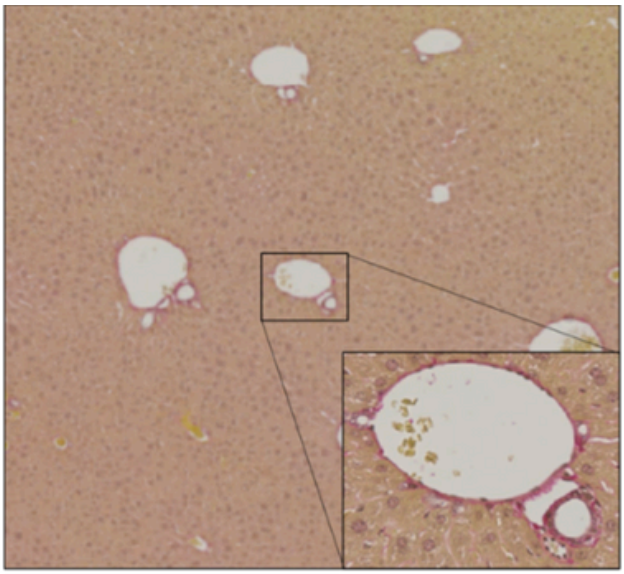
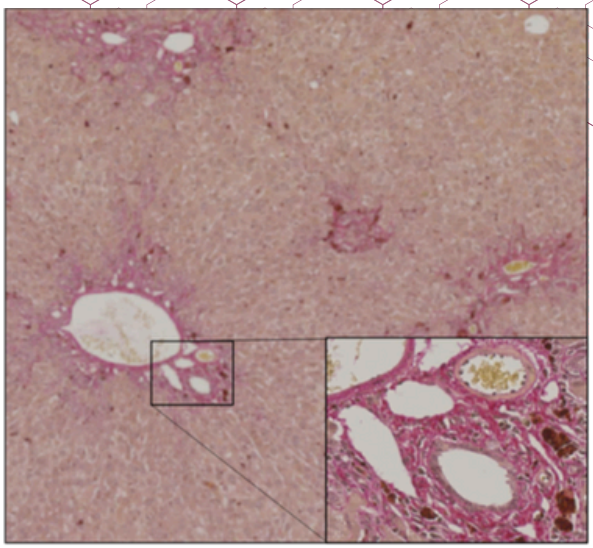
CASE STUDY

Spotlight On: The 3,5-diethoxycarbonyl-1,4-dihydrocollidine (DDC) Mouse Model for Biliary Fibrosis



8 week fed with Chow Diet



8 week fed with DDC Diet

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Overview

Chronic liver diseases, particularly cholangiopathies, are characterized by persistent inflammation, cholestasis, bile duct proliferation, and progressive fibrosis. These complex processes are difficult to replicate in vitro, making translationally relevant animal models essential for drug development.

Why Researchers Choose It

The DDC diet-induced mouse model captures key features of cholangiopathies, especially Primary Sclerosing Cholangitis:

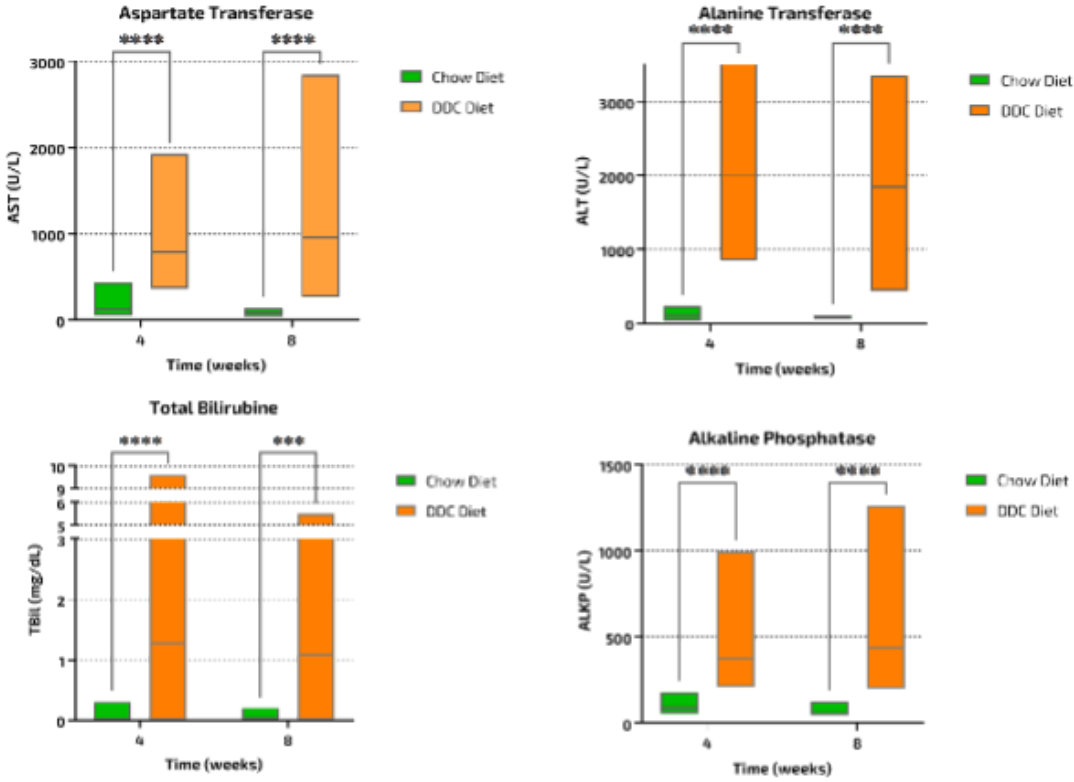
- ✓ Pronounced cholestasis
- ✓ Oxidative stress-induced epithelial injury
- ✓ Inflammatory ductular reaction and bile duct proliferation
- ✓ Hepatocyte dedifferentiation
- ✓ Progressive periductular fibrosis

It provides a **reliable, translational platform** for evaluating **anti-fibrotic and anti-inflammatory drug candidates** in cholestatic liver disease research.

A chemically-induced translational model up to 8 weeks

Let's collaborate! →

Hepatic Injury & Cholestasis Markers (Blood)



- **Alanine transaminase (AST) & Aspartate transaminase (ALT):** Strong elevations at both weeks 4 and 8 (****p≤0.0001), far above physiological ranges, confirming sustained hepatocellular damage.

- **Total Bilirubin:** Significantly increased at both time points (****p≤0.0001) reflecting cholestatic dysfunction.

- **Alkaline Phosphatase (ALP):** Markedly elevated in DDC mice (****p≤0.0001), a hallmark of bile duct injury and cholestasis.

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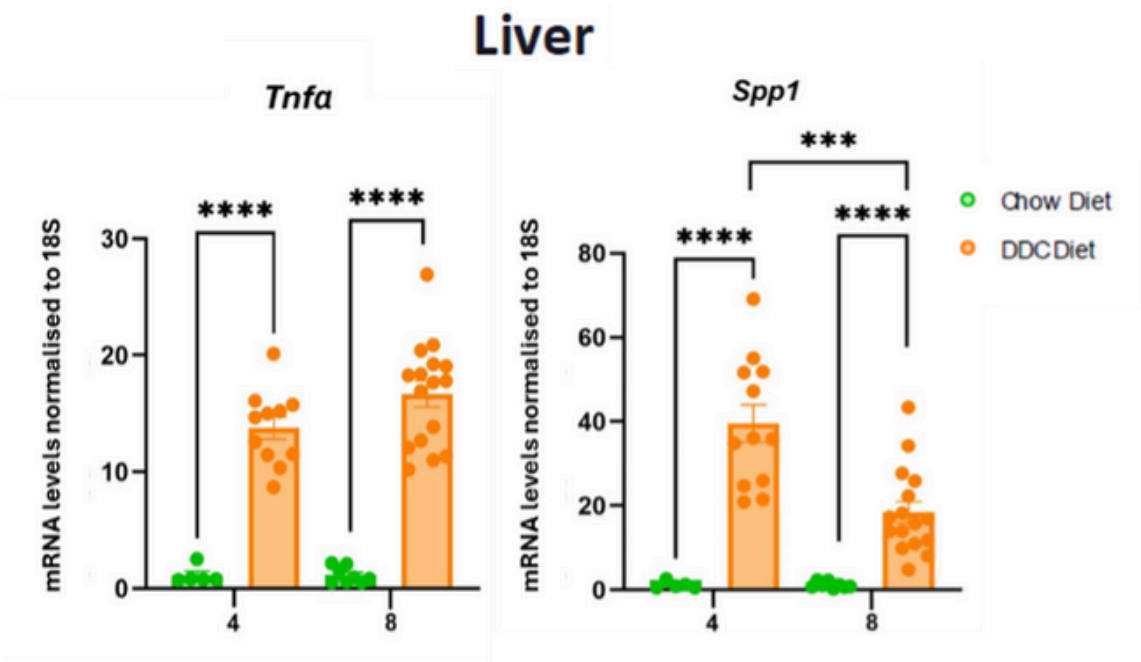
Chronic Inflammation Signatures (qPCR)



- **Tnfα :** tumor necrosis factor alpha gene expression levels markedly upregulated at both week 4 and 8 (****p≤0.0001), confirming persistent pro-inflammatory signaling.

- **Spp1 (osteopontin):** Elevated gene expression at week 4 and sustained at week 8 (****p≤0.0001), supporting a dual inflammatory and fibrogenic role in biliary disease progression.

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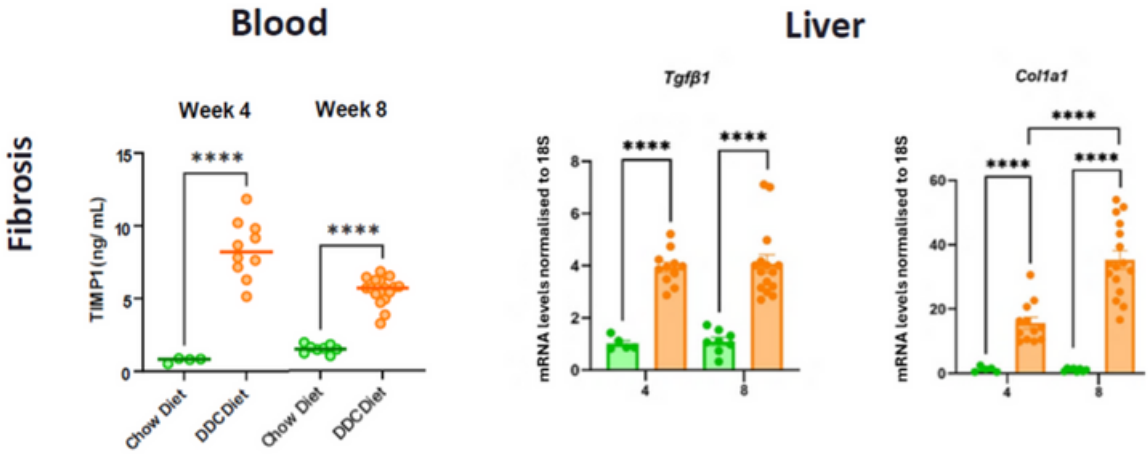
Fibrogenic Remodeling (Blood & Liver)



- **Tissue inhibitor of metallopeptidases 1 (TIMP1) (Blood):** Elevated at both week 4 and 8 (****p≤0.0001), indicating early and maintained fibrogenic activity.

- **Tgfb1 & Col1a1 (qPCR):** Strong upregulation of transforming growth factor beta and collagen type I alpha1 mRNA levels in liver tissue at both time points (****p≤0.0001), confirming active fibrosis progression and extracellular matrix remodeling.

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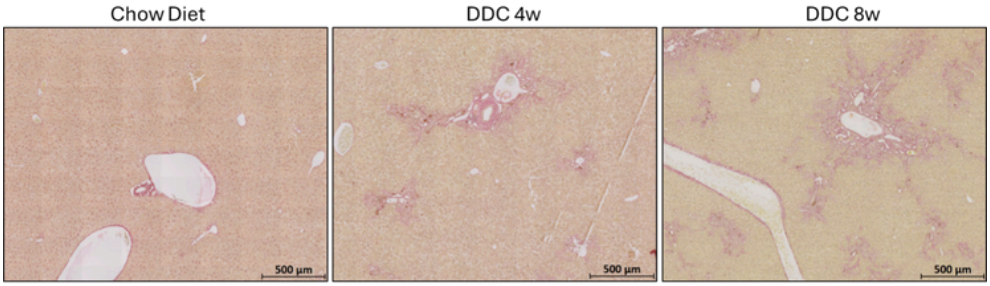
Histology (H&E, Sirius Red)



- **Ductular expansion**
- **Collagen accumulation** in periportal regions (Sirius red staining for collagen deposits detection)

o Marked areas significantly increased in DDC-fed mice

o Inflamed, ulcerated bile ducts associated with **concentric "onion-like" fibrosis**

Conclusion

This model induces chronic inflammation and bile duct injury by week 4, with progressive fibrogenesis and disease stabilization observed by week 8, ideal for evaluating both acute and chronic therapeutic effects.

Are you working on antifibrotic or hepatoprotective compounds? Let's connect to see how the DDC model, or others, can accelerate your liver disease pipeline.

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Let's collaborate!

Dev4All