

CRO services for Acute Liver Failure

Acute liver failure (ALF) carries a high mortality of approximately 40%, which is caused by viral infections (hepatitis A, B and E), drug allergy or autoimmune hepatitis. ALF exhibits symptoms of severe injury such as destruction of hepatocytes or decrease in liver function due to massive necrosis and inflammation.

Thioacetamide (TAA) represents widely used model for the induction of development of acute liver failure. While TAA itself is not hepatotoxic, its reactive metabolites covalently bind to proteins and lipids thereby causing oxidative stress, inflammation and centrilobular necrosis.

SMC, a Tokyo-based biotech company known as the leading nonclinical CRO for nonalcoholic steatohepatitis (NASH), also provides pharmacology study service of acute TAA model in mice. Our expertise in inflammation/fibrosis is now experienced in liver failure R&D.

TAA-induced acute liver failure model

Animal:

- Female C57BL/6J (7 week-old)

Induction of ALF:

- Injection of TAA

Major endpoint:

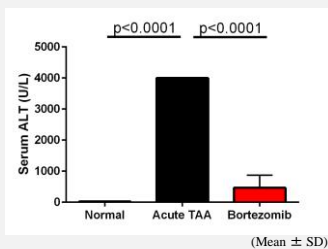
- Histology on liver tissue (HE staining)

Additional endpoints:

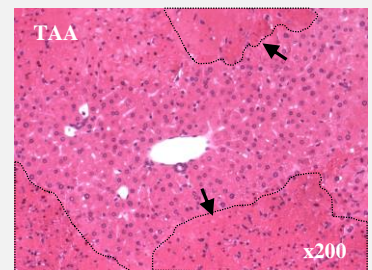
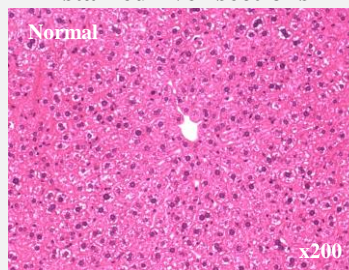
- Blood biochemistry (ALT, AST,...)
- Semi-quantitative RT-PCR (TNF- α , IL-6,...)
- Immunohistochemical analyses for molecular markers
- Cytokines and chemokines in blood and livers by ELISA (TNF- α , IL-6,...)

Evaluation of liver injury

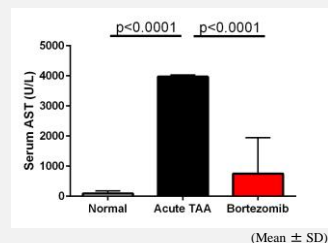
Serum ALT



HE-stained liver sections

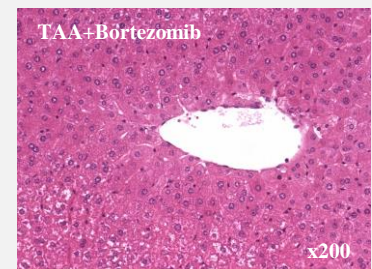


Serum AST



Acute liver injury is induced in the TAA mice model 24 hours after injection of TAA

- Increased serum ALT and AST levels at 24 hours
- Necrotic foci and inflammatory cell infiltration observed in the HE-stained liver sections at 24 hours (Areas surrounded by dot line represent necrotic foci)
- Treatment of Bortezomib, which is a proteasome inhibitor, alleviated TAA-induced liver damage. Thus, the drug is used as a positive control in this model.



For more information, please contact us below.

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