SMC Laboratories,Inc.

Unilateral ureteral obstruction (UUO) renal fibrosis model
SMC's CRO services

Digest version

The **full version** includes the following content.

- All analysis data in UUO on day 7 and 14
- Experience with tested compound targets
- Histology guide
- Drug evaluation data (ALK5 (TGFβ receptor I) inhibitor) etc.

Request for the full version material from here.

SMC Laboratories – Company overview

SMC Laboratories, Inc.

- Founded in October 2006
- A privately-held non-clinical CRO based in Tokyo, Japan;

  specialized in research on ***fibrosis, inflammation and cancer***
- CRO services

  - Non-clinical pharmacology

  - One of the leading CRO in liver research with Proprietary NASH-HCC (STAM™) Model
  - A wide range of In-vivo disease model mice for many different organs

  - Histological imaging services

  - Histological scoring: NAFLD activity score, fibrosis and inflammation scores etc.

CRO capability

- SPF-grade animal room:

  - 2080 mice
- Facility

  *- Accreditation by MEXT**
  - Sponsor audit (QAU)
  - Animal welfare audit by global pharmaceuticals

Tokyo office (Japan)

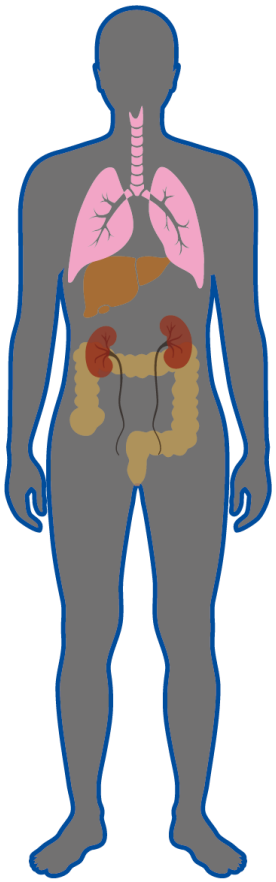
LA office (USA)

*MEXT: Ministry of Education, Culture, Sports, Science and Technology

Extensive disease model lineup

SMC's model lineup

We are able to support the development with various models based on Inflammation and Fibrosis.



【Liver】

♦MASH model
- STAM™

♦Liver fibrosis model
- CDAHFD

♦ Cirrhosis model
- CCl_4 model

♦ HCC models
- STAM™
- DEN + CCl4 model

♦ Cholangitis models
- BDL model
- DDC model

♦ Acute Liver Failure models
- CCl_4
- D-Gal/LPS
- APAP
- TAA
- Con A

【Lung】

♦IPF/SSc-ILD model
- **Bleomycin-induced model**

♦COPD model
- PPE model

♦ALI model
- LPS model

♦Silicosis model
- Silica model

【Kidney】

♦CKD models
- UUO model
- Adriamycin model
- Adenine model
- Folic Acid model

【Skin】

♦SSc/SSc-ILD model
- Bleomycin-induced skin fibrosis model (with Interstitial lung disease)

♦ Psoriasis model
- Imiquimod (IMQ)-induced dermatitis model

【Colon】

♦IBD
- DSS-induced colitis model

【Muscle】

♦Duchenne muscular dystrophy
- MDX mice

【Others】

♦icv-STZ model (Alzheimer's disease)　♦Xenograft model (Subcutaneous/Orthotopic)　♦ Custom model

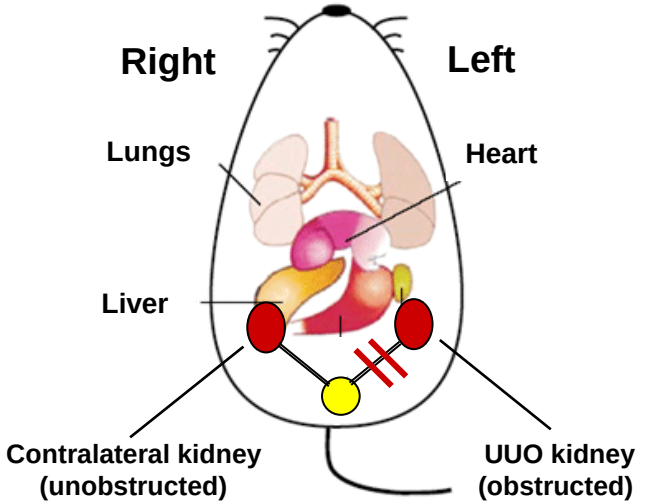
Procedures - mouse unilateral ureteral obstruction

Day 0 → **Surgery and treatment:**

1) Anesthetize and shave off the hair
2) Cut open the abdominal region
3) Ligate the left ureter with 4-0 thread
4) Suture the skin and transfer mice to a clean cage
5) Treat mice with candidate drugs from Day 0

Day 14 → **Sacrifice and sample collection:**

Mouse UUO



Blood → Urea nitrogen (*a marker of renal function*)

Kidney → Hydroxyproline assay (*estimation of renal collagen content*)

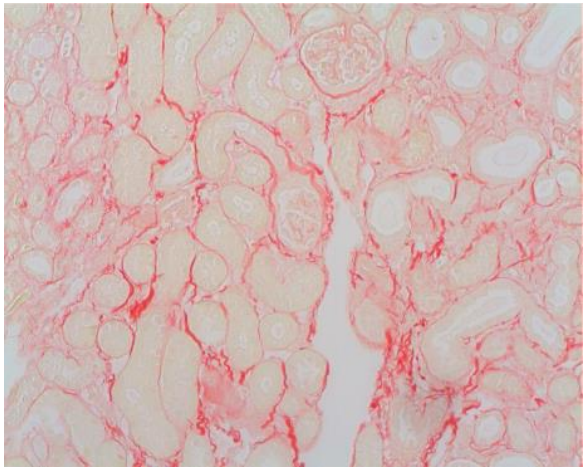
→ Histological analyses (*evaluation of renal injury, collagen deposition*)

→ Gene expression analysis (*for marker genes of fibrosis, inflammation, etc.*)

Sirius red staining

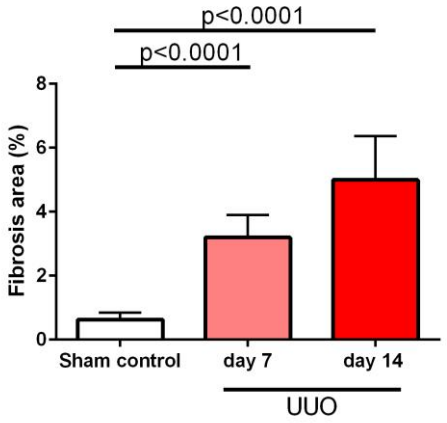
Sham-control

UUO

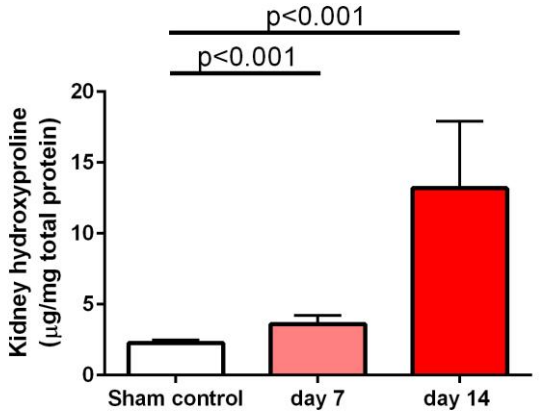


X200, corticomedullar region, Day 14
Positive area: red

Sirius red positive area



Kidney hydroxyproline



Unpaired t-test
Mean ± SD

The UUO model exhibits;

- severe interstitial fibrosis with a statistically significant increase in the Sirius red-positive area
- a 4-5 times increase in kidney hydroxyproline content