Physiogenex
THE METABOLIC DISEASES EXPERTS

Diet-induced NASH mouse models associated with metabolic syndrome

- ✓ Unique diet-induced mouse models of non-alcoholic steatohepatitis (NASH)
- ✓ Associated with obesity and insulin resistance like in a human NAFLD physiopathological context

Key benefits

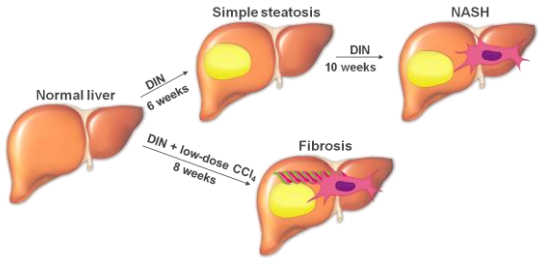
Unique proprietary diet-induced animal models that enables pharmacological studies targeting NASH or fibrosis, in obesity and insulin resistance context.

The diet–induced DIN™ NASH *in vivo* package features:

- Mouse models to study NASH or fibrosis, associated with metabolic syndrome
- Allows to study mechanisms involved in NAFLD progression
- Predictive model: similar to human situation where the diet plays a major role in the development of NAFLD

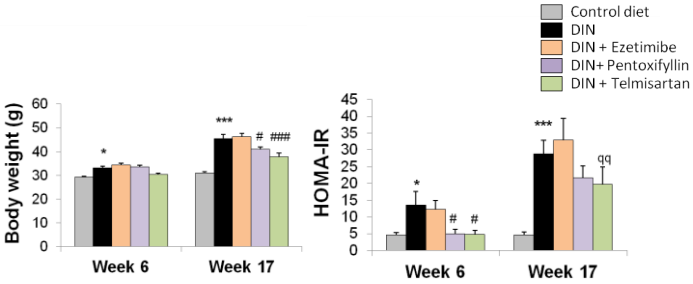
ANIMAL MODEL

- Background strain/gender: C57BL/6J mice, male
- In house "Diet-Induced NASH" (DIN™): High Fat +cholesterol + fructose
- Reference compounds: ezetimibe, pentoxifyllin and telmisartan
- Experimental design:

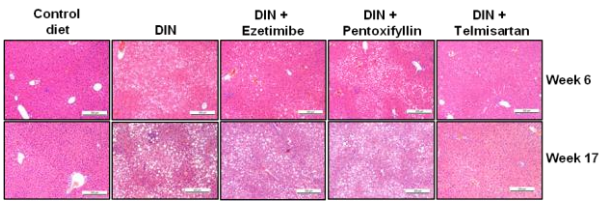


PATHOPHYSIOLOGICAL FEATURES

DIET INDUCED OBESITY AND INSULIN RESISTANCE

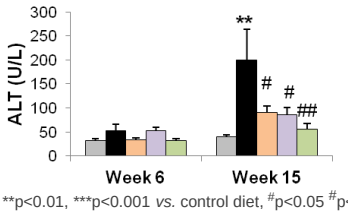


LIVER STEATOSIS (HE staining)



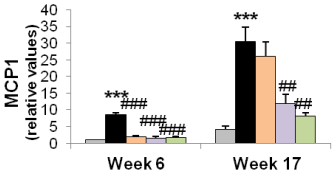
LIVER INJURIES

•Plasma biomarker

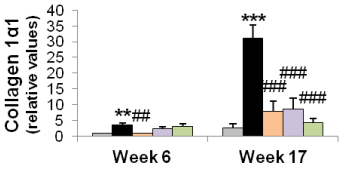


*p<0.05, **p<0.01, ***p<0.001 *vs.* control diet, #p<0.05 #p<0.01 ###p<0.001 *vs.* DIN, qq<0.01 *vs.* DIN without ezetimibe group

Inflammation (qPCR)

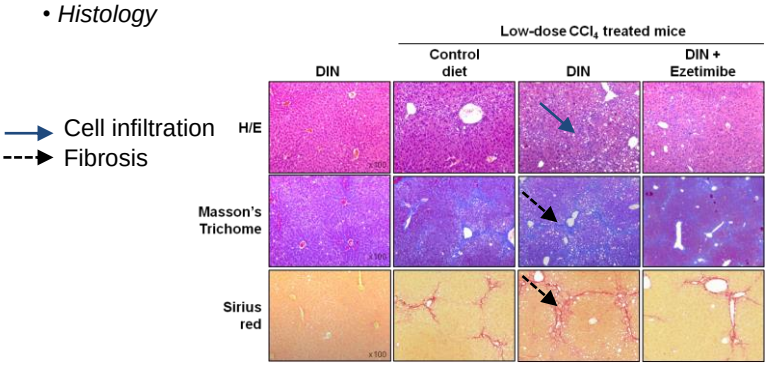


Fibrosis (qPCR)

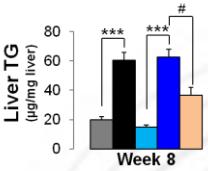


PROGRESSION TO FIBROSIS : DIN + LOW DOSE CCl_4

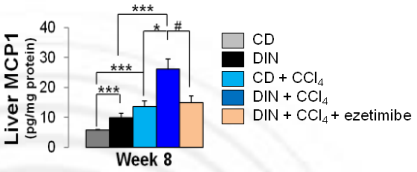
• *Histology*



Steatosis (Triglycerides)



Inflammation (ELISA)



END-POINTS

- Anatomopathology (histology, immunohistology)
- Plasma and liver biomarkers:
  - lipids, inflammation
  - liver enzymes
  - gene expression quantification (qPCR): standard biomarkers and others on request

REFERENCES

Dubuquoy C et *al*. Effects of pharmacological compounds on *in vivo* models of NAFLD associated to metabolic syndrome. SFD, 2014.

Sulpice T. et *al*. Prevention of liver damages by targeting different physiological mechanisms in a new murine NASH model associated with metabolic syndrome. World Diabetes Congress, 2013.

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