Physiogenex
THE METABOLIC DISEASES EXPERTS

Diet-Induced Obese (DIO) rat model

✓ A unique DIO rat model to evaluate your drugs on obesity and cardiometabolic complications

Key benefits

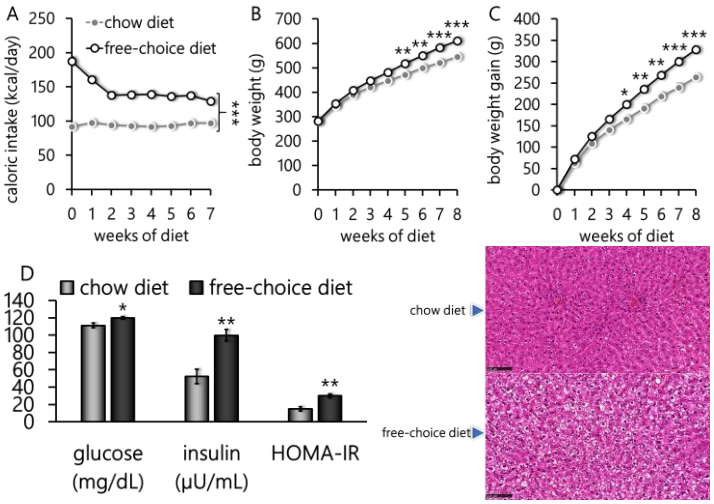
- ✓ ***Demonstrate the efficacy of your drugs in the Physiogenex free-choice diet-induced obese (DIO) rat:*** *an original model developing obesity and insulin resistance with cardiometabolic complications (liver steatosis and diastolic dysfunction).*
- ✓ ***Compare your drug with benchmarks:*** *our model is fully validated with reference drugs lorcaserin, pioglitazone and liraglutide.*

EXPERIMENTAL DESIGN

- **Background strain:** Sprague Dawley rat, male
- **Diet:** free-choice diet-induced obesity (free choice between normal chow or high fat/cholesterol diet and normal water or 10% fructose water) to favor hyperphagia/high energy intake
- **In life study duration:** 13 weeks (8-week diet + 5-week treatment
- **Positive controls**: lorcaserin (5-HT2C receptor agonist), pioglitazone (PPARgamma), liraglutide (GLP-1 receptor agonist)

MODEL CHARACTERISTICS

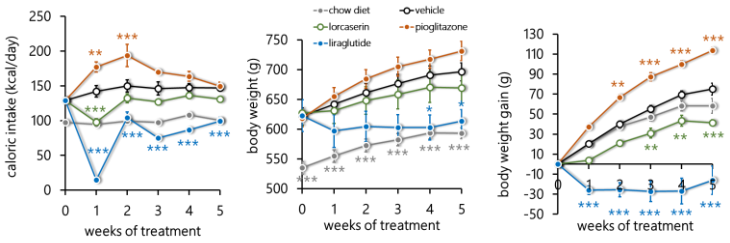
FREE CHOICE DIET FOR 8 WEEKS INDUCES OBESITY, INSULIN RESISTANCE AND LIVER STEATOSIS



Caloric intake (A), body weight (B), body weight gain (C), fasting blood glucose, insulin and HOMA-IR index of insulin resistance (D), representative liver hematoxylin & eosin (right lower panel) in rats fed a chow or free-choice diet for 8 weeks. **p<0.05, **p<0.01 and ***p<0.001 vs. chow diet.*

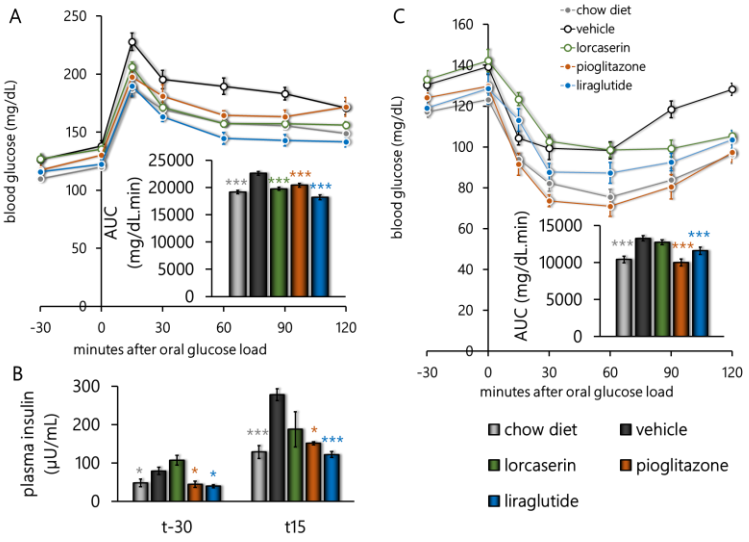
EFFECTS OF BENCHMARKS

BODY WEIGHT GAIN IS REDUCED WITH LORCASERIN AND INCREASED WITH PIOGLITAZONE, WHILE LIRAGLUTIDE INDUCES BODY WEIGHT LOSS



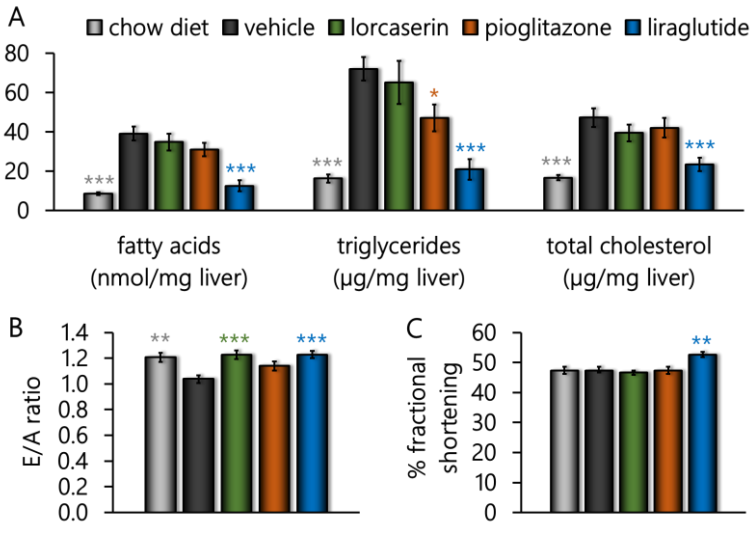
Caloric intake (A), body weight (B), body weight gain (C) in rats treated with vehicle, lorcaserin, pioglitazone or liraglutide for 5 weeks. ***p<0.01 and ***p<0.001 vs. vehicle.*

ALL BENCHMARKS IMPROVE GLUCOSE INTOLERANCE, BUT ONLY PIOGLITAZONE AND LIRAGLUTIDE IMPROVE INSULIN RESISTANCE



Blood glucose levels and glucose area under the curve (A), plasma insulin levels (B) before and after an oral glucose load (oral glucose tolerance test), blood glucose levels and glucose area under the curve (C) after an insulin injection (insulin tolerance test) in rats treated with vehicle, lorcaserin, pioglitazone or liraglutide for 5 weeks. **p<0.05, **p<0.01 and ***p<0.001 vs. vehicle.*

LIRAGLUTIDE SHOWS THE BEST BENEFITS ON HEPATIC LIPIDS AND CARDIAC FUNCTION



Hepatic fatty acids, triglycerides and total cholesterol levels (A), cardiac diastolic function index with E/A ratio (B) and % fractional shortening (C) assessed during echocardiography in rats treated with vehicle, lorcaserin, pioglitazone or liraglutide for 5 weeks. **p<0.05, **p<0.01 and ***p<0.001 vs. vehicle.*

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