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Preclinical Liver Disease Research

Translational Disease Models for Drug Discovery

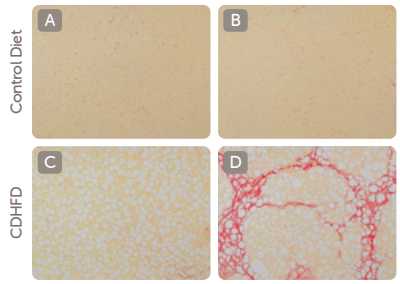
Accelerate liver disease drug discovery with Inotiv's portfolio of translational *in vivo* liver disease models. Our offerings span acute and chronic indications, including fibrosis, MASH, and steatosis. Supported by integrated pharmacology expertise and customizable study design, these models enable robust evaluation of therapeutic efficacy, safety, and disease-relevant mechanisms across multiple stages of liver disease progression.

MASH Rodent Models

Rodent MASH (metabolic dysfunction-associated steatohepatitis) models mimic human disease, showing steatosis, inflammation, and fibrosis. Diet-induced models allow testing of therapies and mechanisms, linking MASH progression to metabolic and cardiometabolic risks.

- Choline Deficient High Fat Diet (CDHFD)-Induced MASH

Figure 1 Collagen Deposition in the CDHFD Model



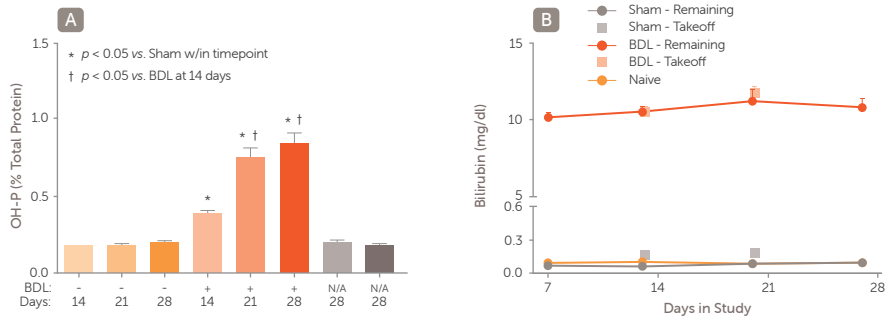
Picrosirius red staining of liver sections from CDHFD-induced MASH and control diet animals at 4 weeks (**A, C**) and 20 weeks (**B, D**). Marked collagen deposition is observed in CDHFD animals at 20 weeks, with minimal staining in controls.

Liver Fibrosis Rodent Models

Rodent liver fibrosis models mimic human disease, including inflammation, matrix buildup, and scarring. They enable testing of anti-fibrotic therapies and support translational liver research.

- Bile Duct Ligation (BDL)-Induced Fibrosis
- Carbon Tetrachloride-Induced Fibrosis
- Thioacetamide-Induced Fibrosis

Figure 2 Fibrosis and Liver Function in the BDL Model



Assessment of fibrosis and liver function in BDL sham control animals. Percent hydroxyproline (OH-P) relative to total liver protein (**A**) and serum total bilirubin levels (**B**) measured at indicated timepoints. OH-P, a collagen-specific amino acid, reflects tissue collagen content. Bilirubin levels are a marker of impaired bile flow and cholestasis.

In Vivo Capabilities

- Survival surgeries
- Glomerular filtration rate (MediBeacon®)
- Blood pressure (tail-cuff, telemetry)
- Body composition (qNMR)
- Ultrasound imaging and analysis
- Blood glucose (Glucometer)
- Glucose (GTT) and insulin (ITT) tolerance tests
- 24-hour urine collection (metabolic cages)
- Sample collection (e.g., blood, BALF, urine, tissue)
- Compound dosing (e.g., i.p., i.v., p.o., s.c., infusion)

Translational Biomarkers and Pathways

- Clinical chemistry
- Hematology
- Flow cytometry
- mRNA expression analysis
- Protein quantification
- Global and targeted proteomics
- Spatial transcriptomics
- Customized analyte development
- Pharmacokinetics and drug metabolism
- Investigative and molecular pathology
- Immunohistochemistry/ Immunofluorescence
- Image analysis by veterinary pathologist

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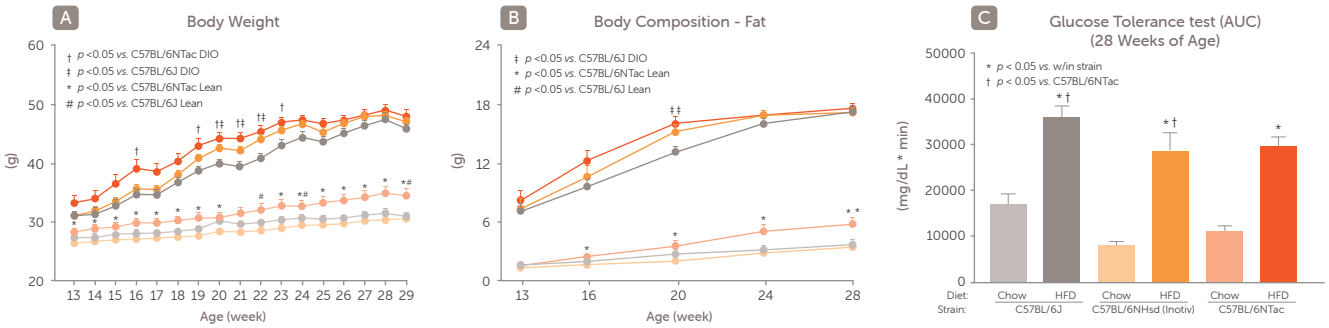
DIO Mouse Model of Liver Steatosis

Diet-induced obesity (DIO) models are widely used to study liver steatosis driven by metabolic dysfunction. In high-fat diet (HFD)–fed mice, obesity, insulin resistance, and hepatic lipid accumulation develop, enabling evaluation of therapeutic strategies targeting metabolic pathways that contribute to fatty liver disease progression.

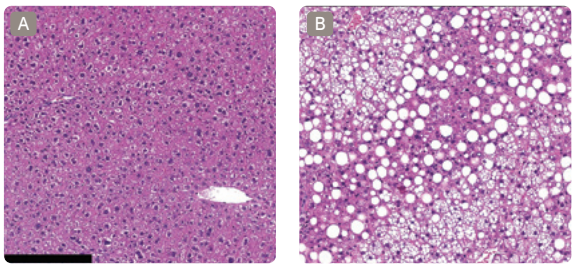
Figure 3 Physiological Characterization of Inotiv's DIO Mouse Model



Inotiv's DIO model, induced in C57BL/6NHsd mice, shows expected body weight gain (A), increased adiposity (B) and impaired glucose handling (C) like existing commercial models.

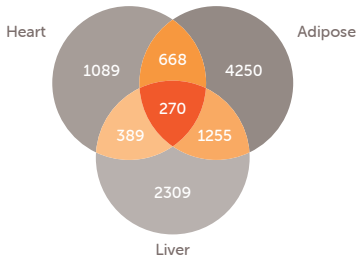
C57BL/6NHsd Lean (Inotiv) · C57BL/6J Lean · C57BL/6NTac Lean
C57BL/6NHsd DIO (Inotiv) · C57BL/6J DIO · C57BL/6NTac DIO

Figure 4 HFD-Induced Hepatic Lipidosis in Mice



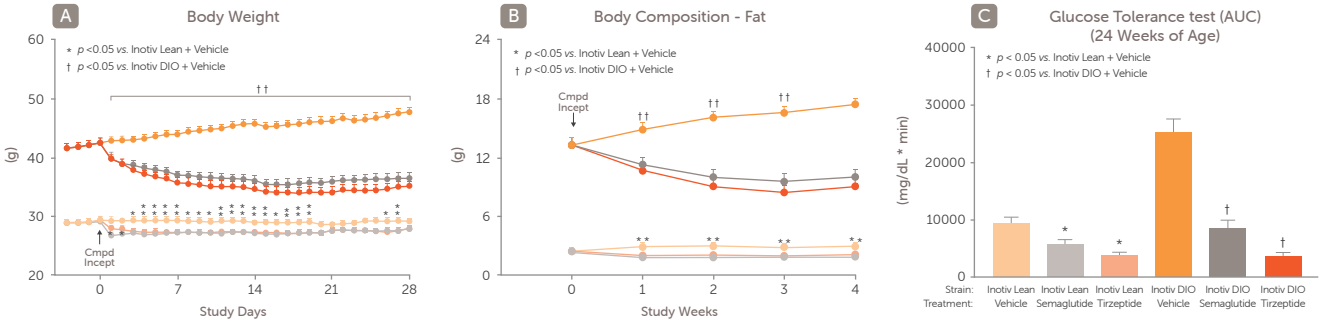
Stained liver sections from mice on standard laboratory diet (A) or HFD (B). Mice on HFDs develop hepatic lipidosis, with hepatocyte cytoplasm expanded by lipid vacuoles, most prominent in centrilobular regions.

Figure 5 Tissue-Specific Proteomic Changes in Inotiv's DIO vs. Lean Mice



Overlap of differentially regulated proteins in DIO vs. lean mice across heart, adipose, and liver (q < 0.05) from proteomic analysis.

Figure 6 Efficacy of Incretin-Based Therapies in Inotiv's DIO Mouse Model



DIO mice fed 60% HFD show increased body weight (A), adiposity (B), and impaired glucose tolerance (C) compared to mice fed a standard diet. Treatment with semaglutide or tirzepatide improves these metabolic parameters.

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Contact us at inotiv.com/contact to discuss how our models and services can support your CVRM drug development program.