GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MICE
Mutant inbred

B6 DIO MASH Mouse

Strain name:
C57BL/6JRj

Type: Inbred mouse

Origin: CSAL (Orléans) - 1993 (F172)

Colour and related genotype:
Black mouse

Presentation of the model

Non-alcoholic fatty liver disease (NAFLD) and its progressive form, metabolic-associated steatohepatitis (MASH), are rapidly growing global health concerns closely linked to obesity, insulin resistance, and metabolic syndrome. To support the preclinical evaluation of novel therapeutics in this field, robust and translational animal models are essential.

The Janvier Labs DIO MASH mouse model (Diet-Induced Obese Metabolic Associated Steatohepatitis) is a nutritionally induced model that replicates key features of human MASH development, including progressive hepatic steatosis, lobular inflammation, ballooning degeneration and fibrosis. This model is generated by exposing genetically predisposed mice to a high-fat, high-fructose, and high-cholesterol diet over an extended period, resulting in a clinically relevant phenotype that mirrors the pathophysiology of human MASH.

We evaluated this model at three key timepoints following start of the diet—week 15, 25, and 35—to monitor the progression of metabolic and hepatic alterations.

Validation data:

Figure 1. Insulin resistance and liver weight progression in DIO MASH model, compared to control C57BL6/JRj mice under a chow diet (n=8 per group)

At week 15, DIO MASH mice exhibit early signs of insulin resistance and a modest increase in liver weight, indicating initial metabolic stress. By week 25, insulin resistance becomes more pronounced, accompanied by a significant increase in liver weight, suggesting hepatic lipid accumulation. At week 35, hepatomegaly sustains in DIO MASH mice. However, insulin resistance parameters have started to decrease, resulting from hepatic lesions whose severity is increased with MASH development.

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Validation data:

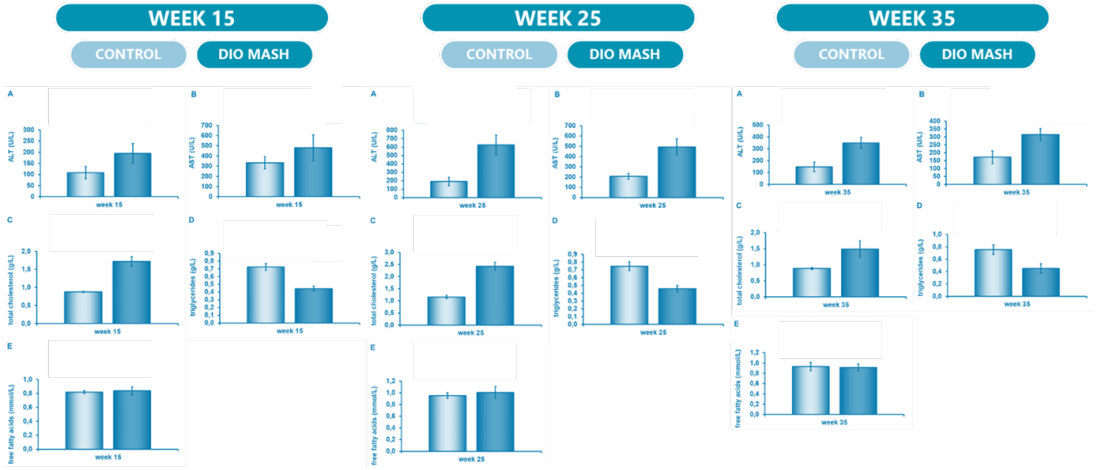

Figure 2. Biochemical characterization of DIO MASH models highlights the progression of liver injury

At week 15, DIO MASH mice show moderate elevations of plasma liver enzymes (ALT and AST), suggesting the onset of hepatocellular injury. Additionally, the increase in total cholesterol reflects early metabolic alterations. At week 25, a clear worsening of liver injury is observed, with further increases in ALT and AST levels. Cholesterol is significantly elevated, indicating advanced steatosis and dyslipidemia. At week 35, DIO MASH mice maintain elevated ALT and AST levels, confirming sustained liver injury. Total cholesterol remains significantly higher than in controls, showing persistent metabolic dysregulation.

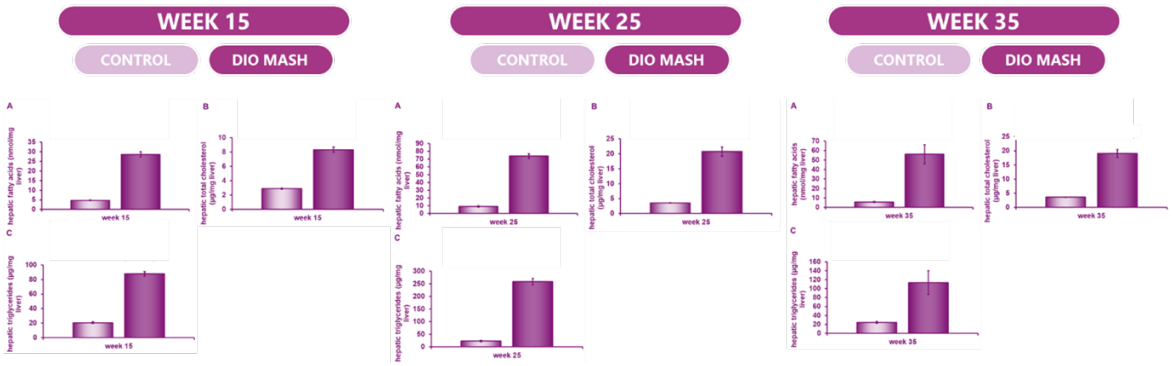

Figure 3. Hepatic lipid accumulation in DIO MASH mice and control mice over time (n=8 per group).

A significant accumulation of liver lipids is observed in DIO MASH mice at week 15 compared to control mice, which is increased by week 25 under high-fat diet. The data reflect progression toward moderate steatosis. At week 35, hepatic lipid levels remain elevated, confirming persistent and advanced steatosis in the DIO MASH model.

Validation data:

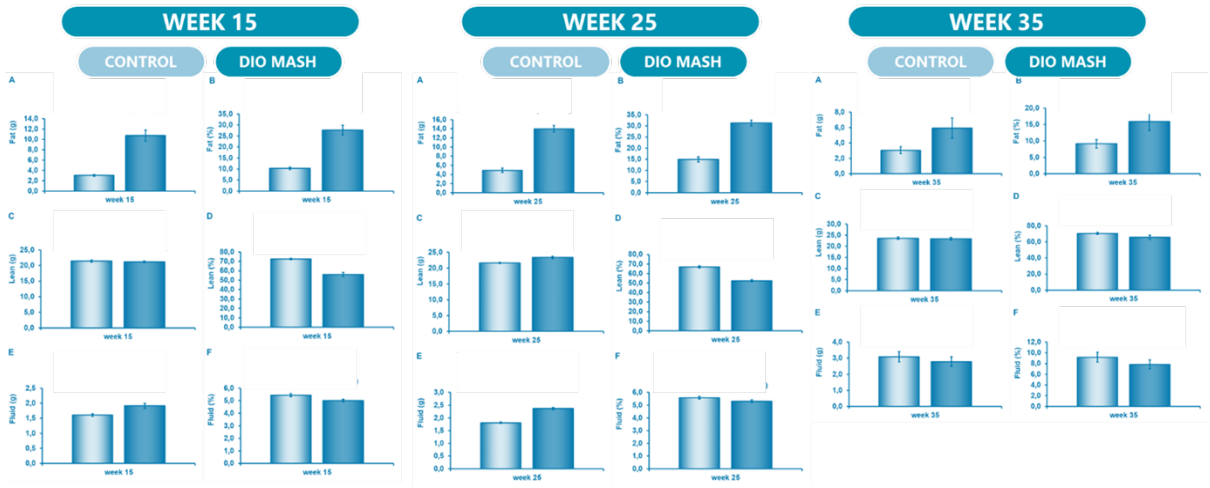

Figure 4. Alterations in body composition in DIO MASH and control mice over time (n=8 per group).

At week 15, DIO MASH mice show increased fat mass compared to controls, with early signs of lean mass reduction. By week 25, fat accumulation intensifies, and lean/fat ratio shifts significantly. At week 35, body composition remains altered, with sustained adiposity and reduced lean mass, consistent with chronic metabolic imbalance.

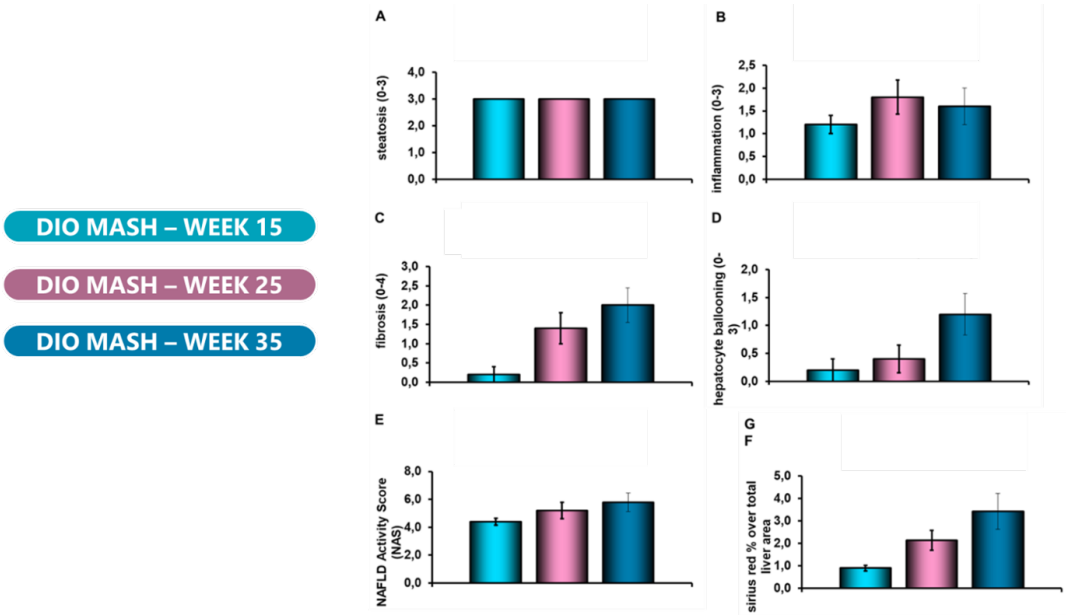

Figure 5. Histological progression of liver pathology in DIO MASH mice

Liver histology (H&E staining) reveals that DIO MASH already features severe steatosis after 15 weeks under high fat diet, confirmed by a high NAFLD activity score. Between week 15 and 25 appears the first signs of inflammation and fibrosis (Sirius Red staining). At week 35, histological analysis confirms advanced steatosis, persistent inflammation, and established fibrosis and hepatocyte ballooning, mirroring the pathological features of human MASH.

Altogether, the Janvier Labs DIO MASH model successfully replicates the progressive nature of human MASH. Key features include the development of insulin resistance, sustained elevations in liver enzymes (ALT and AST), increased hepatic lipid accumulation, and histological evidence of steatosis, inflammation, and fibrosis. These characteristics make the model highly suitable for evaluating therapeutic interventions targeting metabolic dysfunction and liver pathology, as well as for exploring disease mechanisms and biomarker discovery.

Main application and research fields

INFECTIOUS DISEASES

METABOLIC DISORDERS

Our added value

- The «JANVIER LABS Genetic Policy», specific programme, guarantees homozygosity of autosomal pairs
- Animals with the SPF or SOPF standards
- A gentling policy for docile and easy-to-handle animals
- Optimal stability conditions of our models during shipments, thanks to our dedicated and internal transport service
- A scientific support with a team of Veterinarians and PhD

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