

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

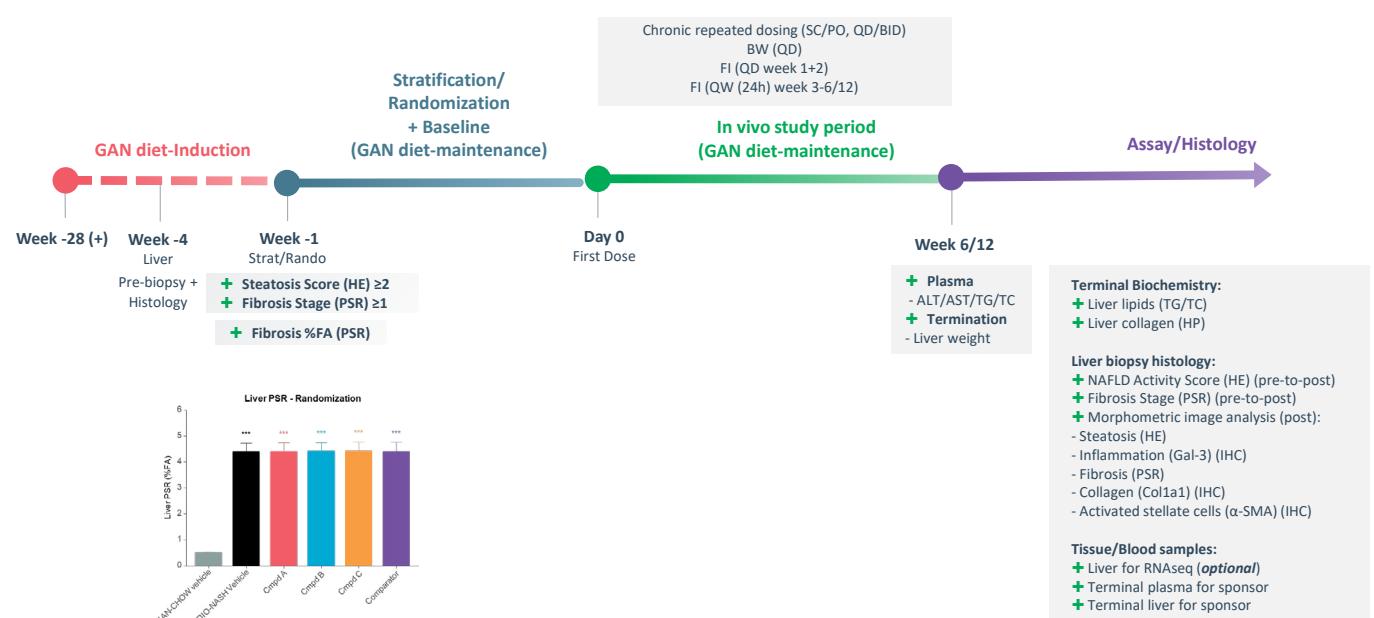
The DIO-NASH mouse model exhibits key hallmarks of metabolic-associated advanced NASH including liver fibrosis, uniquely identified by baseline liver biopsy and objectively evaluated by individual histopathological pre-to-post changes in clinically-derived NAFLD Activity Score and Fibrosis Stage.

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 (stage F3) and 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; D09100310 Research diets Minimum 28 weeks on diet to develop DIO-NASH fibrotic phenotype
Strain	Male and female C57BL/6J mice	

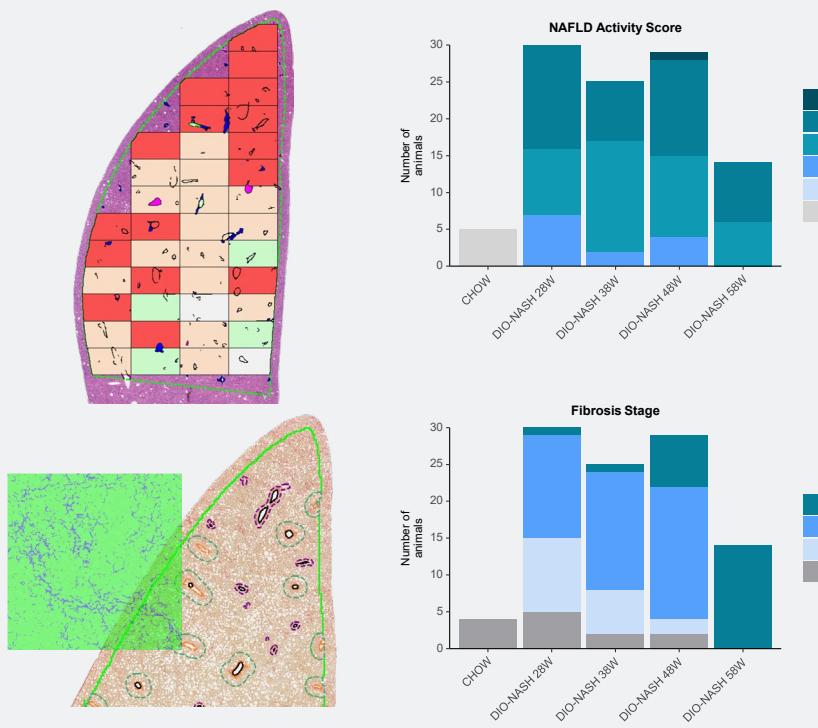
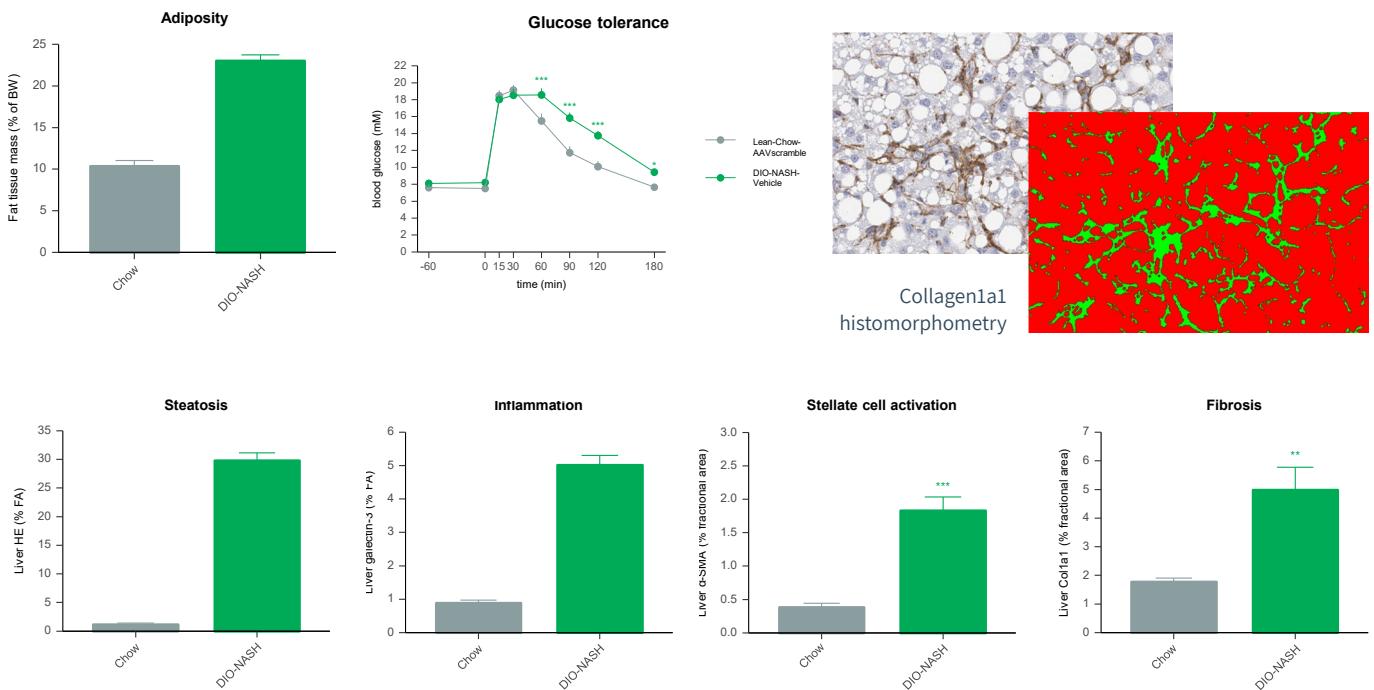
Study outline



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



Clinical histopathological scoring

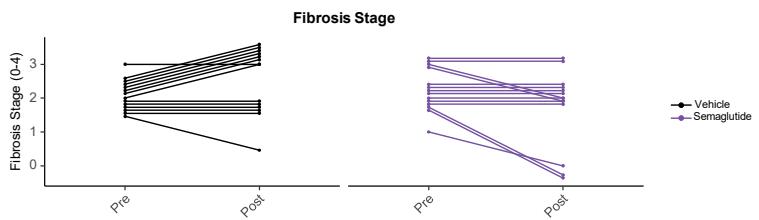
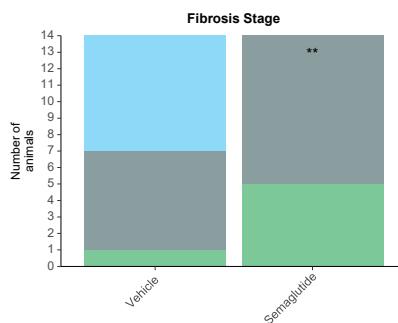
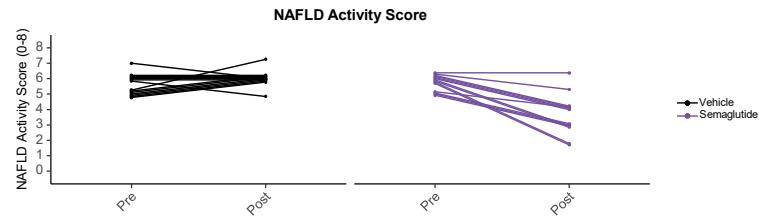
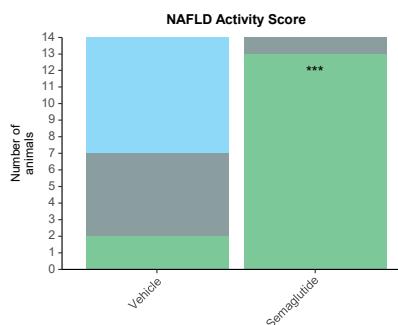
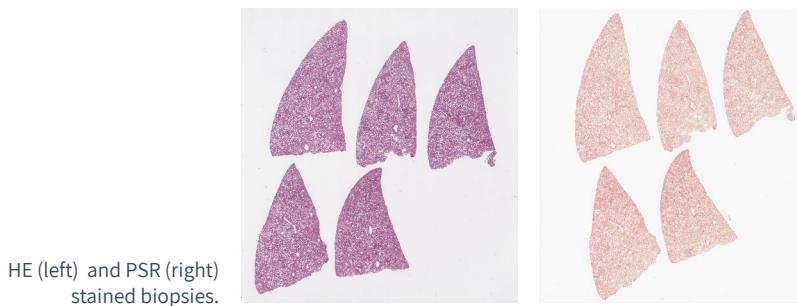
Application of clinical-derived NAFLD Activity Score (NAS) and Fibrosis Stage (Kleiner, 2005). NAS is a composite score of steatosis, lobular inflammation and ballooning degeneration.

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](#)

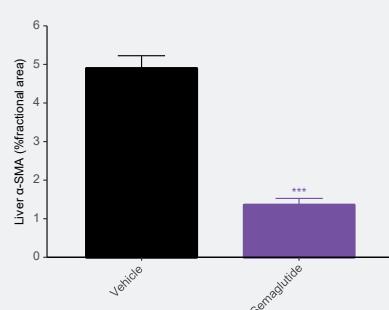
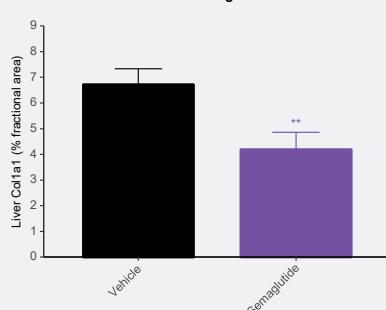
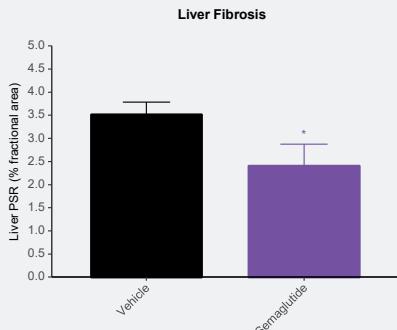
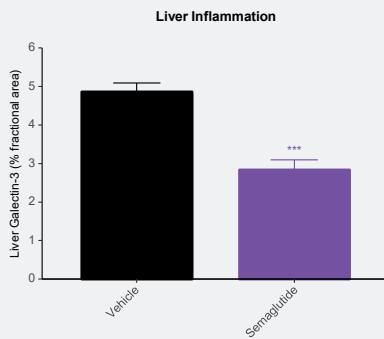
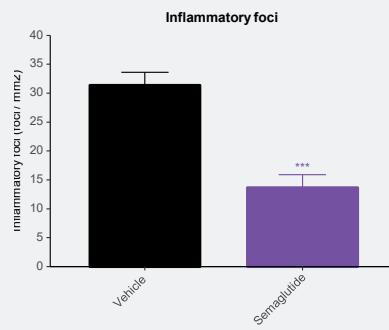
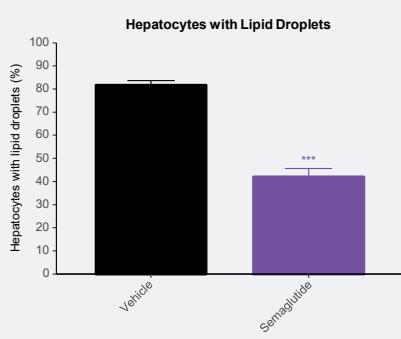
Individual pre-to-post NAFLD Activity Score and Fibrosis Stage

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.



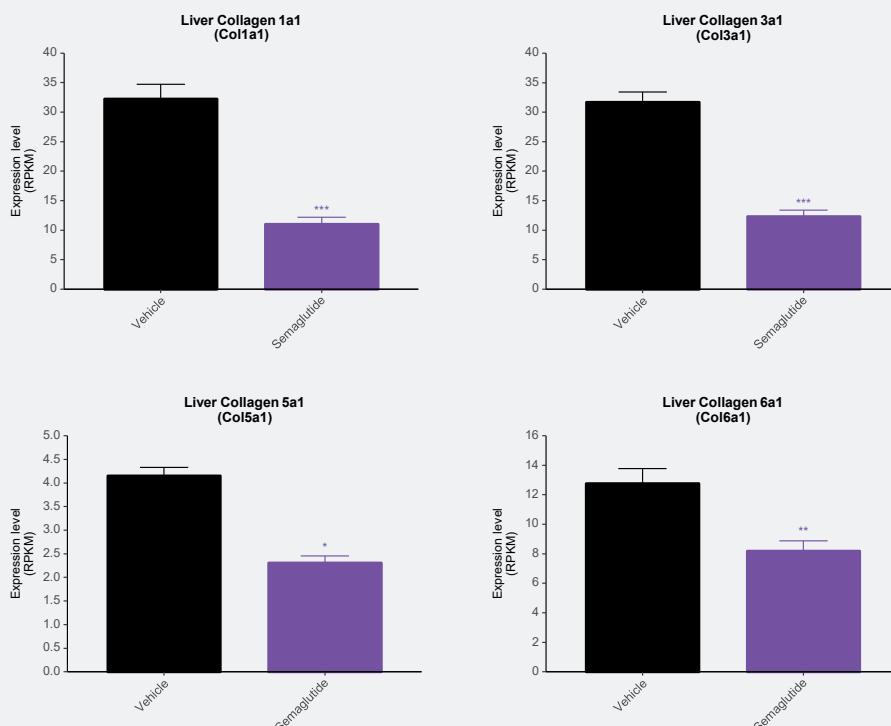
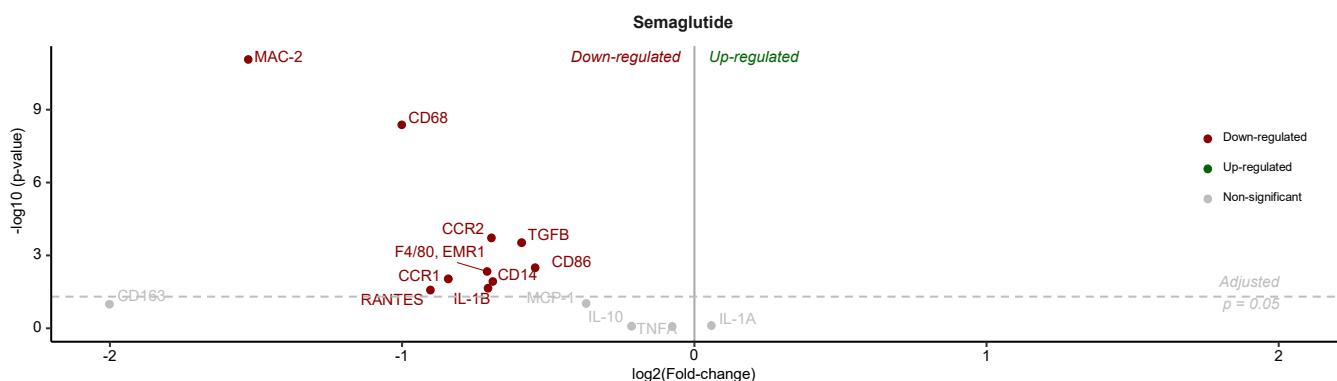
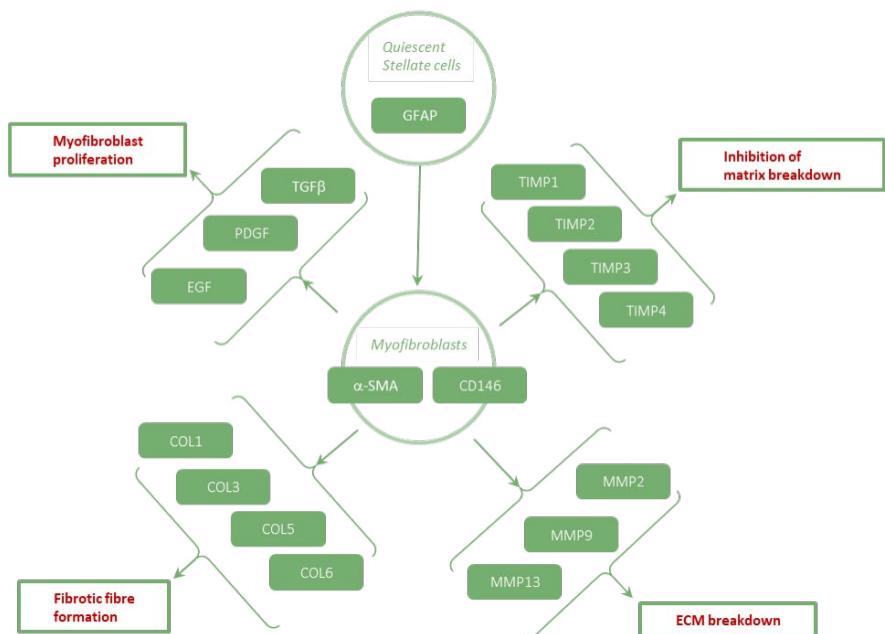
Histomorphometric evaluation of steatohepatitis and fibrosis

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.