Gubra DIO-NASH model

The industry golden standard biopsy-confirmed DIO-NASH fibrotic mouse model.

Gubra diet-induced obese (DIO) and biopsy-confirmed mouse model of NASH with hepatic fibrosis

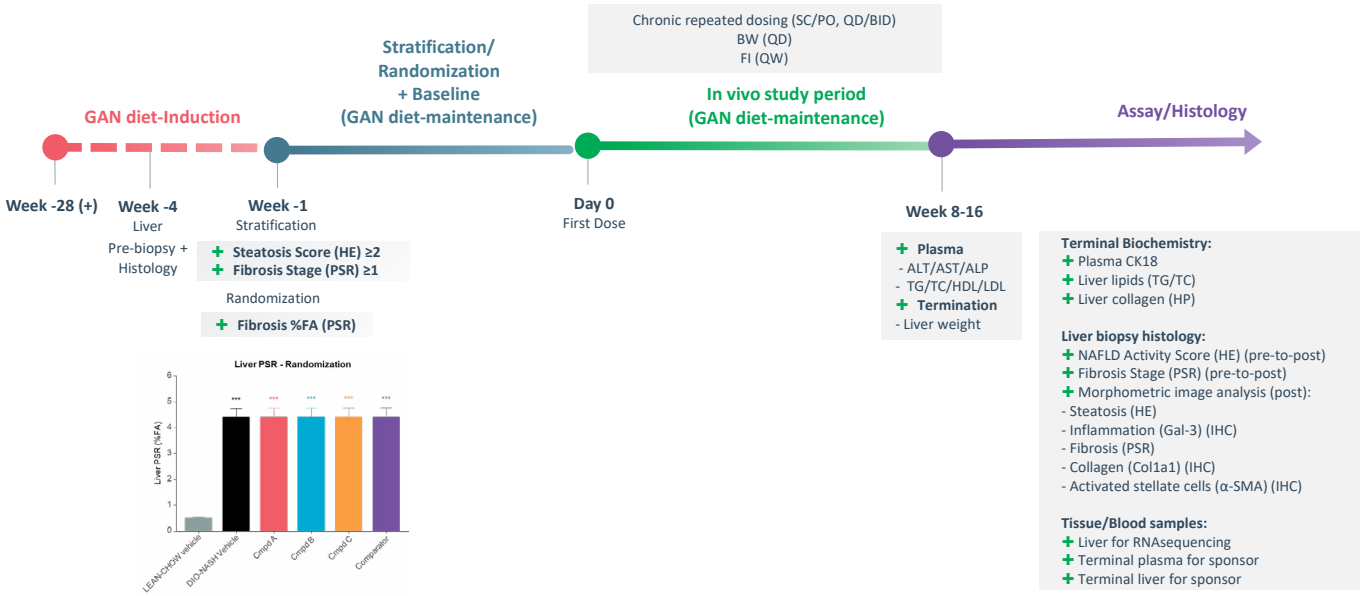
The DIO-NASH mouse model exhibits key hallmarks of metabolic-associated advanced NASH including liver fibrosis, uniquely identified by baseline liver biopsy and objectively evaluated by individual histopathological pre-to-post changes in clinically-derived NAFLD Activity Score and Fibrosis Stage.

Key model traits

- GAN diet high in fat, fructose and cholesterol for ≥28 weeks before study start.
- Diet-induced obesity (DIO) and metabolic disease.
- Chronic onset of biopsy-confirmed steatosis and fibrosis.
- Slow progression to bridging fibrosis (F3) and hepatocellular carcinoma (HCC).
- Clinical histopathological endpoints (pre-to-post).
- Therapeutic evaluation of drug efficacy.

Diet	40% fat (palm oil) 40% carbohydrates (20% fructose) 2% cholesterol	Gubra Amylin NASH (GAN) diet. Minimum 28 weeks on diet to develop DIO-NASH fibrotic phenotype
Strain	Male and female C57BL/6J mice	

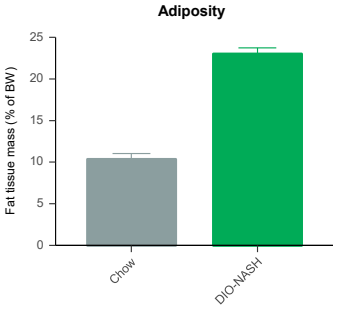
Study outline

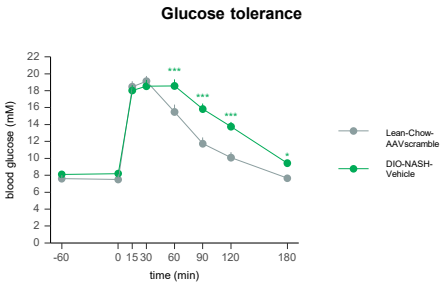


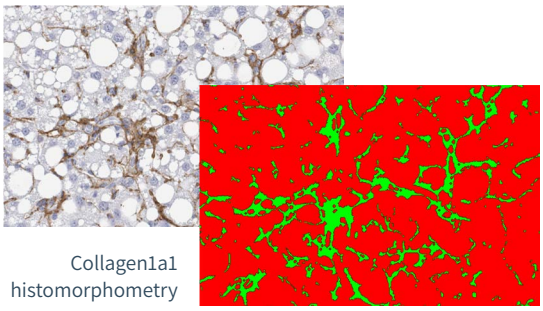
Metabolic, biochemical and histopathological characteristics

DIO-NASH mice develop characteristics of the metabolic syndrome, including obesity and impaired glucose tolerance. DIO-NASH mice display significantly elevated quantitative markers of liver lipid accumulation, inflammation and fibrosis.

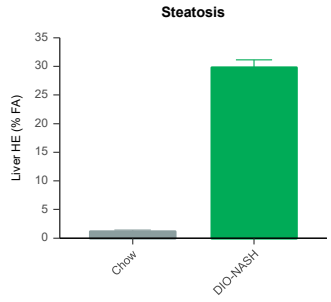
	CHOW	DIO-NASH
Body weight (g)	28.3 ± 0.8	41.6 ± 0.6
Liver weight (g)	1.3 ± 0.1	3.1 ± 0.3
Plasma insulin (pmol/l)	336 ± 39	775 ± 60
Plasma ALT (U/L)	29.5 ± 1.9	166 ± 16
Plasma total CK-18 (ng/ml)	0.11 ± 0.02	0.83 ± 0.12
Liver triglycerides (mg/g tissue)	7.4 ± 0.7	94.0 ± 5.4
Liver MCP-1 (pg/g tissue)	30 ± 4.7	1,759 ± 304
Liver hydroxyproline (µg/mg tissue)	0.03 ± 0.01	0.08 ± 0.01

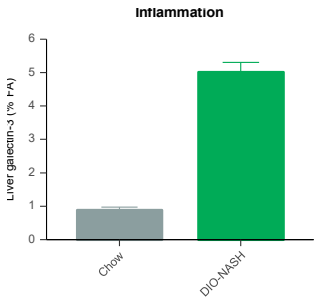


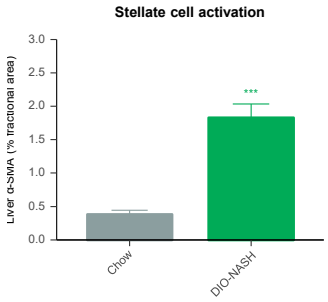


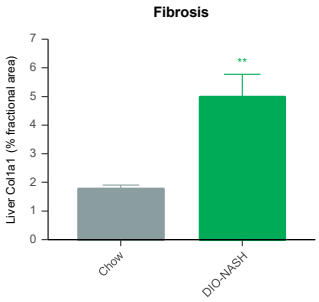


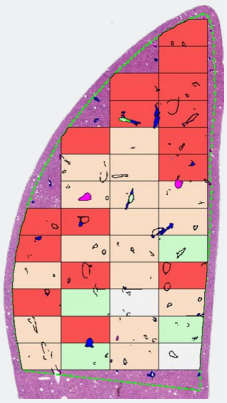
Collagen1a1 histomorphometry

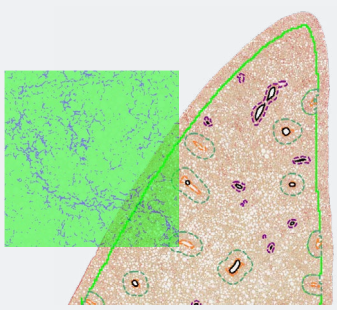


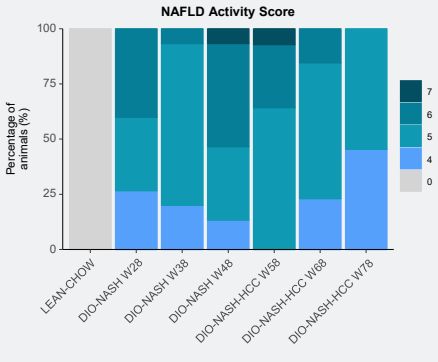


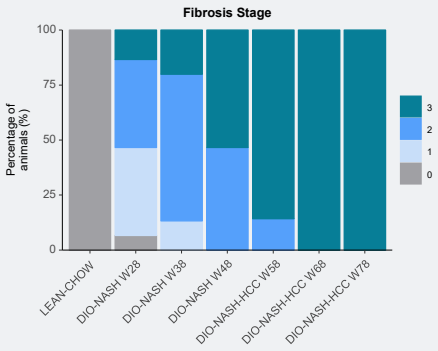












Clinical histopathological scoring

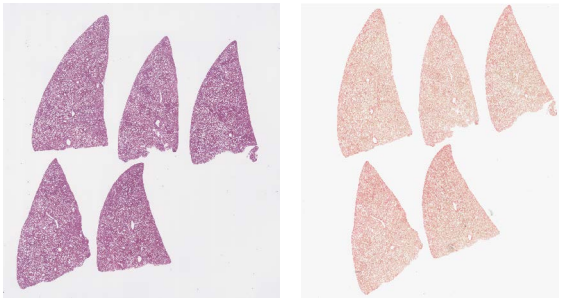
Application of clinical-derived NAFLD Activity Score (NAS) and Fibrosis Stage (Kleiner, 2005). NAS is a composite score of steatosis, lobular inflammation and ballooning degeneration.

All features are assessed using our in-house developed deep learning based APP (GHOST – Gubra Histopathological Objective Scoring Technology).

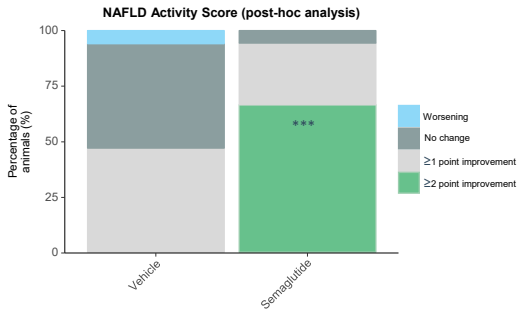
Find more information on GHOST here

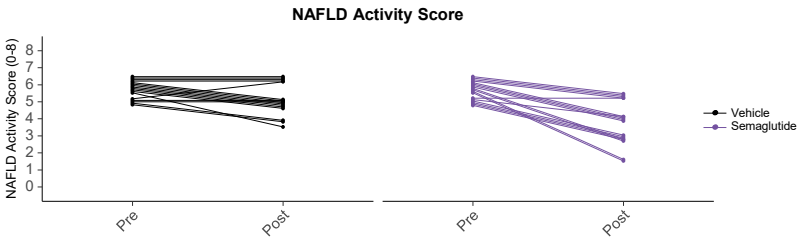
Individual pre-to-post NAFLD Activity Score and Fibrosis Stage

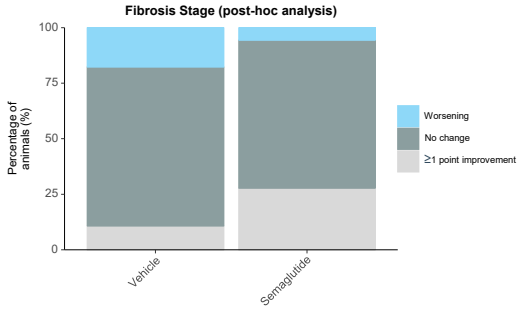
Assessment of pre-to-post NAFLD Activity Score and Fibrosis stage allows for evaluation of individual treatment effects on liver histopathology. Effect of 12 weeks of treatment with the GLP-1 analogue semaglutide.

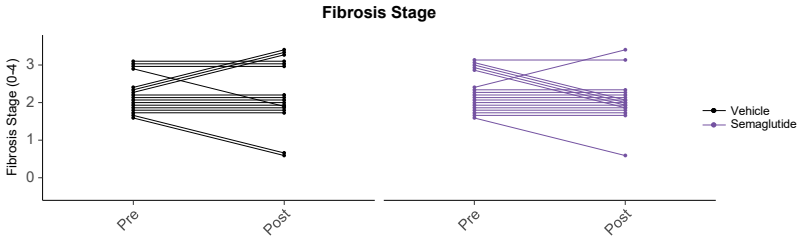


HE (left) and PSR (right) stained biopsies.



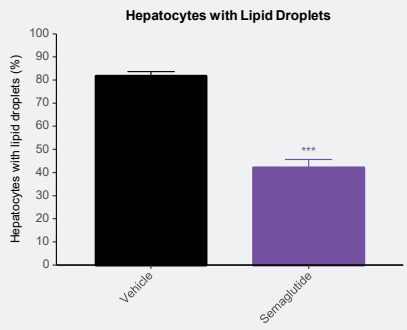


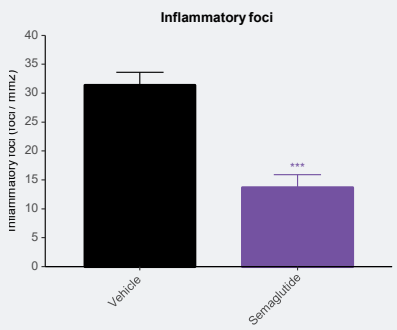


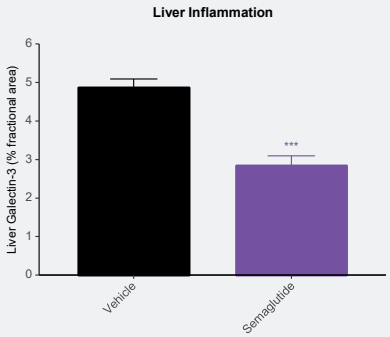


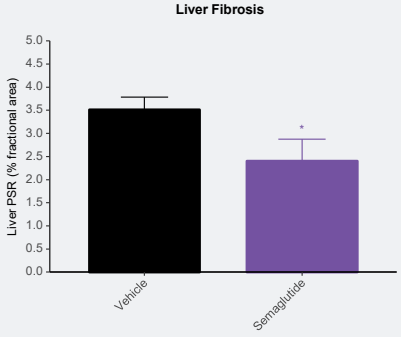
Histomorphometric evaluation of steatohepatitis and fibrosis

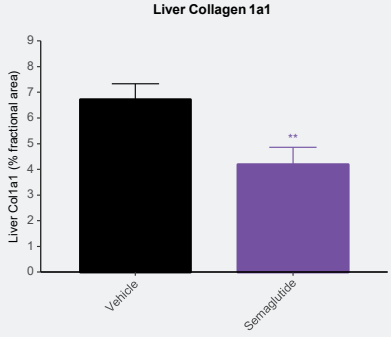
Quantitative assessment of liver steatosis, inflammation and fibrosis by histomorphometric image analysis. Effect of 12 weeks of treatment with the GLP-1 analogue semaglutide.

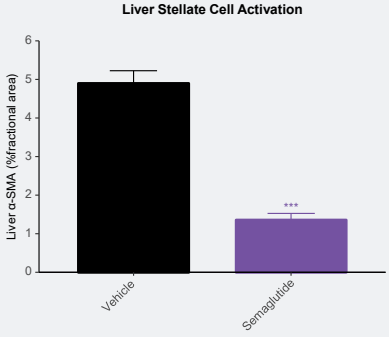






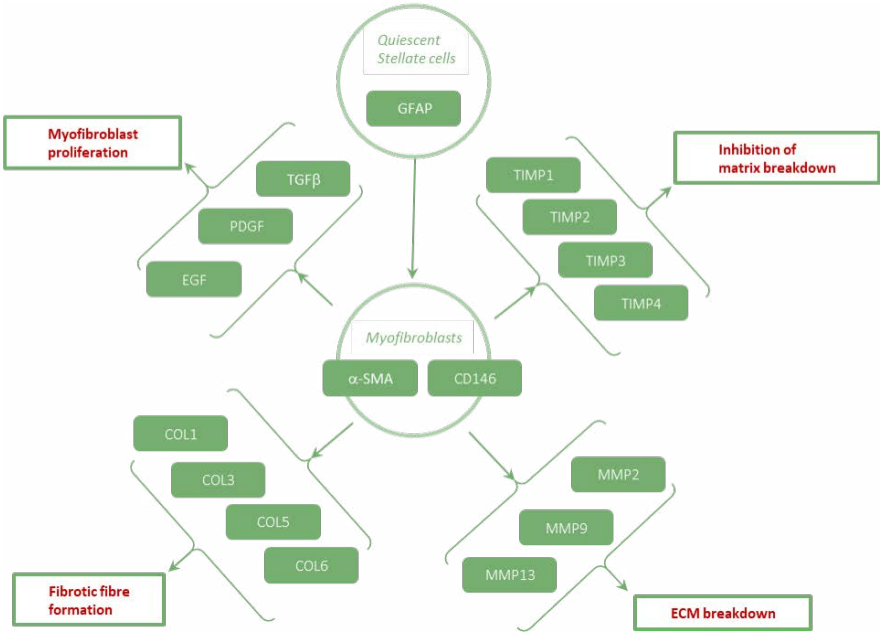


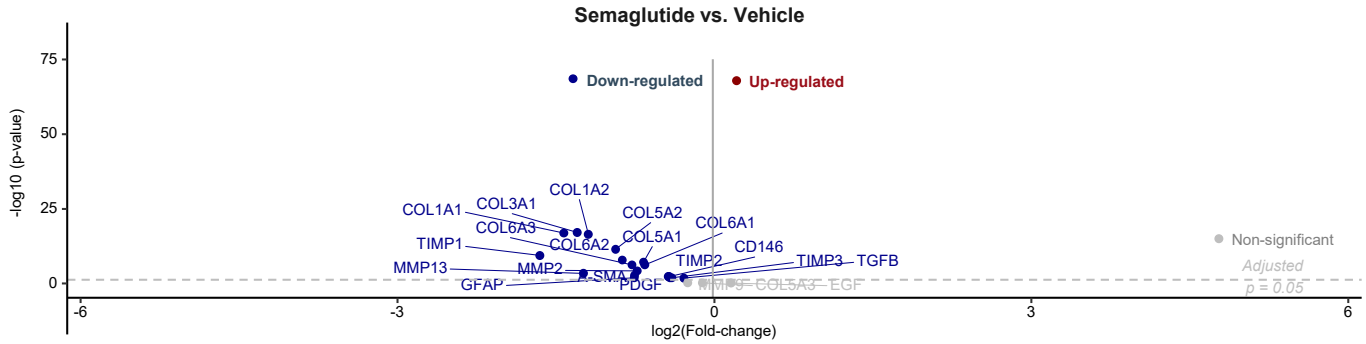


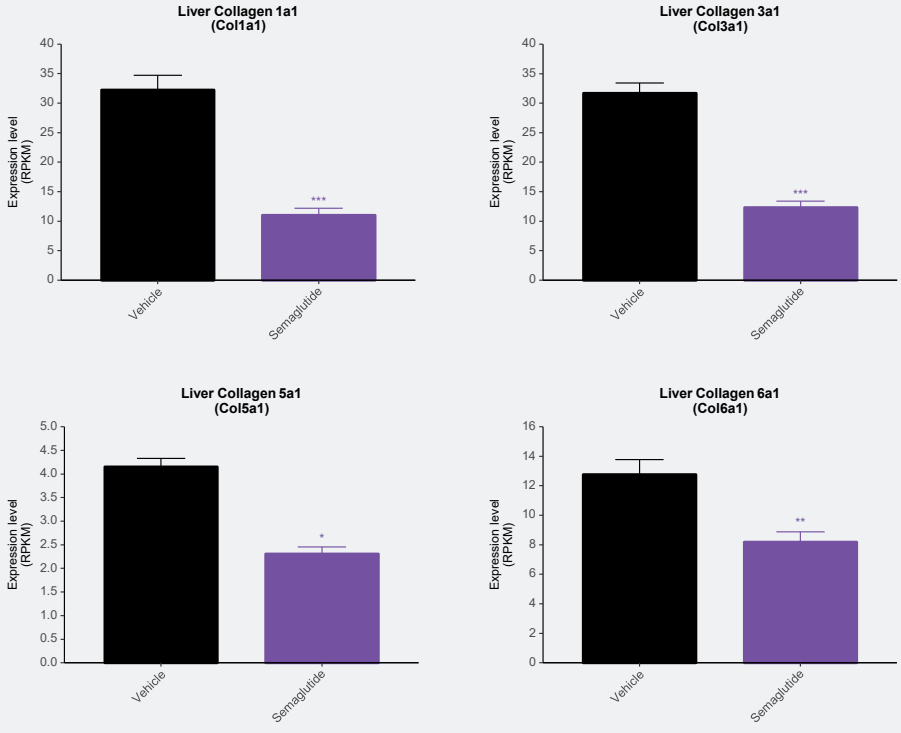


RNAsequencing including bioinformatic analysis

Gubra has developed a customised bioinformatic pathway analysis with key genes involved in NASH and fibrosis progression (**right**). Effect of 12 weeks of treatment with the GLP-1 analogue semaglutide on genes involved in fibrogenesis (**below**).







Gene and Pathway analysis

RNAsequencing gives the full overview of transcriptomic regulation in combination with pathway analysis.

All liver expressed genes are analysed simultaneously and can easily be explored.