Physiogenex
THE METABOLIC DISEASES EXPERTS

CETP apo B100 transgenic mouse under high fat diet

A nutrional animal model with a "human-like" lipoprotein profile to evaluate your compounds affecting both diabetes and dyslipidemia

Key benefits :

- ✓ To test drugs affecting both diabetes and dyslipidemia in an obese, insulin resistant and dyslipidemic model
- ✓ A model specifically designed to perform the most predictive *in vivo* experiments: euglycemic hyperinsulinemic clamp, *in vivo* macrophage-to--feces reverse cholesterol transport and LDL/HDL kinetics

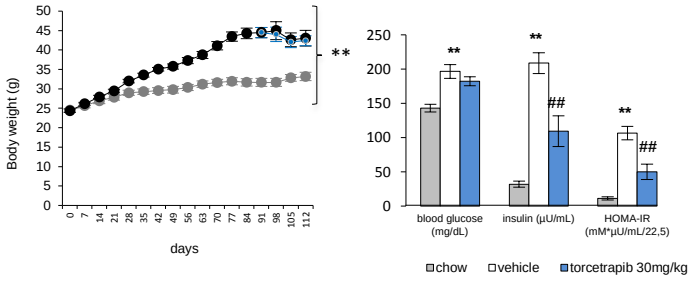
ANIMAL MODEL

- Background strain: C57BL6/J mouse carrying both human CETP and human apoB100
- Gender/age: male, 6-week old
- Diet: 60% high fat diet
- Time on diet: 3 months
- Positive reference compounds: torcetrapib, metformin, sitagliptin

PATHOPHYSIOLOGICAL FEATURES AND PHARMACOLOGICAL RELEVANCE

❖ *Effects of torcetrapib*

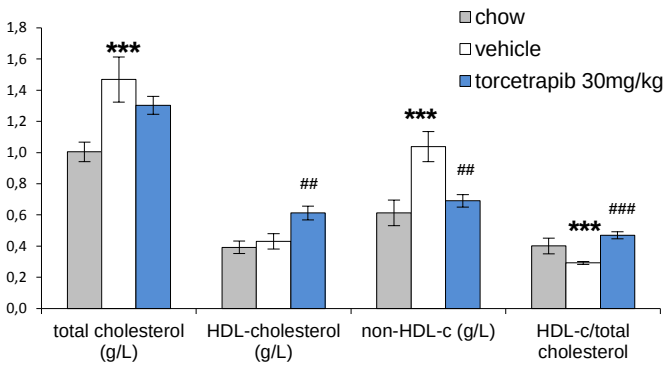
Body weight and biochemical parameters - 3-hour food deprivation



**p<0.01 *vs.* chow ##p<0.01 *vs.* vehicle

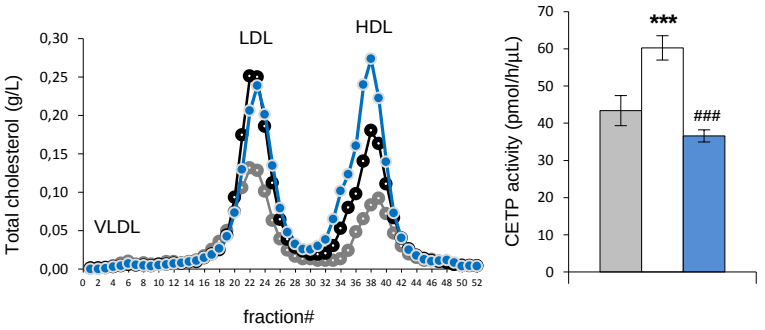
Torcetrapib increases HDL cholesterol

Body weight and biochemical parameters – overnight fasting

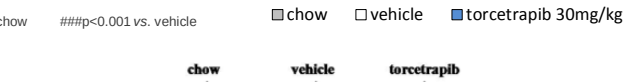


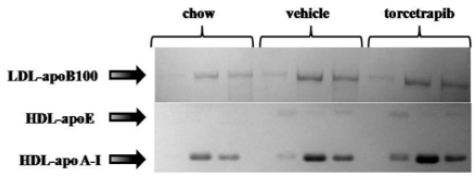
***p<0.001 *vs.* chow; ##p<0.01 *vs.* vehicle; ###p<0.001 *vs.* vehicle

Lipoprotein/apolipoprotein profile and CETP activity - 3-hour food deprivation

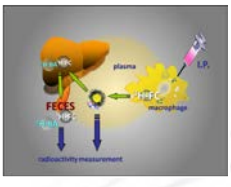


***p<0.001 *vs.* chow ###p<0.001 *vs.* vehicle

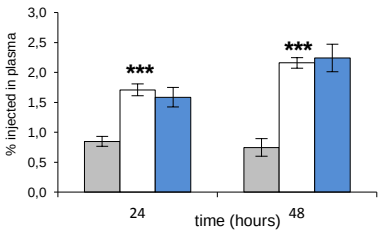


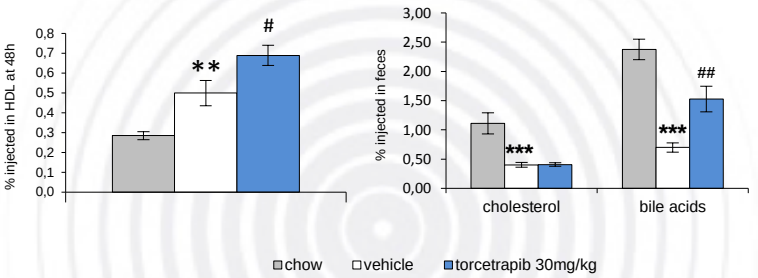


Torcetrapib improves macrophage-to-feces reverse cholesterol transport



Macrophage-to-feces reverse cholesterol transport





#p<0.05 *vs.* vehicle ##p<0.01 *vs.* vehicle

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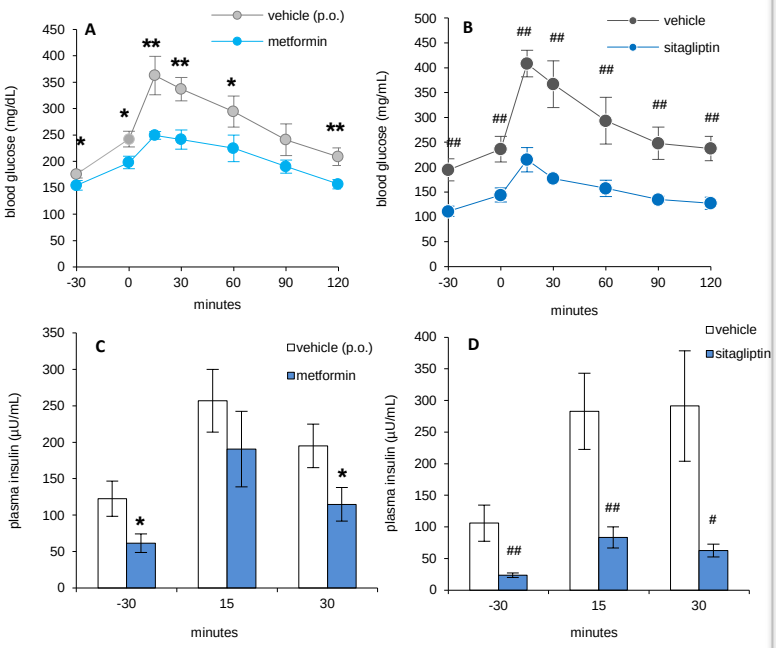
❖ *Effects of sitagliptin and metformin*

Both sitagliptin and metformin improve glucose homeostasis

Oral glucose tolerance test

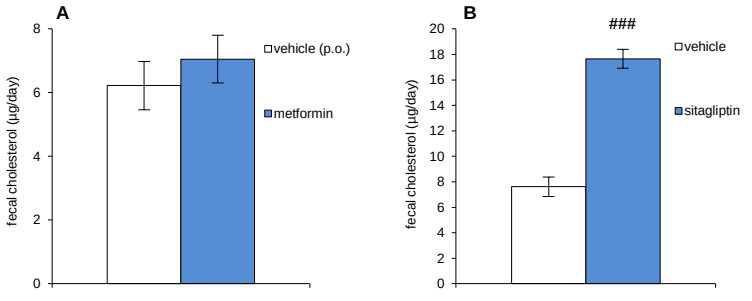


*p<0.05, **p<0.01 *vs.* vehicle
#p<0.05, ##p<0.001 *vs.* vehicle

Blood glucose (A,B) and plasma insulin (C,D) levels after an oral glucose load

Cholesterol mass excreted in feces increases in sitagliptin treated mice

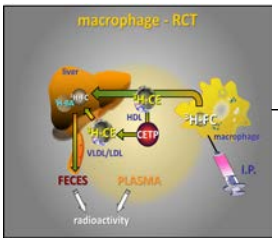
Cholesterol mass excreted in feces

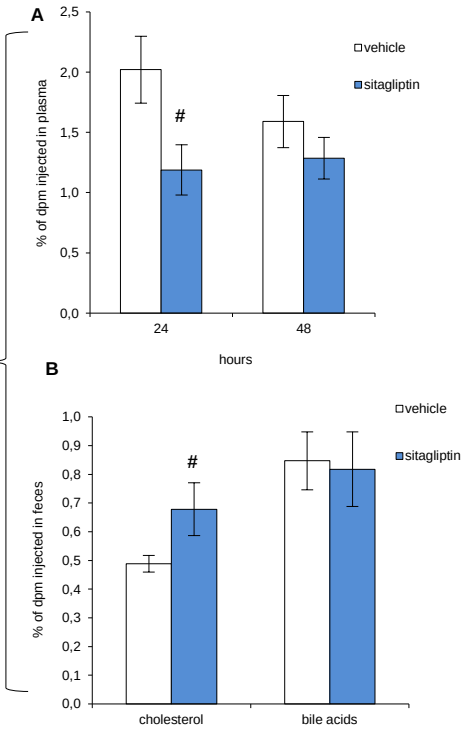


###p<0.001 *vs.* vehicle

Sitagliptin improves macrophage-to-feces RCT through reduced intestinal cholesterol absorption

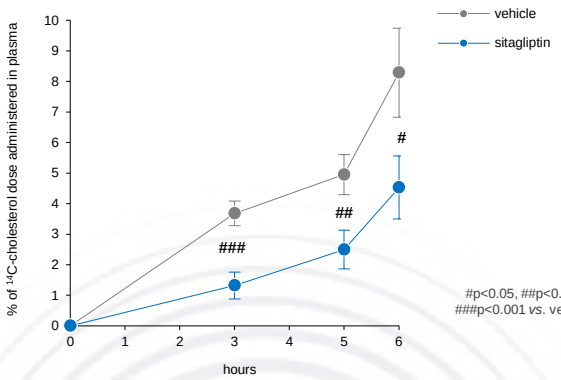
^{3}H-tracer appearance in plasma (A) and feces (B) after ^{3}H-cholesterol labeled macrophages injection





#p<0.05 *vs.* vehicle

Intestinal cholesterol absorption



#p<0.05, ##p<0.01, ###p<0.001 *vs.* vehicle

ADD-ON STUDIES

- Euglycemic hyperinsulinemic clamp
- Hyperglycemic clamp

REFERENCES

Briand F. et *al*. DPP-4 inhibitor sitagliptin improves reverse cholesterol transport through reduced intestinal cholesterol absorption in obese insulin resistant CETP-apoB100 transgenic mice. Presented as a poster during the 71st American Diabetes Association meeting 2011.

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