

Atherosclerosis – apo E ko and LDL-r ko mouse models

✓ Take advantage of Physiogenex expertise in running athero models to demonstrate the benefits of your drugs on atherosclerosis

Key benefits

- ✓ *In vivo* validation of the anti-atherosclerotic effect of your compounds using “*en face*” and histology analysis
- ✓ Combine these athero models with our unique VCAM-1 imaging technique (used in both mice and humans) to detect inflammation inside atherosclerotic plaques

MODEL FEATURES

- **Background strain:** apo E ko or LDL-r ko mouse
- **Diets:** Western (0.15 to 0.20% cholesterol), high fat +/- Paigen diet (1.25% cholesterol, 0.5% cholate) or high fat+2% cholesterol+10% fructose (HFCF) diet
- **In life study duration:** depends on diet (Paigen diet: 6 to 8 weeks; Western diet: 12 weeks; HFCF diet: 16 weeks)
- **Positive drug controls:** ezetimibe, FXR and LXR agonists

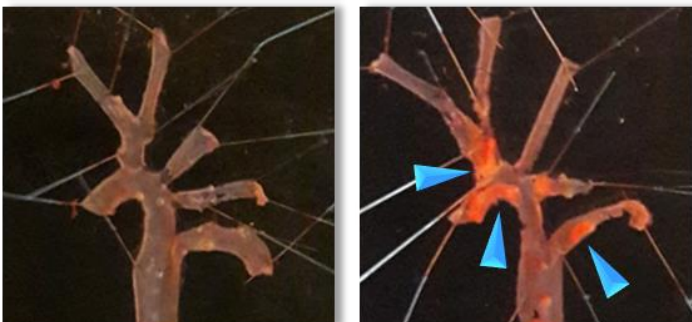
“EN FACE” ANALYSIS

PAIGEN DIET EXPEDITES ATHEROGENESIS IN APO E KO MICE FED A HIGH FAT PAIGEN DIET

2-WEEK DIET



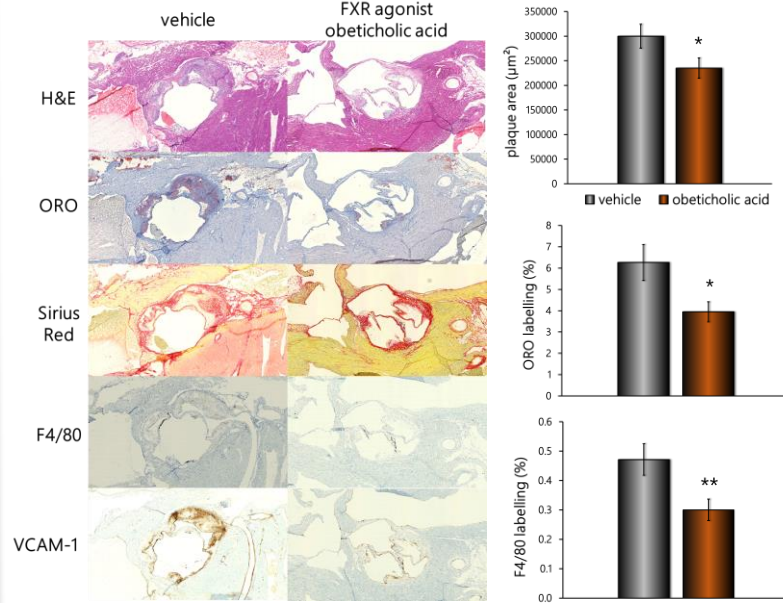
8-WEEK DIET



Representative “*en face*” analysis of aortas collected from apo E ko mice fed a high fat Paigen diet for 2 weeks (left side) or 8 weeks (right side). Upper panel represents the whole dissected aorta after oil red O staining. Lower panel shows a zoom on aortic root/arch of the same aorta. Blue arrows indicates atherosclerotic plaques.

HISTOLOGY & IMMUNO-HISTOLOGY ANALYSIS

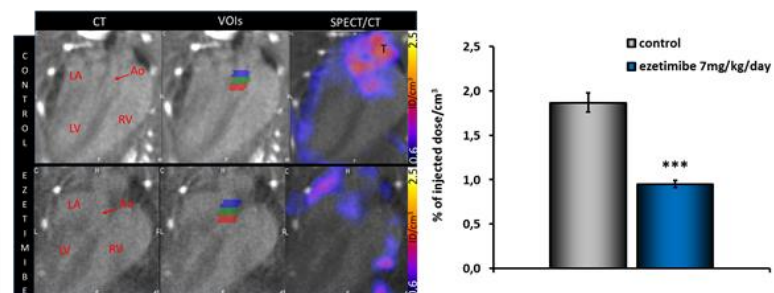
FXR AGONIST OBETICHOLIC ACID REDUCES ATHEROSCLEROSIS IN LDL-R KO MICE FED A HFCF DIET



Representative pictures of H&E (for plaques area), ORO (lipid deposition) and Sirius Red (collagen deposition) staining, F4/80 (macrophages) and VCAM-1 (inflammation) immunostaining (left panel); plaque area, lipid deposition and macrophages quantification from H&E, ORO and F4/80 staining (right panel) in LDL-r KO fed a HFCF diet treated with vehicle or obeticholic acid (*p<0.05 and **p<0.01 vs. vehicle).

VCAM-1 IMAGING TO QUANTIFY INFLAMMATION INSIDE PLAQUES

INTESTINAL CHOLESTEROL ABSORPTION INHIBITOR EZETIMIBE REDUCES PLAQUE INFLAMMATION IN APOE KO FED A PAIGEN DIET



⁹⁹mTc-cAbVCAM1-5 uptake in aortic valves and ascending aorta (left panel) and quantification (right panel) by SPECT/CT imaging