

Diet-Induced NASH (DIN™) hamster model associated with metabolic syndrome

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

Key benefits

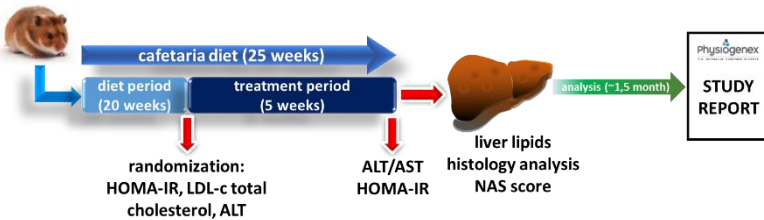
Unique proprietary diet-induced hamster model that enables the evaluation of novel drugs targeting NASH and fibrosis in comparison with the benchmark obeticholic acid, in a human-like context.

The diet-induced DIN™ NASH hamster provides:

- Unlike mice and rats, a nutritional model closer to the human situation with similar 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.

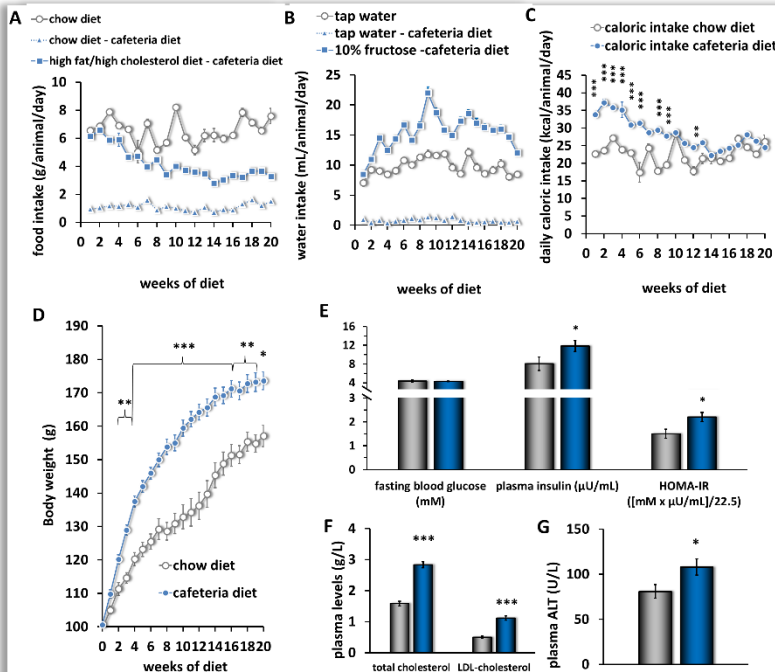
ANIMAL MODEL

- **Background strain/gender:** Golden Syrian Hamster, male
- **In house "Diet-Induced NASH" (DIN™):** cafeteria diet (choice between a normal chow diet + normal tap water or high fat/high cholesterol + fructose in drinking water for 25 weeks)
- **Reference compounds:** FXR agonist Obeticholic Acid (OCA) 15mg/kg/day in the diet
- **Experimental design:**



MODEL CHARACTERISTICS

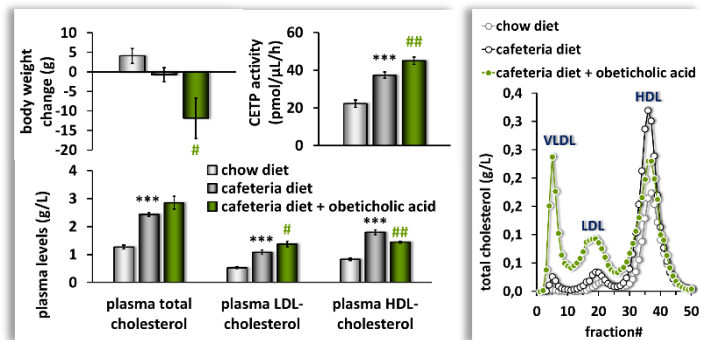
CAFETERIA DIET INDUCES OBESITY, INSULIN RESISTANCE, HYPERCHOLESTEROLEMIA AND HIGHER ALT LEVELS



Food intake (A), water intake (B), daily caloric intake (C), body weight (D), fasting blood glucose, plasma insulin and HOMA-IR index of insulin resistance (E), plasma total cholesterol and LDL-cholesterol (F), plasma ALT after 20 weeks of chow or cafeteria diet.

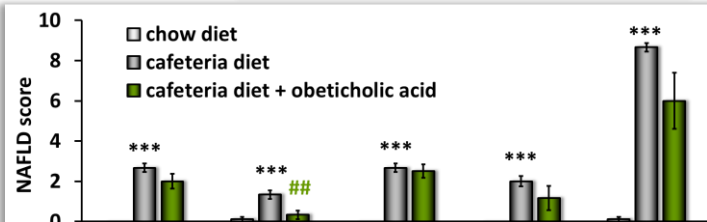
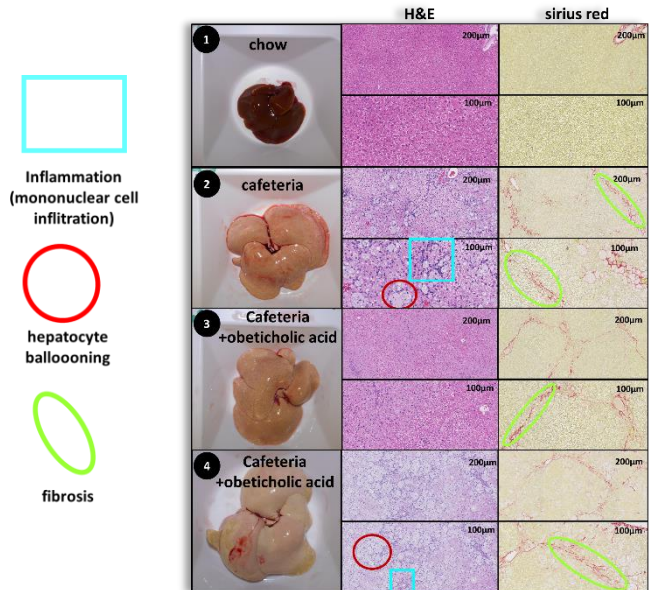
*p<0.05, **p<0.01 and ***p<0.001 vs. chow

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



***p<0.001 cafeteria vs. chow, #p<0.05 and ##p<0.01 cafeteria vs. cafeteria + obeticholic acid

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



Liver aspect, representative histology (1: chow; 2: cafeteria; 3: cafeteria + obeticholic acid showing NAFLD improvement; 4: cafeteria + obeticholic acid showing no NAFLD improvement), and NAFLD scoring.