Physiogenex
THE METABOLIC DISEASES EXPERTS

The free choice diet-induced obese NASH hamster model

- ✓ Unique diet-induced hamster model of non-alcoholic steatohepatitis (NASH)
- ✓ The only preclinical model replicating the side-effects observed with FXR agonist obeticholic acid in humans

Key benefits

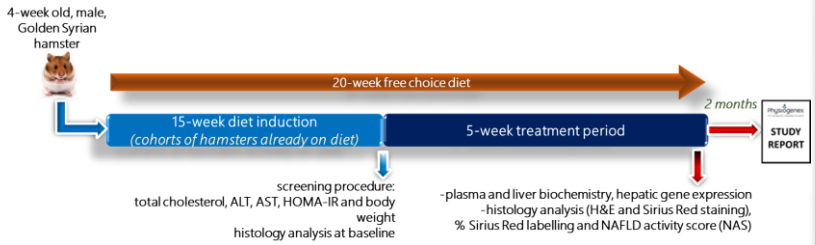
Unique proprietary diet-induced hamster model that enables the evaluation of novel drugs targeting NASH and fibrosis in comparison with the benchmark obeticholic acid, in a human-like context.

The free choice diet–induced obese NASH hamster provides:

- Unlike mice and rats, a nutritional model closer to the human situation with similar NASH lesions, cholesterol and bile acids metabolism.
- A pharmacologically validated model with the benchmark FXR agonist obeticholic acid with the similar benefits (body weight, liver inflammation reduction) and side-effects (increased LDL-cholesterol and reduced HDL-cholesterol) observed in humans.

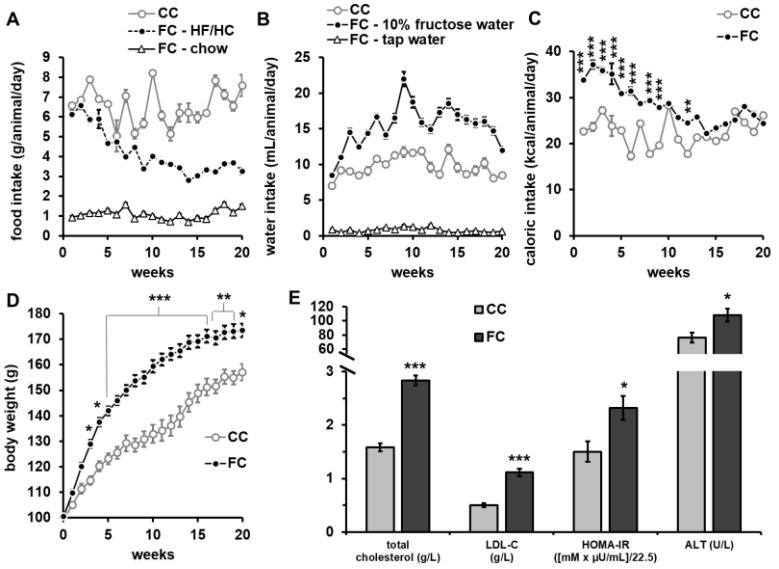
ANIMAL MODEL

- **Background strain/gender:** Golden Syrian Hamster, male
- **In house "free choice diet-induced NASH":** choice between a normal chow diet + normal tap water or high fat/high cholesterol + fructose in drinking water for up to 20 weeks
- **Reference compounds:** obeticholic acid (OCA), elafibranor, semaglutide, resmetirom, firsocostat
- **Experimental design:**



MODEL CHARACTERISTICS

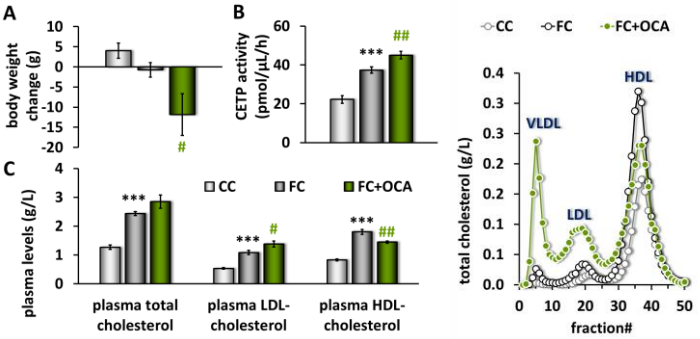
FREE CHOICE DIET INDUCES OBESITY, INSULIN RESISTANCE, HYPERCHOLESTEROLEMIA AND HIGHER PLASMA ALT LEVELS



Food intake (A), water intake (B), daily caloric intake (C), body weight (D), plasma total cholesterol, LDL-cholesterol, HOMA-IR index of insulin resistance and plasma ALT levels (E) after 20 weeks of chow (CC) or free choice (FC) diet.

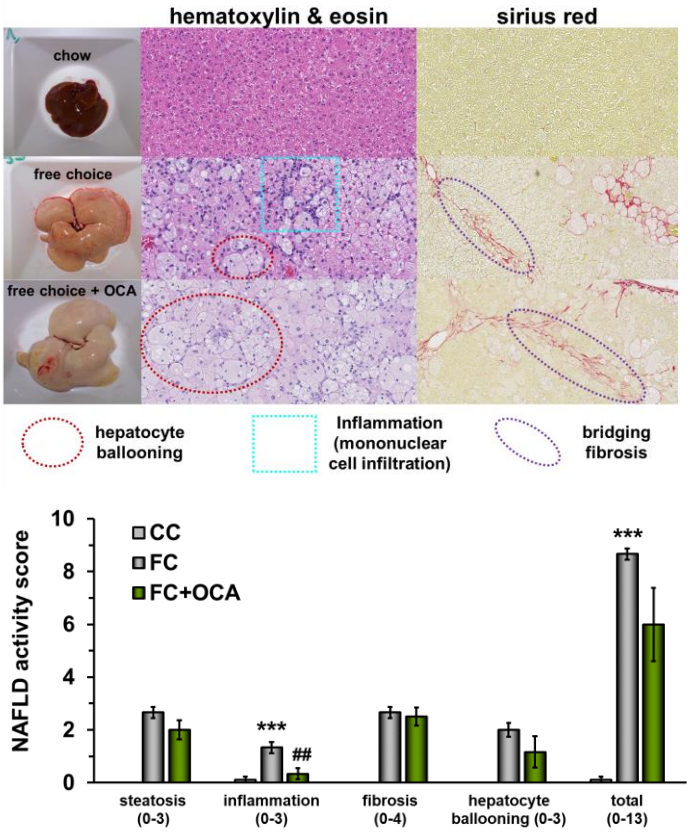
***p<0.05, **p<0.01 and ***p<0.001 free choice (FC) vs. chow (CC)**

OCA INDUCES BODY WEIGHT LOSS, BUT RAISES CETP ACTIVITY AND LDL-CHOLESTEROL, AND REDUCES HDL-CHOLESTEROL LEVELS



*****p<0.001 free choice (FC) vs. chow (CC), #p<0.05 and ##p<0.01 free choice vs. free choice + OCA**

OCA REDUCES LIVER INFLAMMATION BUT DOES NOT IMPROVE NAFLD SCORE IN ALL INDIVIDUALS



Liver aspect, representative H&E and Sirius Red staining (upper panel) and NAFLD activity scoring (lower panel). ***p<0.001 free choice (FC) vs. chow (CC), ##p<0.01 free choice vs. free choice + OCA.

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