



[Print this Page for Your Records](#) [Close Window](#)

Control/Tracking Number: 2026-A-2179-SOT

Activity: Abstract

Current Date/Time: 2/23/2026 10:31:11 AM

FXIII-B deficiency increases APAP-induced liver injury without impacting hepatic fibrin(ogen) crosslinking

Author Block: C. D. Schneider¹, Z. Wei¹, K. Kangro², Y. Sang², A. S. Wolberg², and J. P. Luyendyk¹. ¹Michigan State University, East Lansing, MI; and ²University of North Carolina, Chapel Hill, NC.

Abstract:

Background and Purpose: Hepatic deposition of the coagulation protein fibrin(ogen) is a hallmark of acetaminophen (APAP)-induced hepatotoxicity in mice and humans. The transglutaminase coagulation factor XIII (FXIII) covalently crosslinks the majority of fibrin(ogen) deposits in the APAP-injured liver. FXIII circulates in plasma as a heterotetramer (FXIII-A₂B₂) composed of two catalytic (FXIII-A) subunits stabilized by two regulatory (FXIII-B) subunits, the latter synthesized by the liver. FXIII-A₂ is also stored intracellularly in certain cell types (e.g., platelets, macrophages). We tested the hypothesis that plasma FXIII-A₂B₂ drives hepatic fibrin(ogen) crosslinking in the APAP-injured liver.

Methods: To test this hypothesis, we generated novel mice with a selective reduction in plasma FXIII-A₂B₂ by deleting the gene encoding FXIII-B (*F13b*^{-/-} mice). *F13b*^{-/-} mice were then challenged with APAP (300 mg/kg, i.p.) and analyzed after 24 hours.

Results: FXIII-B was not detectable in plasma of *F13b*^{-/-} mice. As anticipated, plasma FXIII-A levels were reduced to less than 3%, while platelet intracellular FXIII-A levels were not impacted. Wild-type mice challenged with APAP developed acute hepatocellular injury indicated by centrilobular necrosis and elevated plasma alanine aminotransferase activity. Hepatic deposition of fibrin(ogen) with abundant Fibrin-γ crosslinking, a modification imposed by FXIII-A, was evident in the liver of APAP-challenged wild-type mice. Unexpectedly, FXIII-B deficiency dramatically increased APAP-induced hepatic necrosis and sinusoidal congestion, an observation that was not present in *F13a1*^{-/-} mice. This increase in injury was not attributable to an increase in APAP adduct formation. Additionally, extravascular fibrin(ogen) deposition and crosslinking (Fibrin-γ) was preserved in the APAP-injured liver of *F13b*^{-/-} mice.

Conclusions: The results indicate that selective loss of plasma FXIII-B (*F13b*^{-/-} mice) does not impact extravascular fibrin(ogen) crosslinking in experimental hepatocellular necrosis, suggesting a potential role of cellular FXIII-A in fibrin(ogen) crosslinking. Furthermore, the results suggest a hepatoprotective effect of FXIII after APAP overdose that is mediated by mechanisms independent of traditional fibrin crosslinking.

Presentation Acknowledgment (Complete): None selected

Category (Complete): Liver: In Vivo ; Clinical and Translational Toxicology

Sponsor (Complete):

Are you or another author of the abstract an SOT member? : Yes

COI/Keyword (Complete):

The authors declare there exist no real or perceived conflict of interest : True

Keyword 1: Liver

Keyword 2: Toxicity; Acute

Abstract Submission Fee (Complete): Your credit card order has been processed on Wednesday 12 November 2025 at 4:30 PM.

Status: Complete

Society of Toxicology
65th Annual Meeting and ToxExpo
March 22–25, 2026

Society of Toxicology
11190 Sunrise Valley Drive, Suite 300
Reston, VA 20191
703-438-3115 Office
sothq@toxicology.org
<http://www.toxicology.org/>

Feedback

Powered by cOASIS, The Online Abstract Submission and Invitation System SM

© 1996 - 2026 CTI Meeting Technology. All rights reserved. [Privacy Policy](#)