Physiogenex
THE METABOLIC DISEASES EXPERTS

Demonstrate further your drug benefits on atherosclerosis reduction with radio-tracer based methods in validated athero models

Going beyond the classical athero studies
with ApoE and LDL-r KO models

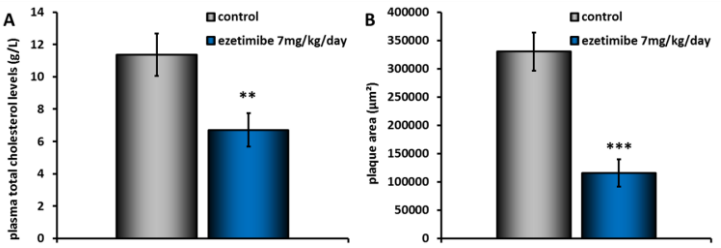
Key objectives:

- ✓ ***In vivo*** **validation of the anti-atherosclerotic effect of your compounds**
- ✓ **Highlights additional benefits of your drug through radio-tracer based in vivo experiments**
- ✓ **Take advantage of the VCAM-1 imaging technique to detect inflammation inside atherosclerotic plaques**

PROOF OF EFFICACY IN VALIDATED MODELS WITH ACTIVE COMPARATORS

- Apolipoprotein E knock out or LDL-receptor knock out mice
- Western or Paigen diet
- Active comparators: ezetimibe, others on request

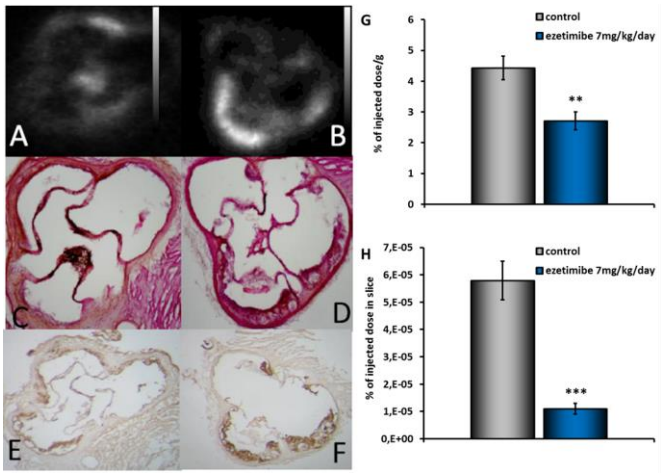
1. REDUCTION IN HYPERCHOLESTEROLEMIA AND PLAQUE SIZE



Plasma total cholesterol levels (A) and atherosclerotic plaques area (B) in apolipoprotein E ko mice fed a Paigen diet w/o (control) or w/ ezetimibe

Ezetimibe substantially reduces hypercholesterolemia and atherosclerosis plaque area in apoE ko mice

2. BIOMARKER OF PLAQUE INFLAMMATION (VCAM-1 UPTAKE)

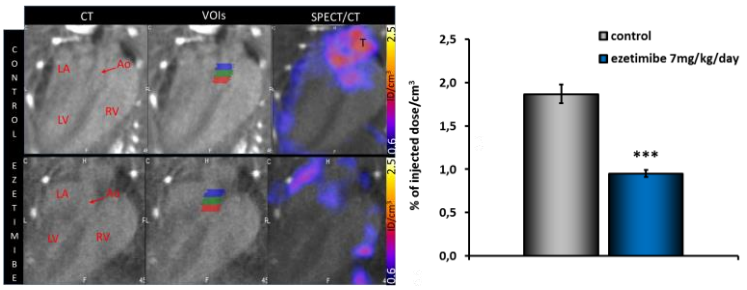


Autoradiography (A,B), H&E staining (C, D) and anti-MAC2 immunostaining (E, F) in apo E ko mice treated w/ ezetimibe (A, C and E) or w/o ezetimibe (B, D and F).
^{99m}Tc-cAbVCAM1-5 uptake evaluated by autoradiography was quantified per (G) volume or (H) slice.

Ezetimibe strongly reduces atherosclerosis and plaque inflammation

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

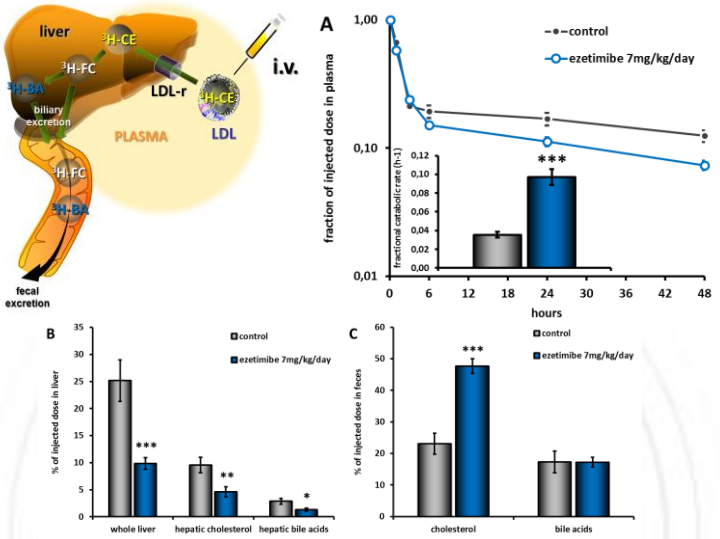
3. VCAM-1 IMAGING TO QUANTIFY INFLAMMATION INSIDE PLAQUES



^{99m}Tc-cAbVCAM1-5 uptake in aortic valves and ascending aorta by SPECT/CT imaging

Ezetimibe significantly reduces VCAM-1 expression in aortic valves and ascending aortas

4. REDUCTION OF LDL-C AND ITS EXCRETION OUT OF THE BODY



^{3}H-tracer plasma disappearance rate and LDL-cholesterol catabolism (A), ^{3}H-tracer recovery in liver (B) and feces (C) after ^{3}H-cholesteryl oleate labeled LDL i.v. injection in apoE ko mice treated w/o or w ezetimibe

Ezetimibe promotes anti-atherosclerotic mechanisms through higher LDL-cholesterol catabolism and LDL-derived cholesterol fecal excretion

Prologue Biotech – 516, rue Pierre et Marie Curie
31670 Labège - FRANCE
Phone : +33 561 287 040
Fax : +33 561 287 043
www.physiogenex.com
business@physiogenex.com

Member of cardio metabolic 2