

# 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.

**Concanavalin A (ConA)-induced acute liver failure model** is widely used for acute immune-mediated hepatitis in contrast to several other models, which is primarily driven by the activation and recruitment of T cells to the liver. The outcome of ALF by ConA is leading to severe liver inflammation, tissue necrosis and terminal organ failure.

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

## ConA-induced acute liver failure model

### Animal:

- Male C57BL/6J (6 week-old)

### Induction of ALF:

- Injection of Concanavalin A

### Major endpoint:

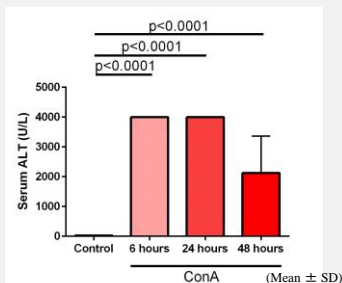
- Histology on liver tissue (HE staining)

### Additional endpoints:

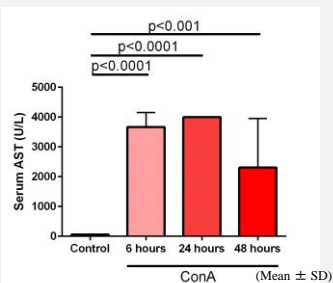
- Mortality rate
- Blood biochemistry (ALT, AST,...)
- Semi-quantitative RT-PCR (IL-6, TNF- $\alpha$ , ...)
- Immunohistochemical analyses for molecular markers
- Cytokines and chemokines in blood and livers by ELISA

## Evaluation of liver injury

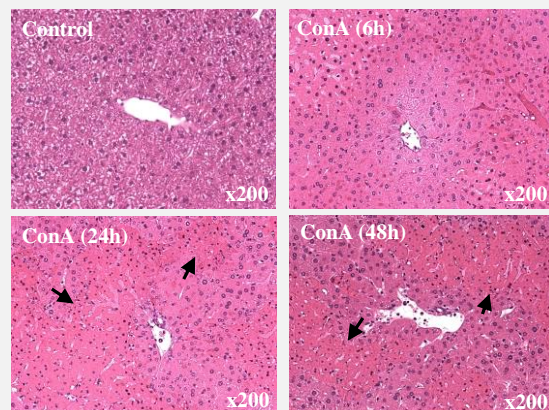
### Serum ALT



### Serum AST



### HE-stained liver sections



**Acute liver injury is induced in the ConA mice model 6, 24 and 48 hours after injection of ConA**

- Increased ALT and AST levels
- Necrotic foci and inflammatory cell infiltration observed in the HE-stained liver sections (Arrows represent lesion area)

### Table. Survival rate

Treatment	No. of survivors/total no. of mice used	Survival rate
Control	10/10	100%
Concanavalin A -6h	10/10	100%
Concanavalin A -24h	5/10	50%
Concanavalin A -48h	5/10	50%



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