

oxLDL-RCT METHOD

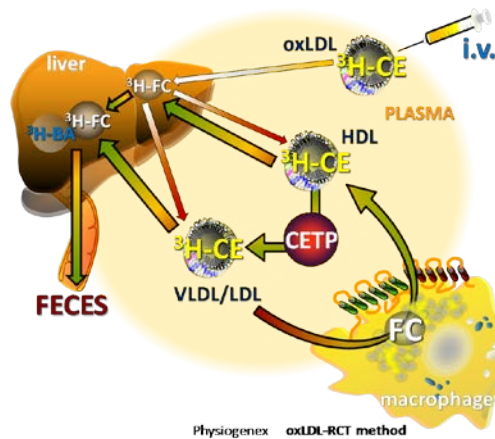
Innovative and proprietary technique only available at Physiogenex. This method will demonstrate if your compound promotes reverse cholesterol transport and has therefore the potential to prevent cardiovascular diseases.

Key benefits :

- ✓ *In vivo* reverse cholesterol transport using ^3H -cholesteryl oleate labeled oxidized LDL to evaluate compounds affecting **cholesterol metabolism** and **reverse cholesterol transport**
- ✓ Essential and robust data to demonstrate that your compound promotes the transport of cholesterol from atherogenic lipoprotein particles to the feces and has therefore the potential to prevent atherosclerosis

DESCRIPTION AND PARAMETERS EVALUATED

- Species: hamster, mouse, rat
- Plasma total cholesterol, HDL-c and HDL-c/TC ratio.
- ^3H -tracer appearance in plasma, HDL, liver, bile and feces

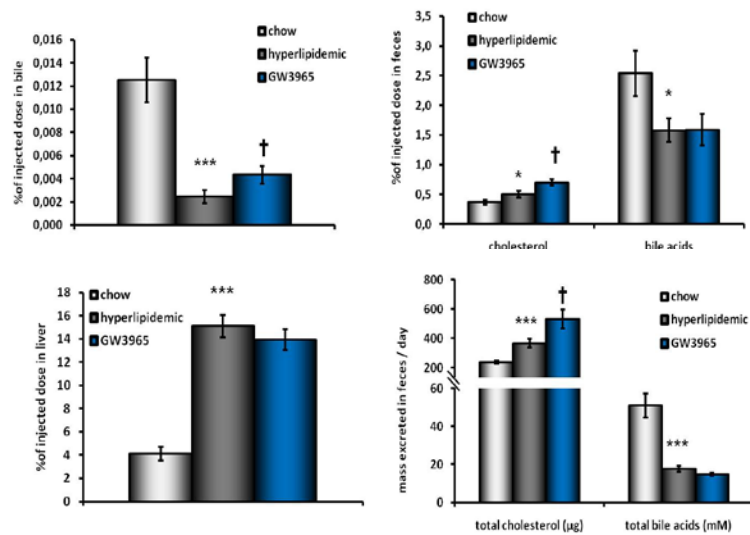
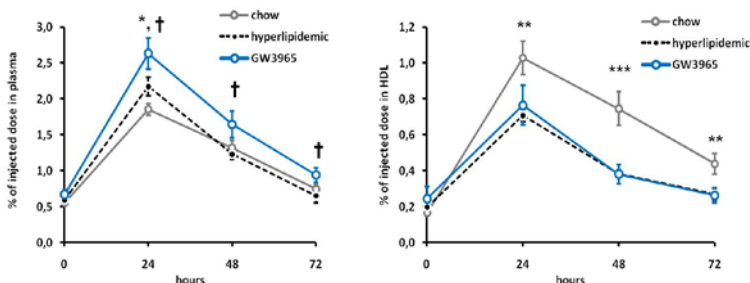


SCIENTIFIC AND PHARMACOLOGICAL RELEVANCE

- Hamsters fed a chow or hyperlipidemic diet over 3 weeks then treated with vehicle or LXR agonist GW3965
- Treatment: LXR agonist GW3965 30mg/kg, twice daily
- Duration: 10 days
- Other reference compounds: please contact our experts

LXR activation promotes *in vivo* reverse cholesterol transport in hamster fed a hyperlipidemic diet:

- High fat feeding severely compromises the efflux of oxidized LDL-derived cholesterol to HDL particles
- High fat feeding lowers the fecal excretion of oxidized LDL-derived cholesterol to fecal bile acids
- LXR agonist GW3965 increase ^3H -tracer and mass fecal cholesterol excretion



ADD-ON STUDIES

- Macrophage-to-feces RCT method
- HDL-cholesterol turn over
- Insulin resistance and liver studies
- Biochemical analysis: plasma lipids, HDL-c, lipoprotein profiles, transfer protein activity assays (CETP, PLTP), etc...

REFERENCES

Briand F, Thieblemont Q, Muzotte E, Sulpice T. **Upregulating reverse cholesterol transport with cholesteryl ester transfer protein inhibition requires combination with the LDL-lowering drug berberine in dyslipidemic hamsters.** *Arterioscler Thromb Vasc Biol.* 2013 Jan;33(1):13-23.

Briand F, Thieblemont Q, Muzotte E, Sulpice T. **An alternative method to measure *in vivo* reverse cholesterol transport in hyperlipidemic hamsters.** *Circulation.* 2011; 124: A11835.