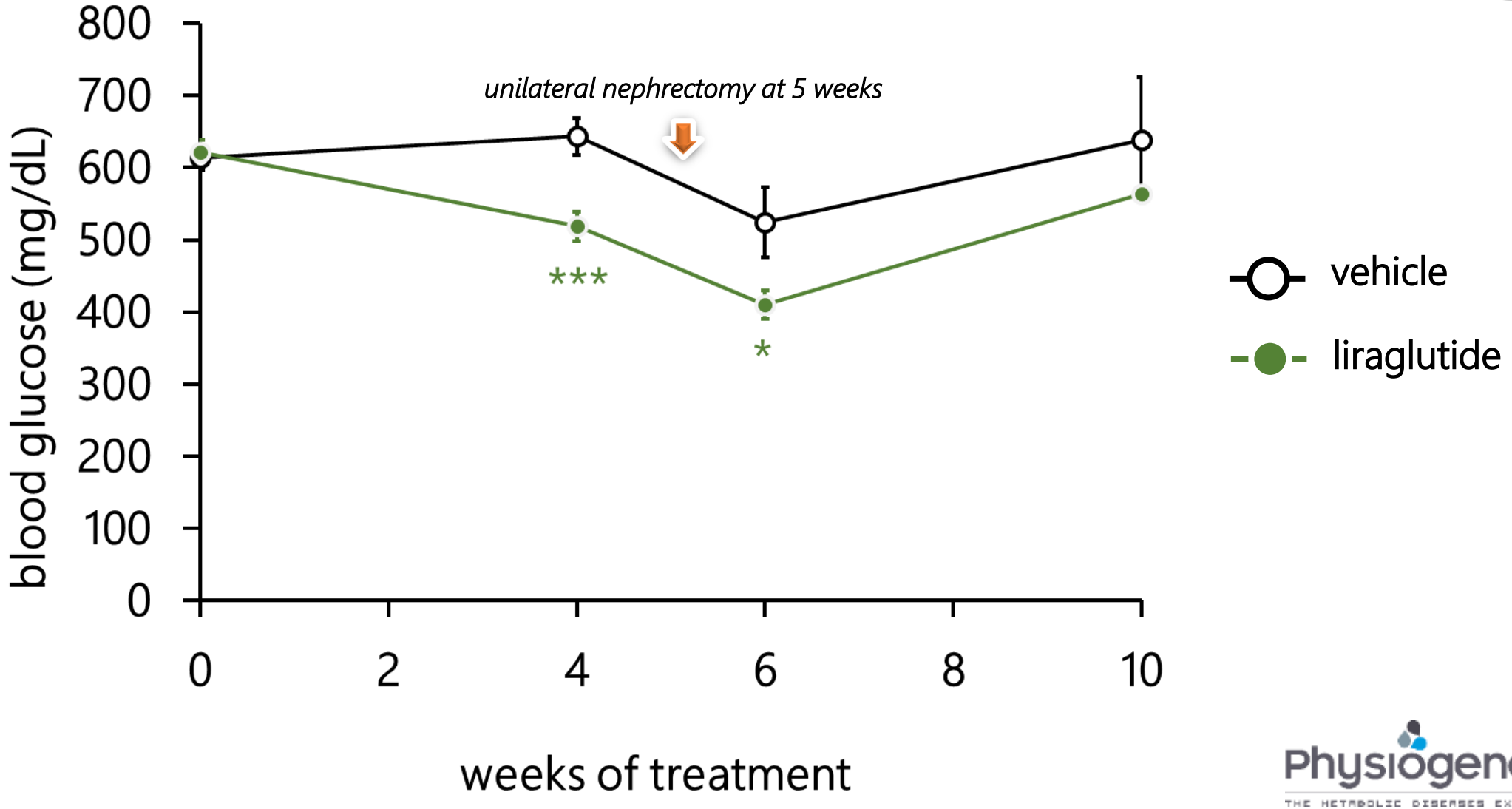
Fed blood glucose follow-up



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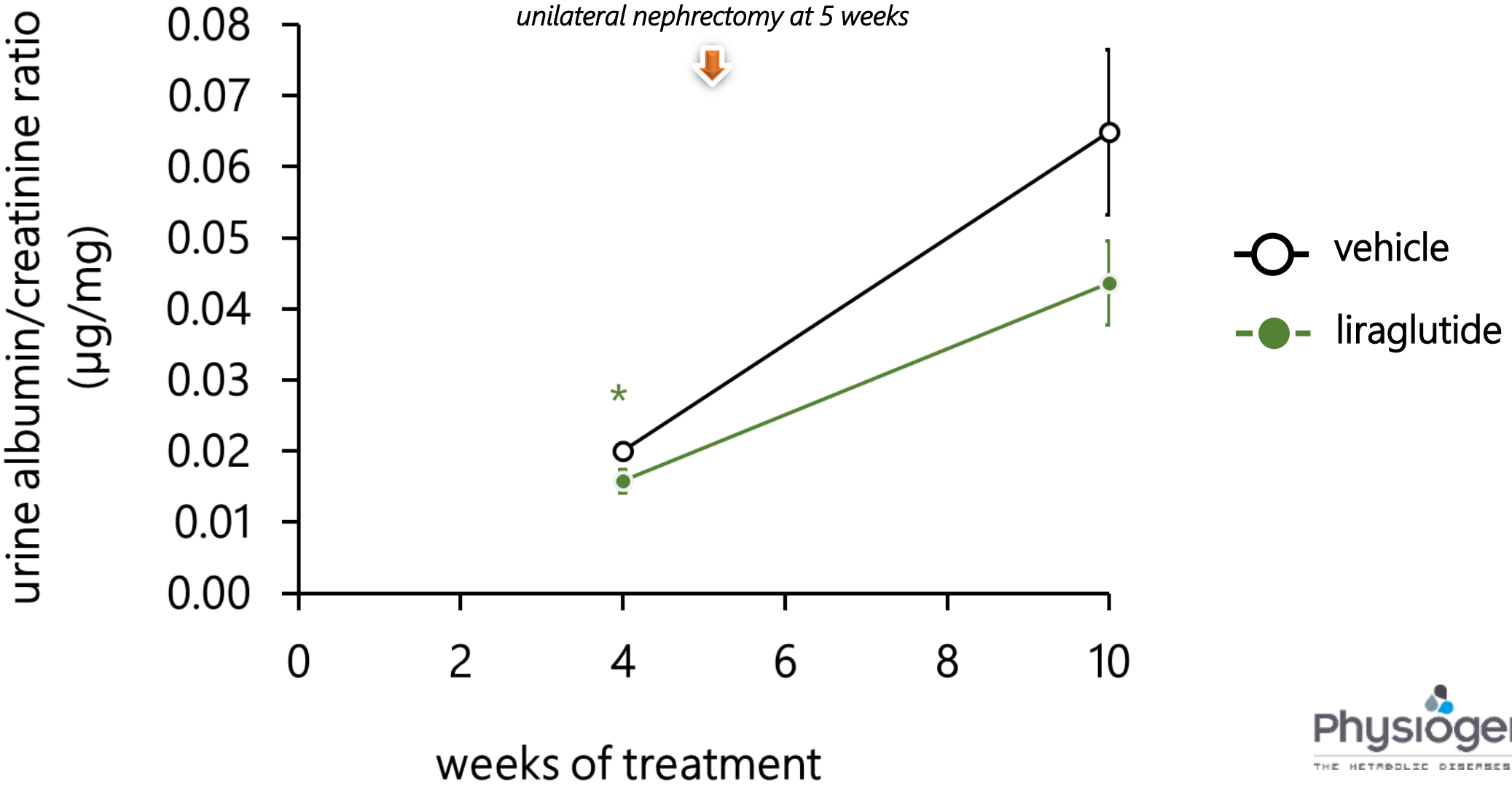
Urine albumin/creatinine ratio follow-up



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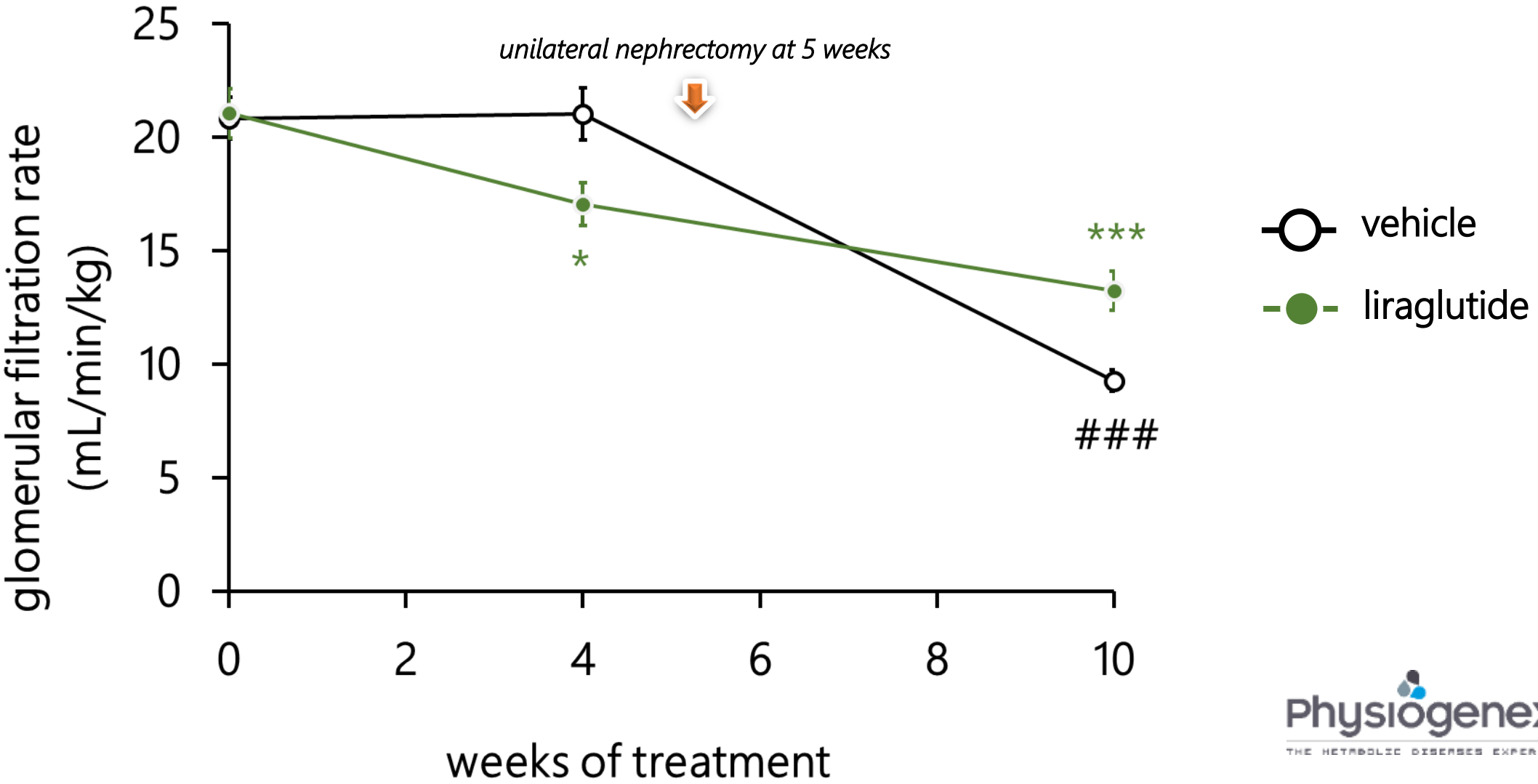
Glomerular filtration rate follow-up (FITC-sinistrin & Medibeacon transdermal monitor)



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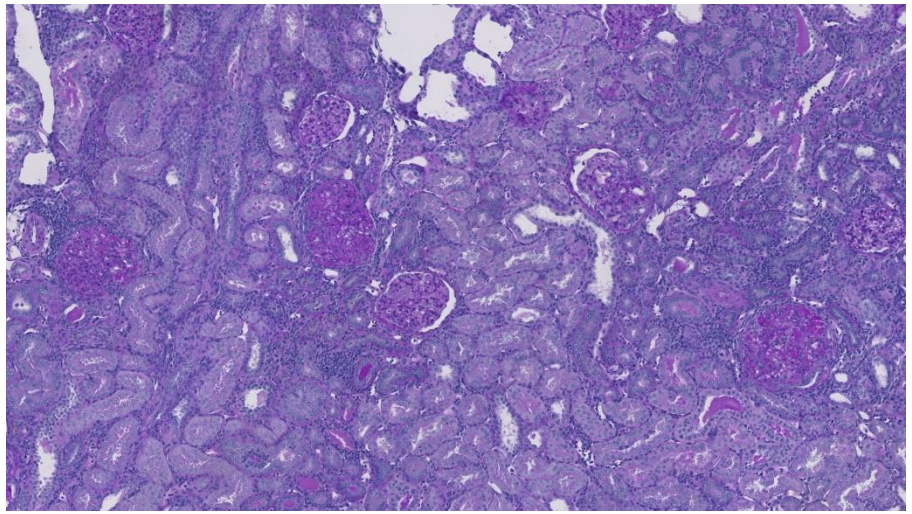
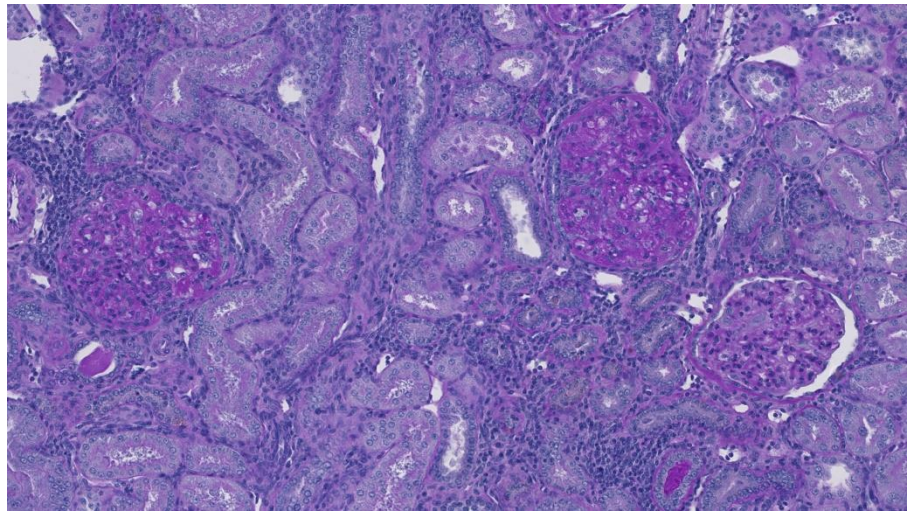
Kidney histopathology (PAS staining - glomerulosclerosis)

x10

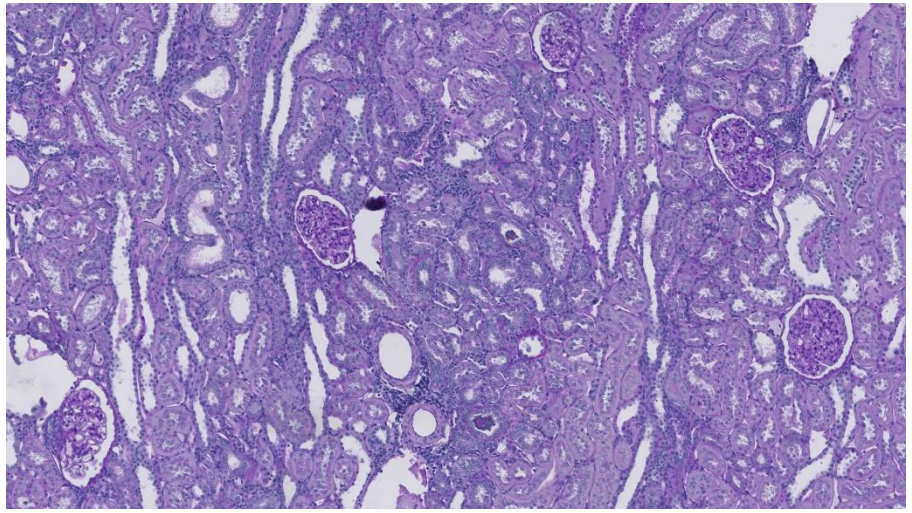
x20

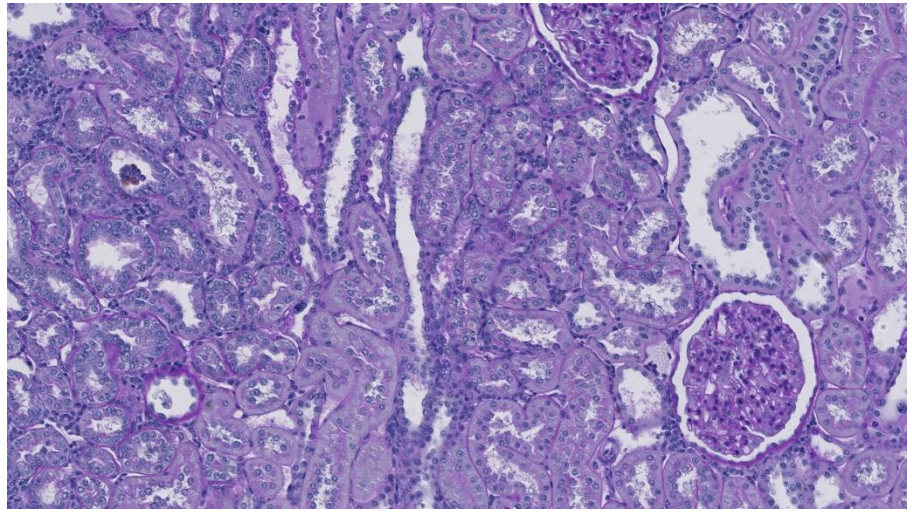
vehicle





LIRA





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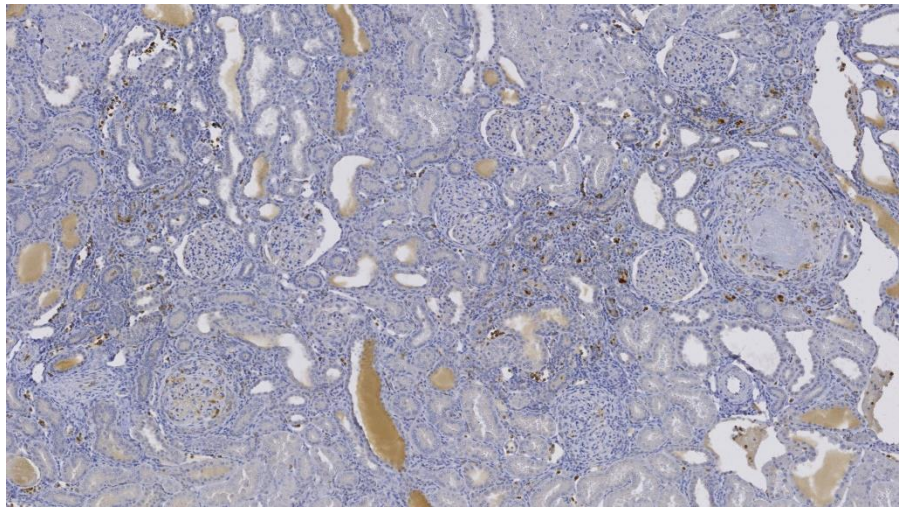
THE METABOLIC DISEASES EXPERTS

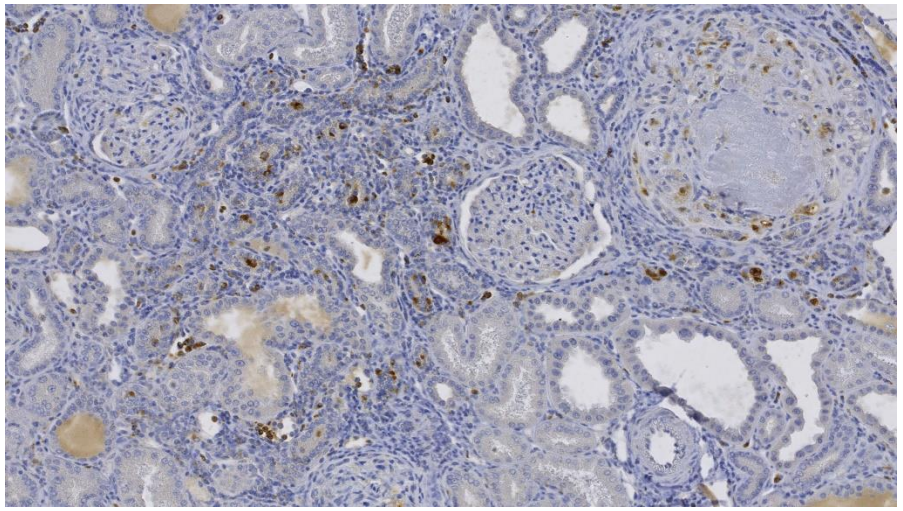
Kidney histopathology (ED1 staining - inflammation)

x10

x20

vehicle





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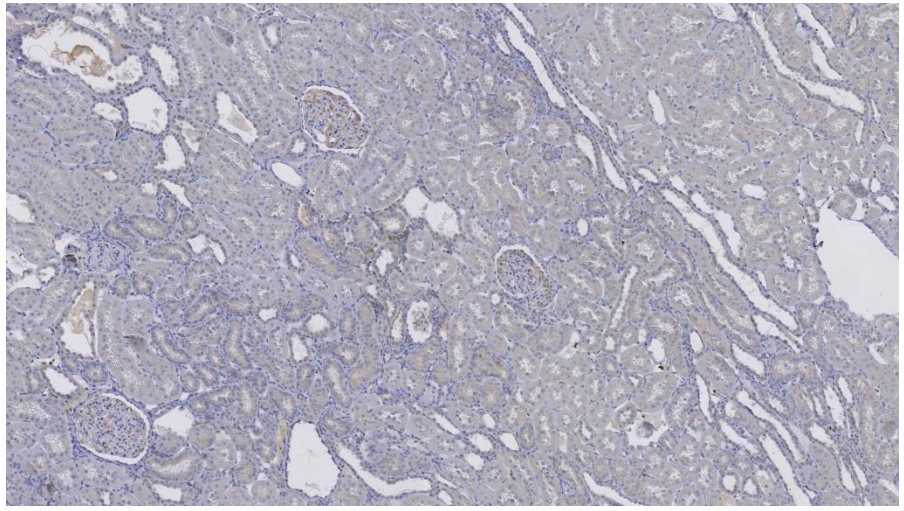

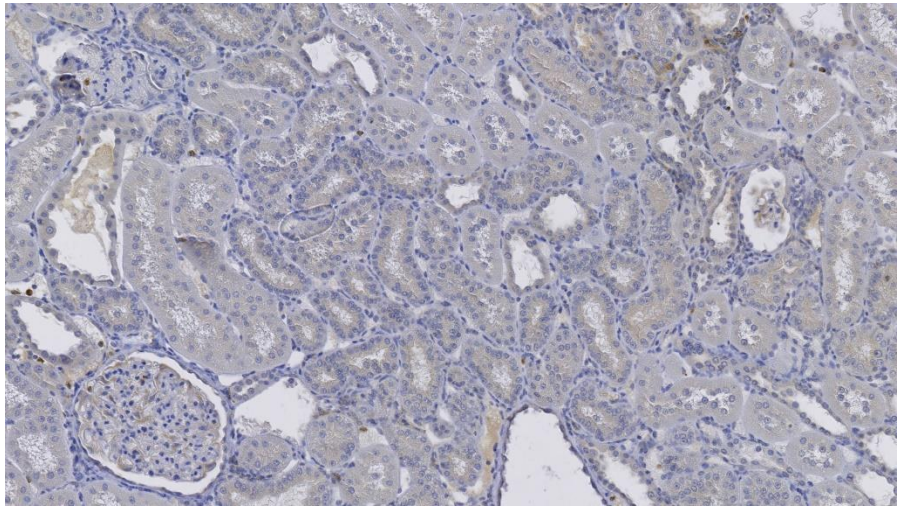

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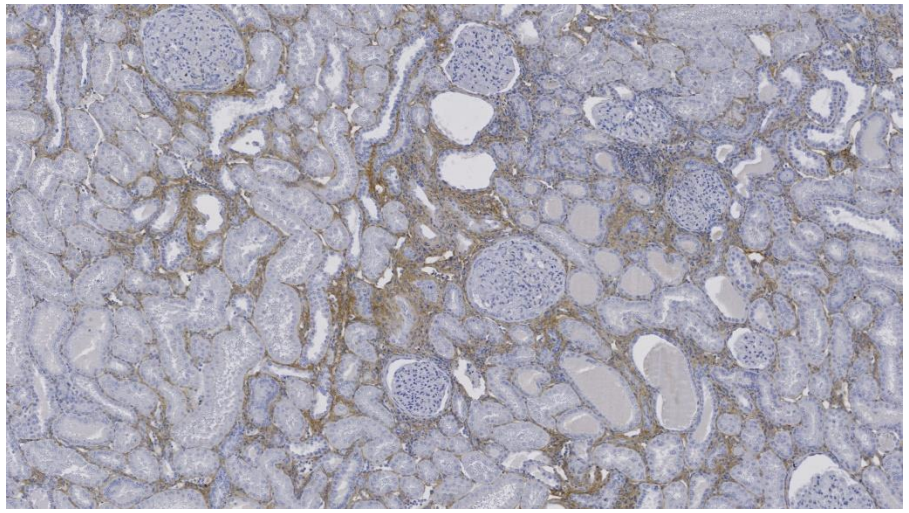
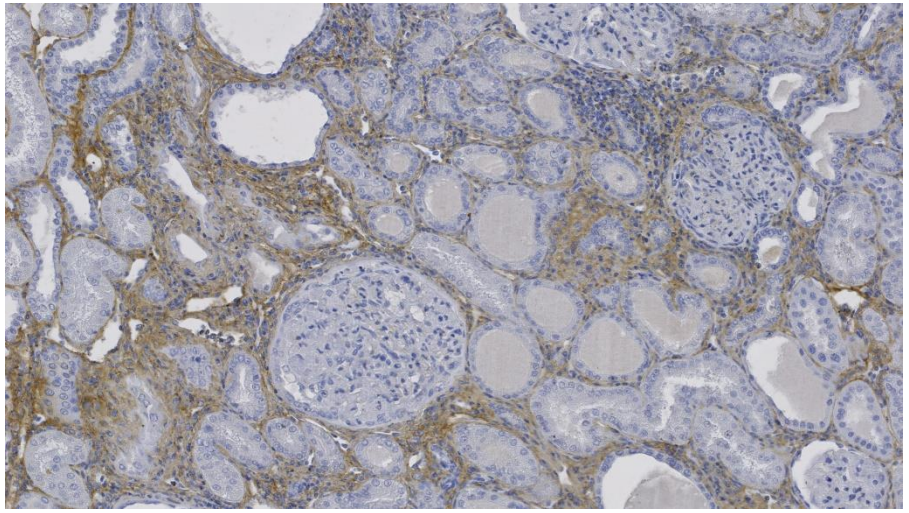
Kidney histopathology (collagen III staining - fibrosis)

x10

x20

vehicle





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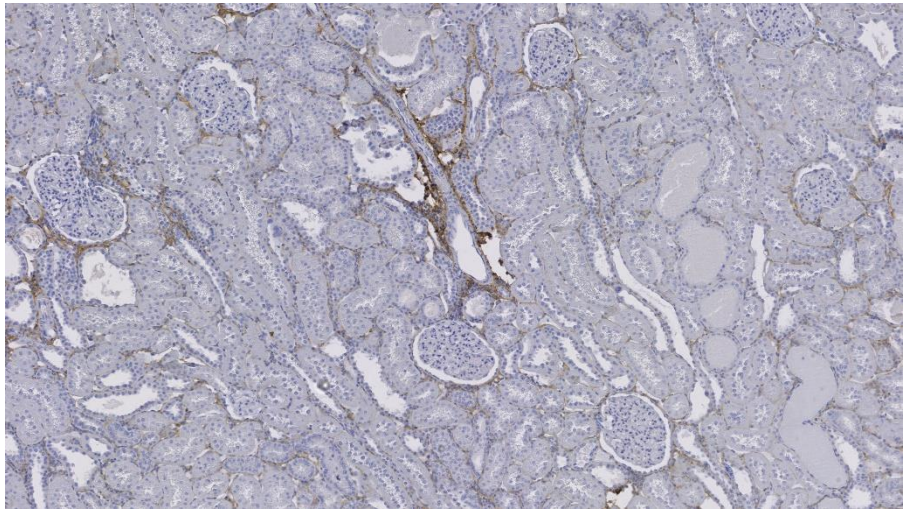

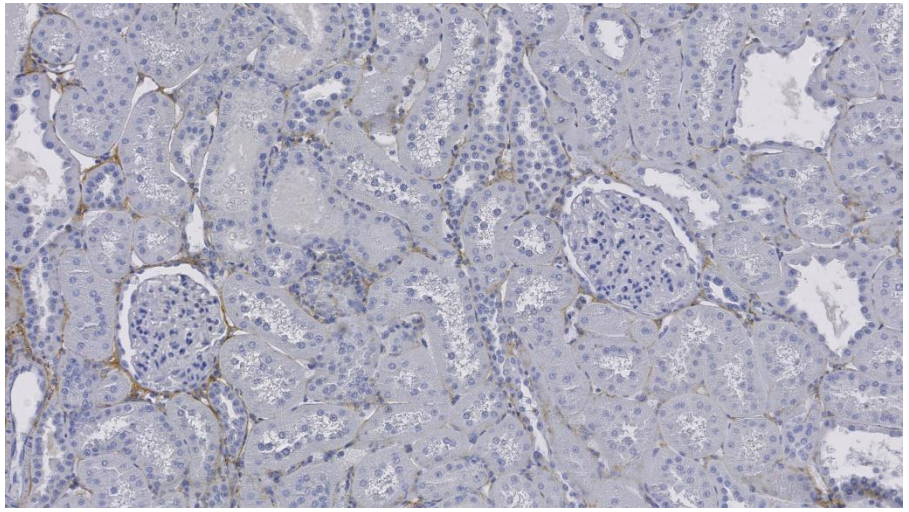

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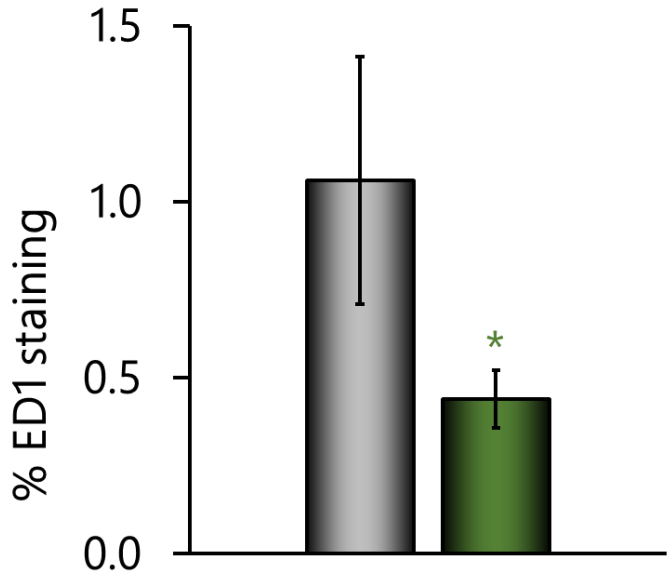
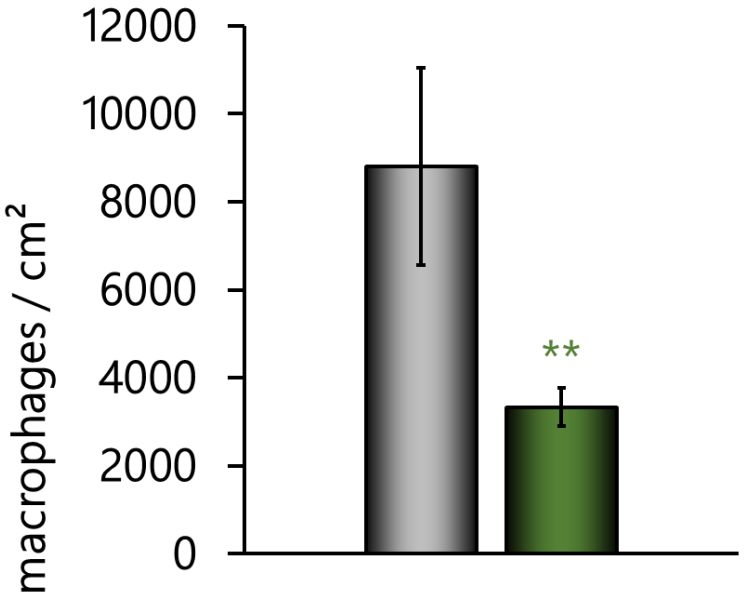
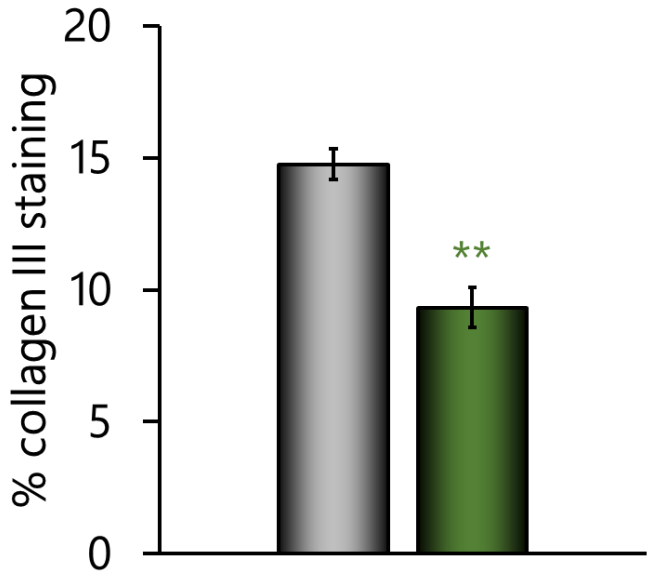
Kidney histopathology







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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.

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

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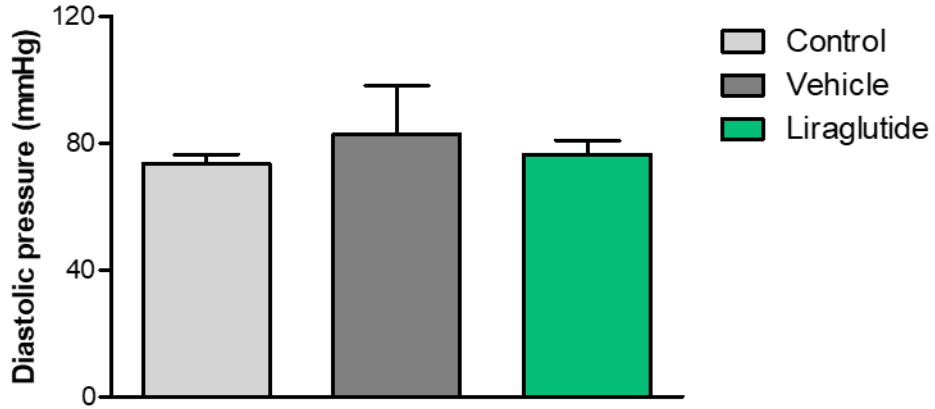
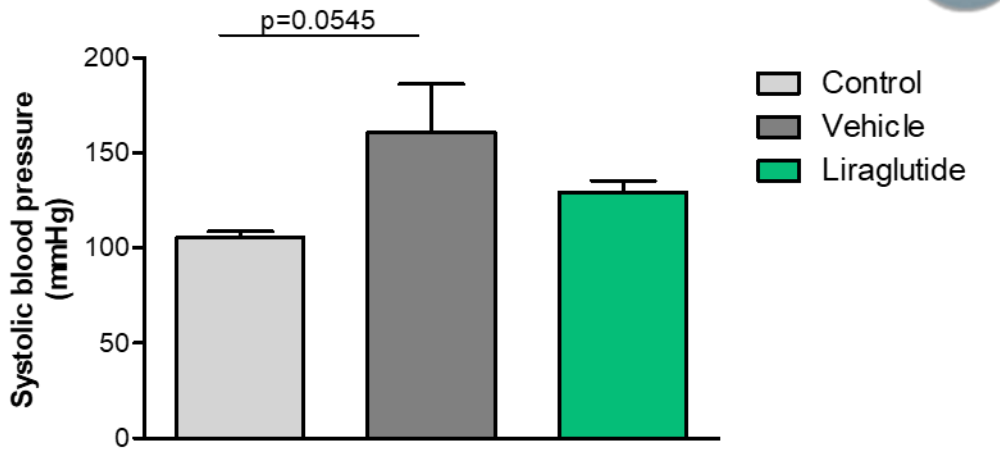
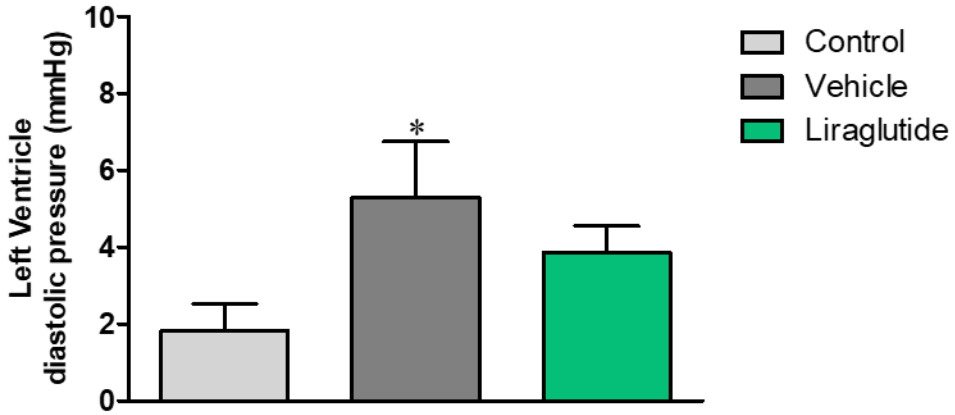
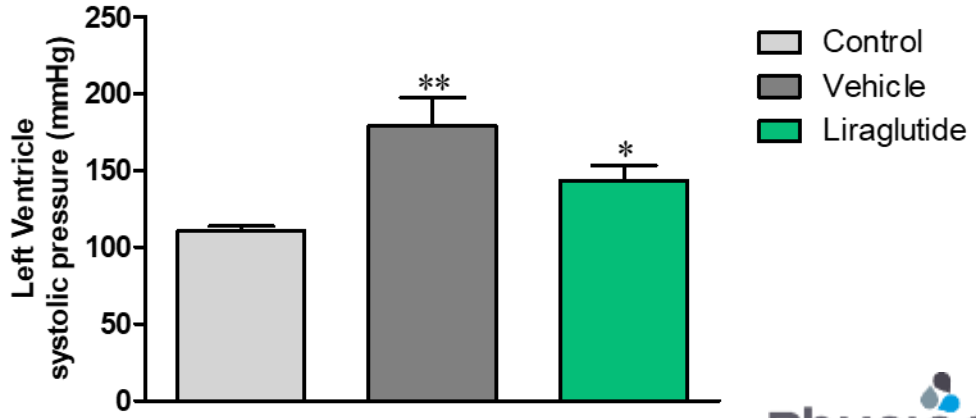
Blood pressure and intraventricular pressure









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

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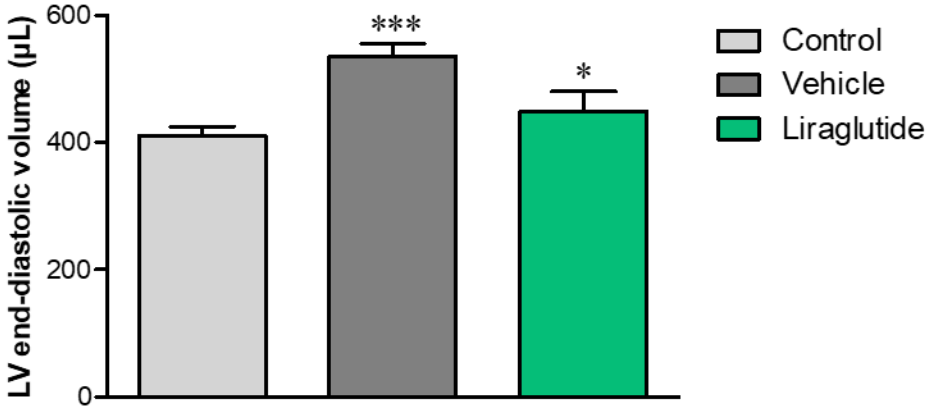
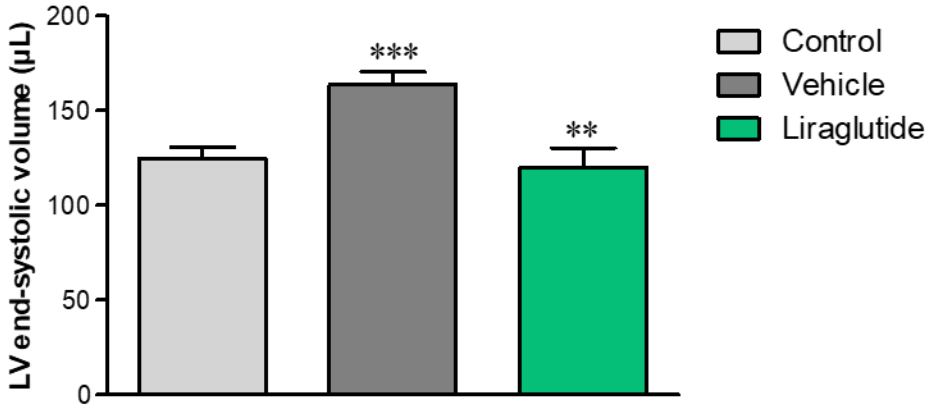
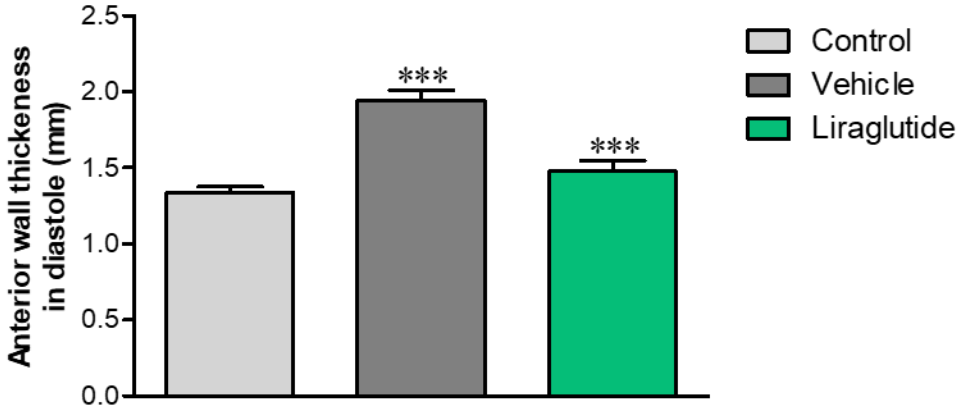
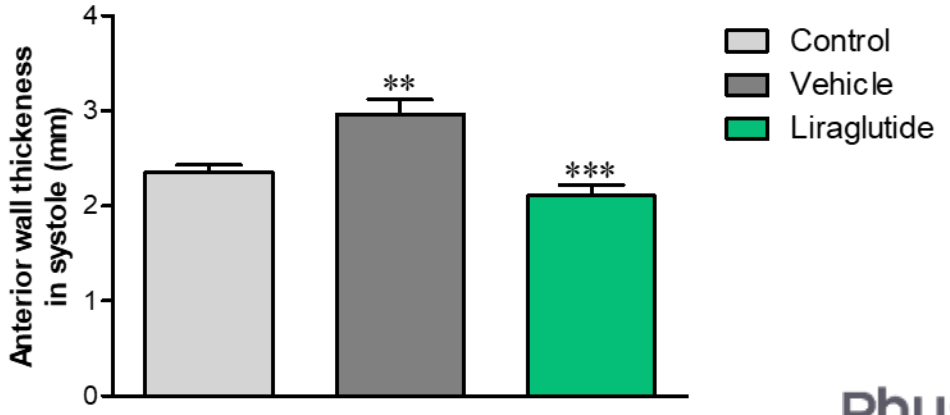
Left ventricular volume and wall thickness









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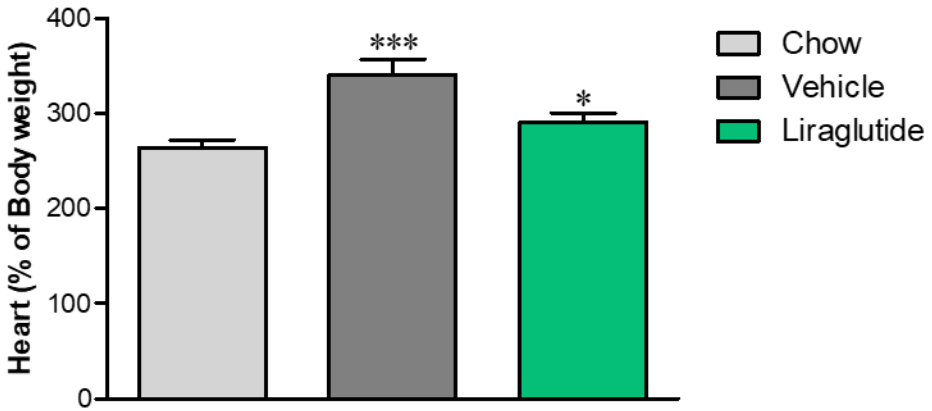
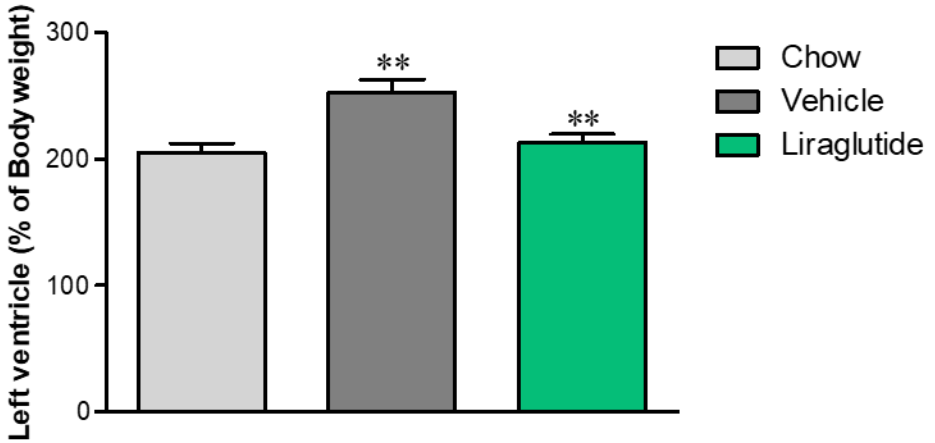
Heart and left ventricle weight





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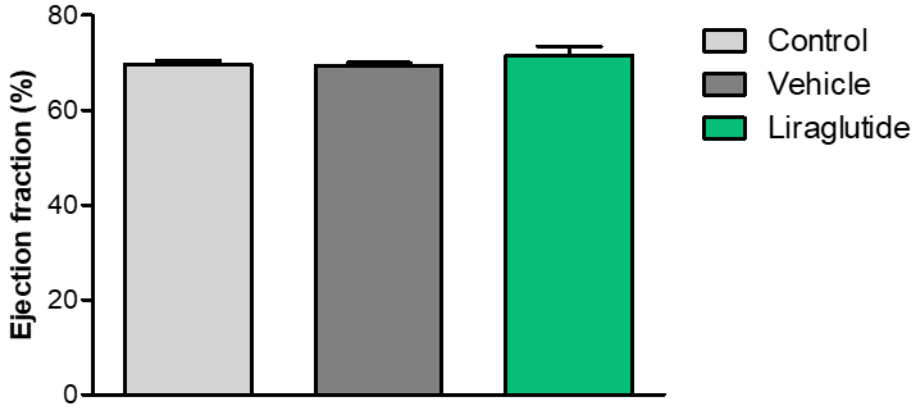
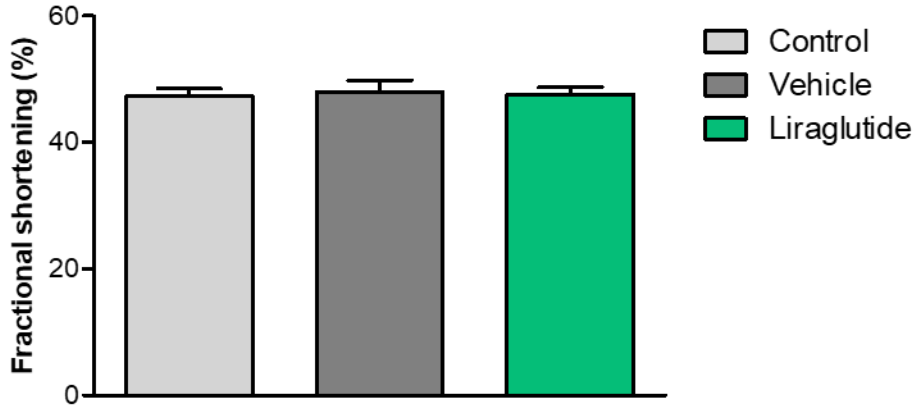
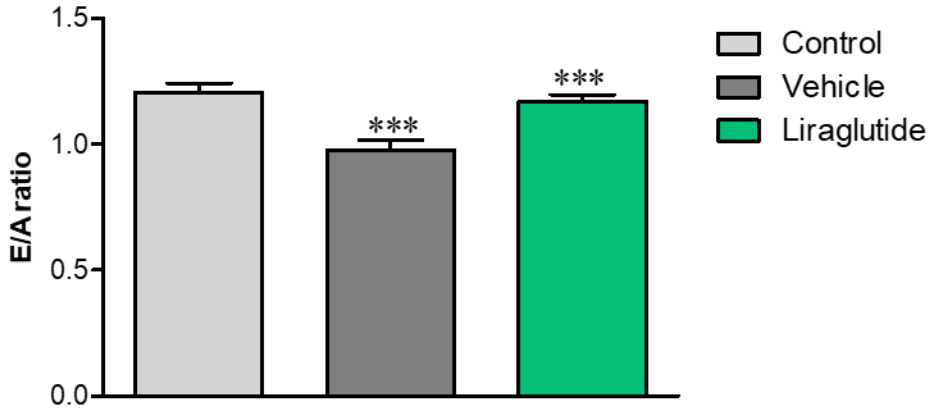
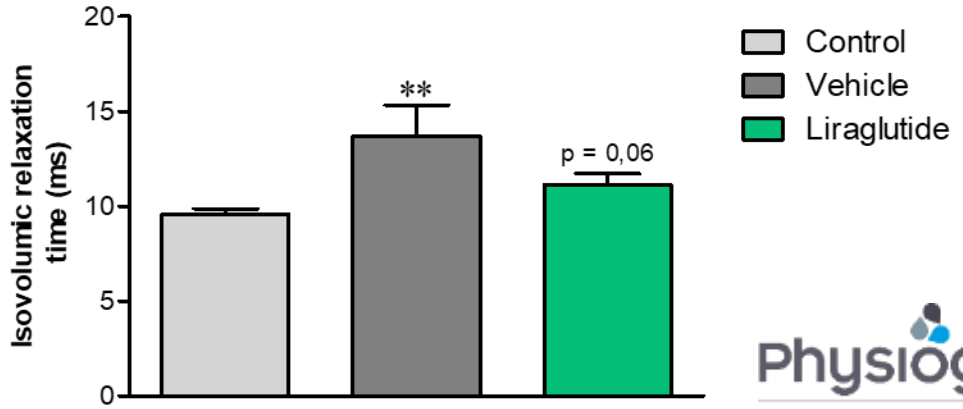
Diastolic and systolic function









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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.

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