CETP apo B100 transgenic mouse under high fat diet

**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

- **Torcetrapib increases HDL cholesterol**
  - Body weight and biochemical parameters - overnight fasting
  - ** ***p<0.001 vs. chow**
  - ** ###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**
  - ** ***p<0.001 vs. chow**
  - ** ###p<0.001 vs. vehicle**
  - ** #p<0.05 vs. vehicle**
**Effects of sitagliptin and metformin**

Both sitagliptin and metformin improve glucose homeostasis

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

Blood glucose levels after oral glucose load:

- **Vehicle** (p.o.)
- **Metformin**
- **Sitagliptin**

![Blood glucose levels](image)

Plasma insulin levels:

- **Vehicle** (p.o.)
- **Metformin**
- **Sitagliptin**

![Plasma insulin levels](image)

Cholesterol mass excreted in feces increases in sitagliptin treated mice

- **Vehicle** (p.o.)
- **Metformin**
- **Sitagliptin**

![Cholesterol mass excreted in feces](image)

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.