A pre-clinical CRO bridging innovation and human healthcare.

SERVICE CATALOG

NIHON BIORESEARCH INC.

株式会社日本バイオリサーチセンター

A pre-clinical CRO bridging inno and human healthcare.

NIHON BIORESEARCH INC.

Nihon Bioresearch Inc. is a preclinical CRO specializing in efficacy and safety studies for pharmaceuticals, medical devices, cell therapies, regenerative medicine products, food, and more.

Distinctive Features

- Conducted more than 300 varieties of pharmacology studies.
- Expertise in handling **diverse animal models**, including minipigs, mice, rats, rabbits, and more.
- Over Twenty years of experience in **mini-pig testing**, marking the longest-standing achievement in Japan.
- Extensive achievements in **medical devices** and **regenerative medicine research**.
- Specialized in conducting **infection studies at Biosafety Level 2 (BSL2)**.
- In-house capabilities for **developing animal models** and **custom testing services**.

Commitment to Quality

- **GLP-Compliance:** Complied with GLP standards, and our facilities are certified by PMDA.
- **High-Quality Data:** In both GLP and non-GLP trials, the study director and technical staff perform thorough quality control protocols, raw data, and reports, including tables and appendices.
- **High Standards for Animal Welfare:** Third-party accreditation or certification from AAALAC International or Japan Pharmaceutical Information Center.

vation

Facilities in Japan

- **Hashima Laboratory:**
  Certified by Japan Pharmaceutical Information Center (JAPIC)
- **Shuzenji Branch:**
  Accredited with the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International)
- **Kisosansen Branch:**
  Certified by Japan Pharmaceutical Information Center (JAPIC)

Contact us

Nihon Bioresearch Inc.
104, 6-chome, Majima, Fukuju-cho,
Hashima, Gifu, 501-6251 Japan
Tel: +81-58-392-6222
E-mail: nbrkikaku@nisshin.com
Website: https://www.nbr.co.jp/en/

NIHON BIORESEARCH INC.

Expertise in Pharmacology Efficacy Studies

- **Central Nervous System:** depression, anxiety, schizophrenia, dementia, cerebral infarction, allodynia, etc.
- **Respiratory and Cardiovascular Systems:** myocardial infarction, hyperpiesia, arrhythmia, etc.
- **Metabolic System:** arteriosclerosis, diabetes, hyperlipemia, obesity, etc.
- **Liver, Kidney, and Urinary System:** hepatopathy, nephritis, frequent micturition, renal failure etc.
- **Digestive System:** ulceration, hemorrhoid, constipation, diarrhea, etc.
- **Inflammation and Allergy:** atopic dermatitis, hay fever, asthma, arthritis, wound, etc.
- **Infection:** *in vivo/in vitro* studies with viral, bacterial, fungal, etc.
- **Others:** muscles/bones, dentistry/oral surgery, skin, aged related diseases, etc

Expertise in Safety Studies

- Single dose toxicity studies
- Repeated dose toxicity studies
- Reproductive and developmental toxicity studies
- Mutagenicity studies
- Irritation studies
- Antigenicity studies
- Skin sensitization studies
- Skin photosensitization studies
- Safety pharmacology studies
- Hemolysis studies
- Cytotoxicity studies
- Implantation studies

Pharmacology Studies 10

1. Central Nervous System

2. Inflammation/Immune Diseases

3. Kidney/Urinary Systems

4. Metabolic System

5. Digestive System

6. Circulatory/Respiratory Systems

7. Muscles/Bones

8. Dentistry/Oral Surgery

9. Skin

10. Age-Related Diseases

11. Infection

12. *In Vitro*

13. Medical Devices

14. Regenerative Medical Products

Safety Pharmacology Studies **70**

Core Battery/Confirmation Test of Adverse Reactions to Test Articles

Follow-up or Supplement/Confirmatory Study

Safety Studies 74

Safety Studies (Pharmaceuticals)

Safety Studies (Health Foods)

Safety Studies (Medical Devices)

Safety Studies (Regenerative Medical Products)

Pharmacology Studies

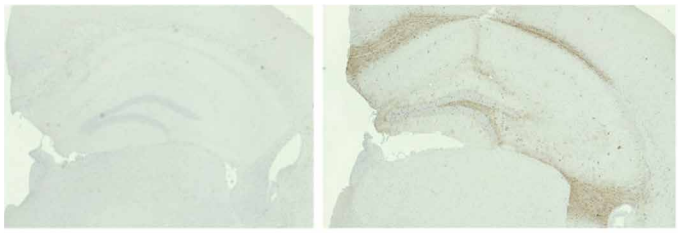
Pharmacology Studies

1. Central Nervous System

Dementia

Tauopathy mouse model

- **Mouse**
  Tau injection into hippocampus
- **Evaluation**
  Y maze test, passive avoidance test

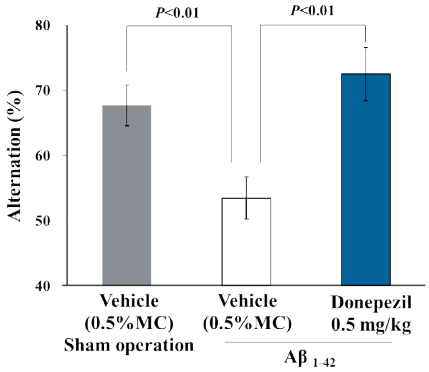


Control group　　Fibrotic tau group(6 months after injection)

Provided by: Tokyo Metropolitan Institute of Medical Science

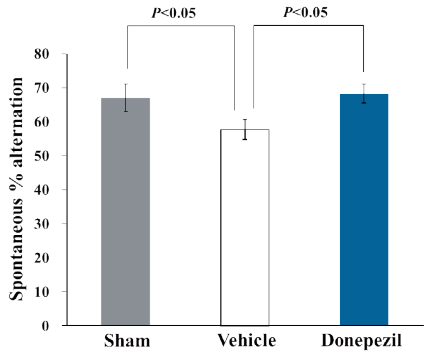
Amyloid-β induced mouse model

- **Mouse**
  Intracerebroventricular injection of amyloid-β
- **Evaluation**
  Y maze test, passive avoidance test



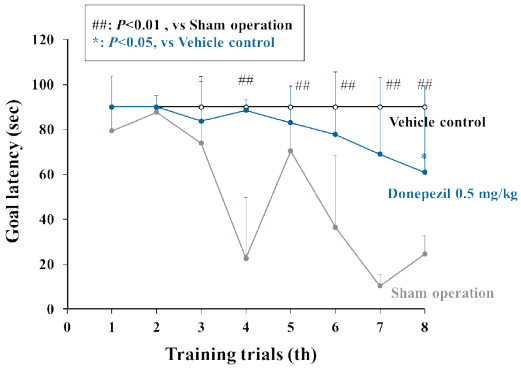
α-Synuclein induced mouse model

- **Mouse**
  Intracerebroventricular injection of α-synuclein
- **Evaluation**
  Y maze test



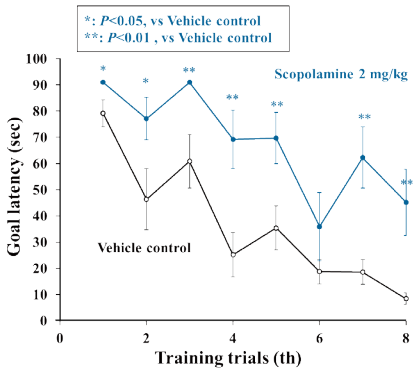
Ibotenic acid injection model

- **Rat**
  Ibotenic acid injection into the basal ganglia
- **Evaluation**
  Morris water maze test



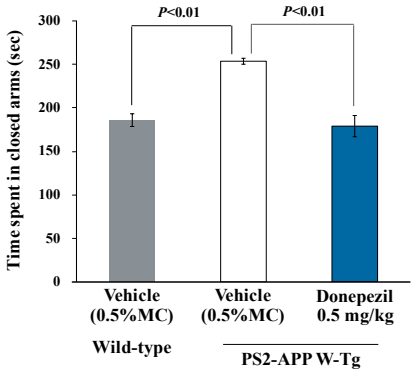
Scopolamine model

- **Rat**
  Scopolamine injection
- **Evaluation**
  Passive avoidance test, Morris water maze test



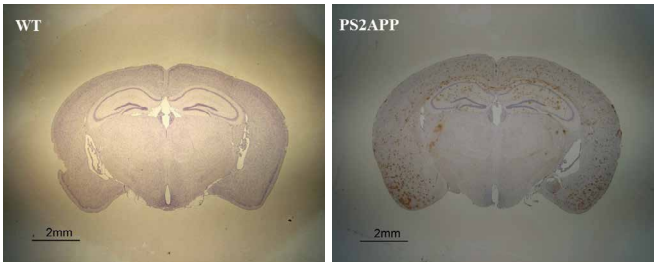
PS2xAPP transgenic mice (peripheral symptoms)

- **Mouse**
  PS2xAPP transgenic
- **Evaluation**
  Elevated plus maze test, open field test, social interaction test



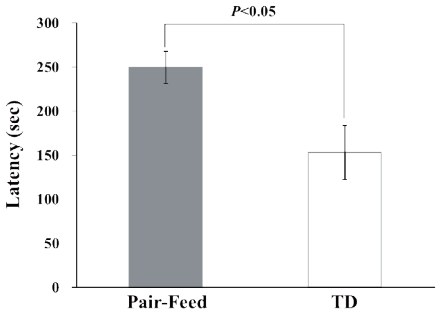
PS2xAPP transgenic mice (core symptoms)

- **Mouse**
  PS2xAPP transgenic
- **Evaluation**
  Y maze test, novel object recognition test, Morris water maze test, passive avoidance test, fear conditioning test, microdialysis, histopathological examination (β amyloid staining)



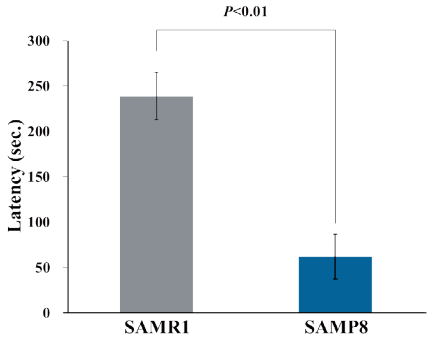
Thiamine deficiency model (core symptoms)

- **Mouse**
  Thiamine-deficient diet
- **Evaluation**
  Passive avoidance test



Senescence-Accelerated Mouse (SAM)

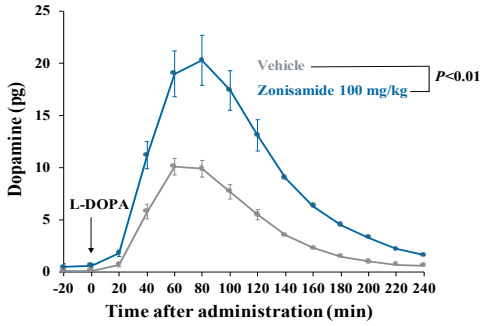
- **Mouse**
- **Evaluation**
  Passive avoidance test



Parkinson's disease

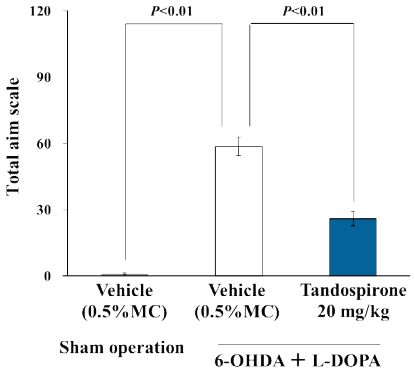
6-OHDA-induced model

- **Rat**
  Medial forebrain bundle injection of 6-OHDA
- **Evaluation**
  L-DOPA-induced rotational behavior, microdialysis



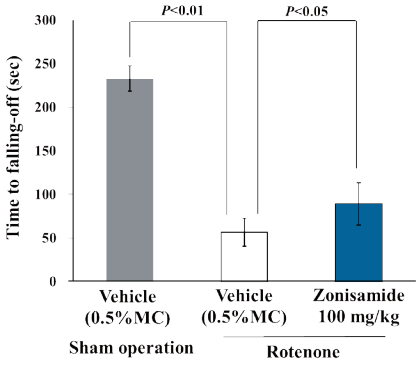
Dyskinesia model

- **Rat**
  Induced by L-DOPA
- **Evaluation**
  Abnormal involuntary movement (AIM) score, brain monoamine content



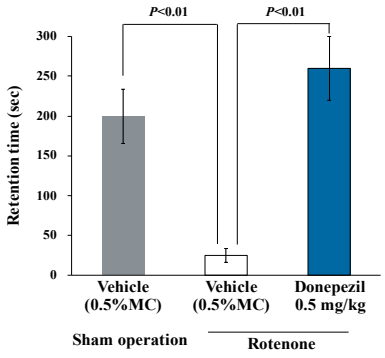
Rotenone-induced model

- **Rat**
  Intra-substantia nigra injection of rotenone
- **Evaluation**
  Locomotor activity, rotarod test, brain monoamine content, histopathological examination (TH staining)



Rotenone-induced model (cognitive dysfunction)

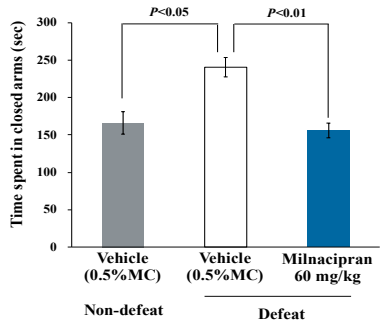
- **Rat**
  Intra-substantia nigra injection of rotenone
- **Evaluation**
  Morris water maze test, passive avoidance test



Anxiety

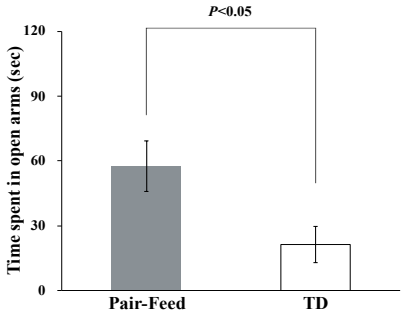
Social defeat stress model

- **Mouse**
  Social defeat
- **Evaluation**
  Elevated plus maze test, number of sexual activities, brain monoamine content



Thiamine deficiency model (peripheral symptoms)

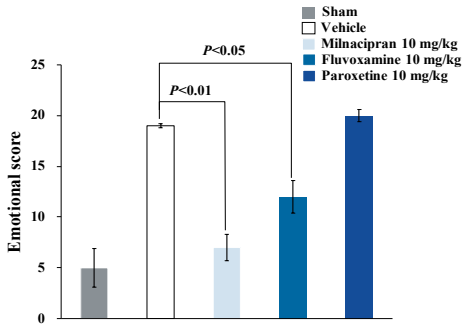
- **Mouse**
  Thiamine-deficient diet
- **Evaluation**
  Elevated plus maze test



Depression

Olfactory bulbectomy model

- **Rat**
  Olfactory bulbectomy
- **Evaluation**
  Emotional hyperreactivity, elevated plus maze test, open field test, brain monoamine content, microdialysis, histopathological examination (TUNEL staining, GFAP staining)



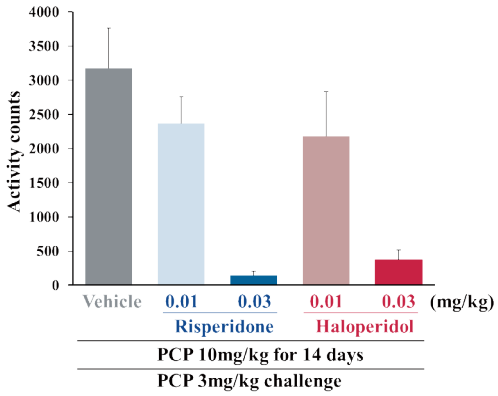
Thiamine deficiency model (peripheral symptoms)

- **Mouse**
- **Evaluation**
  Forced swimming test

Schizophrenia

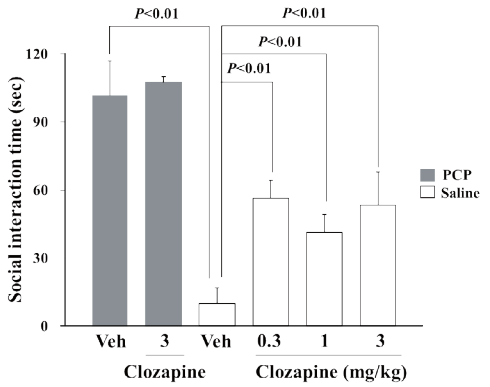
Phencyclidine (PCP) sub-chronic administration model

- **Mouse**
  PCP sub-chronic administration
- **Evaluation**
  Forced swimming test, PCP-induced locomotor activity



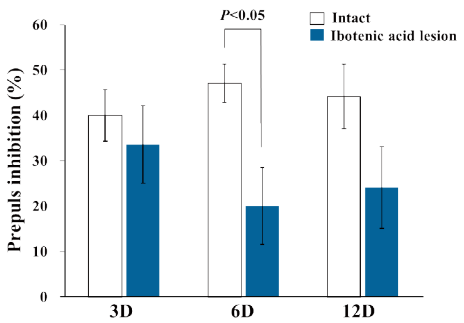
Neonatal phencyclidine (PCP) administration model

- **Rat, Mouse**
  Neonatal PCP administration
- **Evaluation**
  Social interaction test, Morris water maze test, phencyclidine-induced locomotor activity



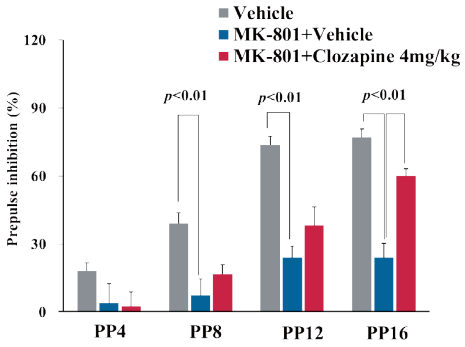
Neonatal ventral hippocampal lesion model

- **Rat**
- **Evaluation**
  Daily activity amount, prepulse inhibition (PPI) test, Morris water maze test, brain monoamine content



Acute MK-801 administration model

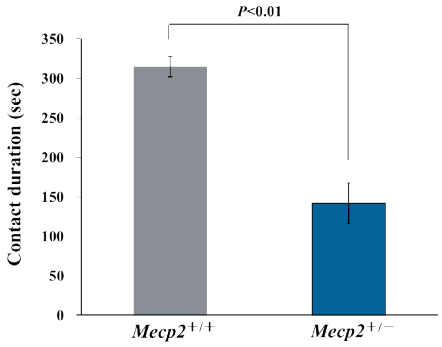
- **Mouse**
  MK-801 injection
- **Evaluation**
  MK-801-induced locomotor activity, prepulse inhibition (PPI) test



Autism spectrum disorder

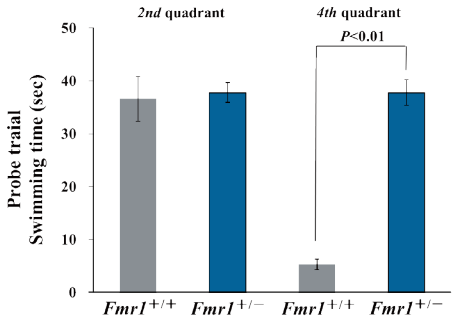
Genetically modified model (Mecp2 KO)

- **Rat**
- **Evaluation**
  Social interaction test, Morris water maze test, acetylcholine content, brain monoamine content



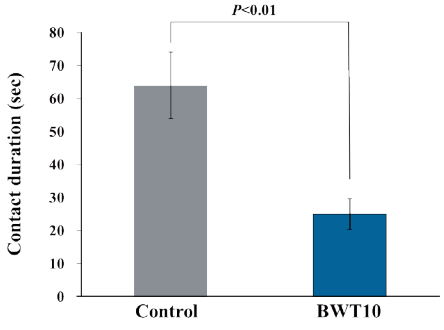
Genetically modified model (Fmrl KO)

- **Rat**
- **Evaluation**
  Social interaction test, reversal learning in Morris water maze, brain monoamine content



Somatosensory processing disorder model

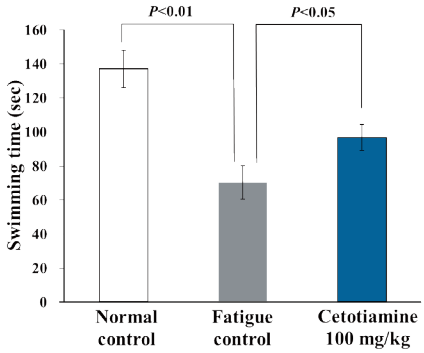
- **Mouse**
- **Evaluation**
  Social interaction test, gap crossing test, acetylcholine content, brain monoamine content



Mental fatigue

Water immersion breeding model

- **Rat**
- **Evaluation**
  Forced swimming test



Sleeping disorder

Normal sleep brain wave measurement

- **Rat, Mouse**
- **Evaluation**
  EEG measurement

Sleep inhibition model (evaluation of sleep-inducing effect)

- **Rat**
- **Evaluation**
  EEG measurement

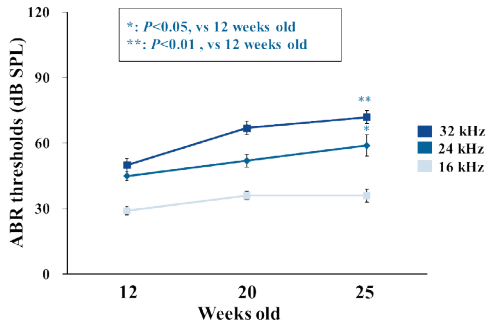
Sleep deprivation model (evaluation of awakening function)

- **Rat**
- **Evaluation**
  EEG measurement

Hearing loss

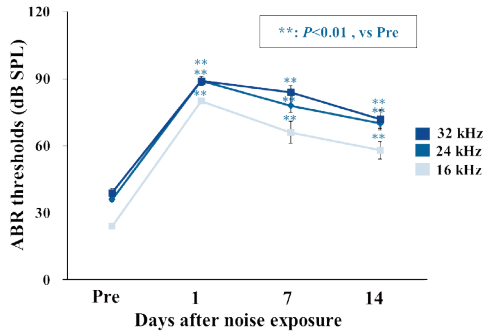
Age-related hearing loss model

- **Mouse**
- **Evaluation**
  Auditory brainstem response (ABR)



Noise-induced hearing loss model

- **Mouse, Guinea pig**
  Noise-induced
- **Evaluation**
  Auditory brainstem response (ABR)



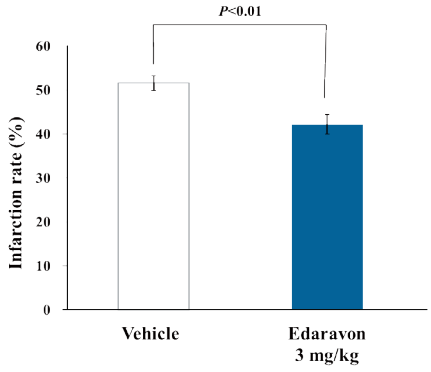
Tympanic membrane perforation model

- **Guinea pig**
  Tympanic perforation
- **Evaluation**
  Auditory brainstem response (ABR)

Brain stroke

Middle cerebral artery occlusion/ reperfusion model (MCAO/R model)

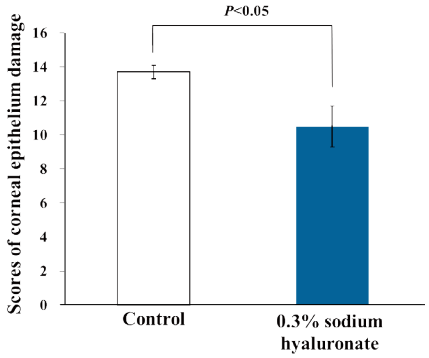
- **Rat**
- **Evaluation**
  Neurological symptoms, histopathological examination



Corneal damage

Corneal epithelial disorder model

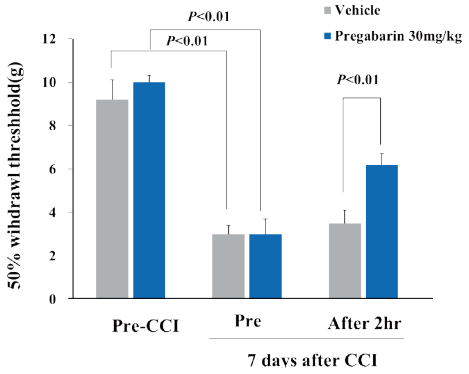
- **Rabbit**
- **Evaluation**
  Dye staining area



Pain

Sciatic nerve constriction (CCI) model (Bennett model)

- **Rat**
- **Evaluation**
  Thermal stimulation (withdrawal latency), tactile stimulation (withdrawal threshold)

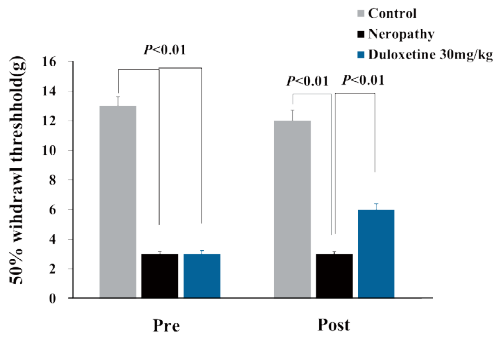


Spinal nerve ligation (SNL) model (chung model)

- **Rat**
- **Evaluation**
  Thermal stimulation (withdrawal latency), tactile stimulation (withdrawal threshold)

Chemotherapy-induced peripheral neuropathy: CIPN/Oxaliplatin-induced peripheral neuropathy model

- **Rat**
  Oxaliplatin-induced
- **Evaluation**
  Cold stimulation (withdrawal latency), tactile stimulation (withdrawal threshold)



Chemotherapy-induced peripheral neuropathy: CIPN/Paclitaxel-induced peripheral neuropathy model

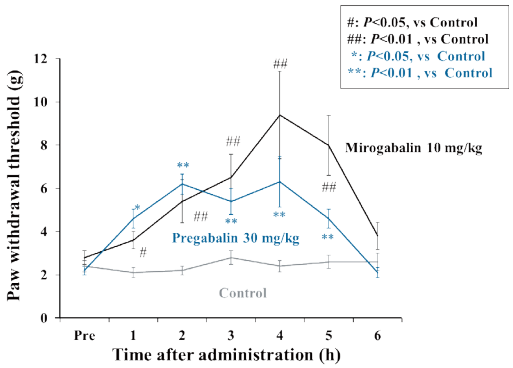
- **Rat**
  Paclitaxel-induced
- **Evaluation**
  Tactile stimulation (withdrawal threshold)

Chemotherapy-induced peripheral neuropathy: CIPN/Cisplatin-induced peripheral neuropathy model

- **Rat**
  Cisplatin-induced
- **Evaluation**
  Tactile stimulation (withdrawal threshold)

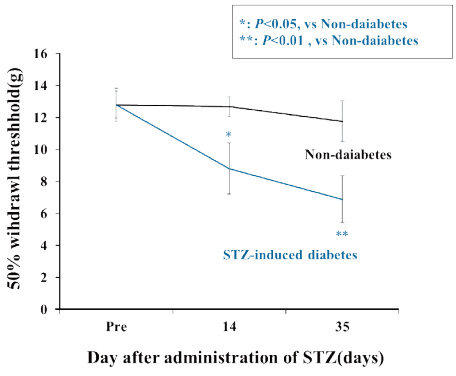
Fibromyalgia (Sluka) model

- **Rat**
- **Evaluation**
  Tactile stimulation (withdrawal threshold)



Diabetic peripheral neuropathy model

- **Rat**
- **Evaluation**
  Tactile stimulation (withdrawal threshold), motor nerve conduction velocity



Adjuvant-induced hyperalgesia model

- **Rat**
- **Evaluation**
  Thermal stimulation (withdrawal latency), tactile stimulation (withdrawal threshold), vocalization response, pressure stimulation

Carrageenin-induced hyperalgesia model

- **Rat, Mouse**
- **Evaluation**
  Tactile stimulation (withdrawal threshold)

Capsaicin patch hyperalgesia model

- **Rat**
- **Evaluation**
  Thermal stimulation (withdrawal latency), tactile stimulation (withdrawal threshold)

Acetic acid-induced abdominal pain model

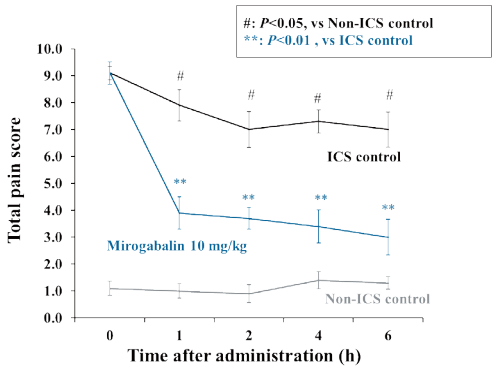
- **Rat, Mouse**
- **Evaluation**
  Writhing number

Acetylcholine-induced abdominal pain model

- **Mouse**
- **Evaluation**
  Writhing number

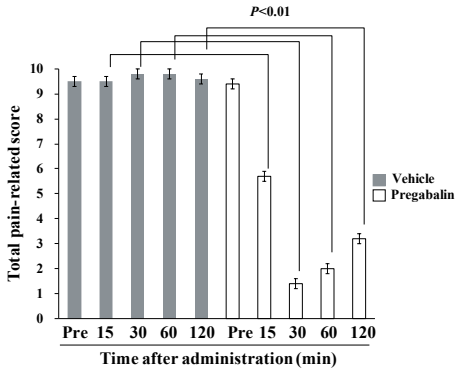
Intermittent cold stress (ICS) model

- **Mouse**
- **Evaluation**
  Tactile stimulation (withdrawal threshold)



Postherpetic neuralgia model

- **Mouse**
  Dermal inoculation of herpesvirus
- **Evaluation**
  Tactile stimulation (withdrawal threshold)

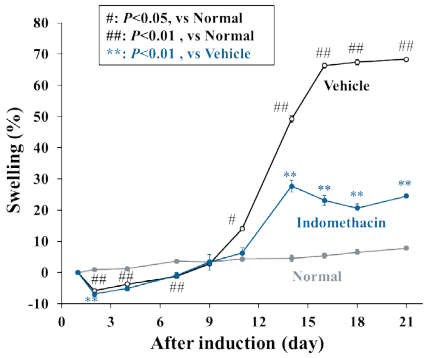


2. Inflammation/Immune Diseases

Rheumatoid arthritis

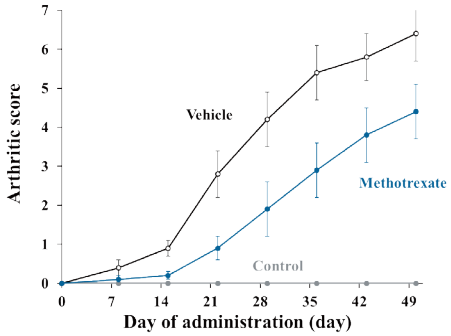
Adjuvant arthritis model

- **Rat**
- **Evaluation**
  Edema rate, arthritis score, histopathological examination



Collagen-induced arthritis model

- **Rat, Mouse**
- **Evaluation**
  Edema rate, arthritis score, histopathological examination



Osteoarthritis

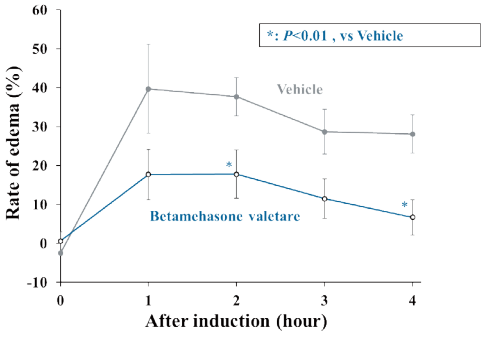
MIA-induced osteoarthritis model

- **Rat**
  Mono-iodoacetate (MIA)-induced
- **Evaluation**
  Histopathological examination

Edema

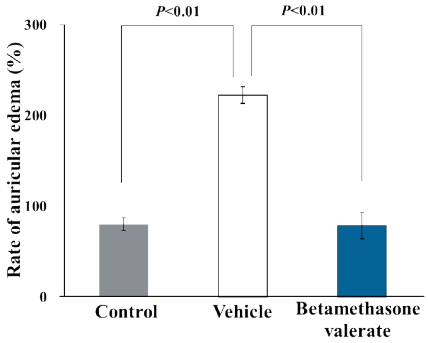
Croton oil-induced ear edema model

- **Rat, Mouse**
- **Evaluation**
  Ear weight, ear thickness



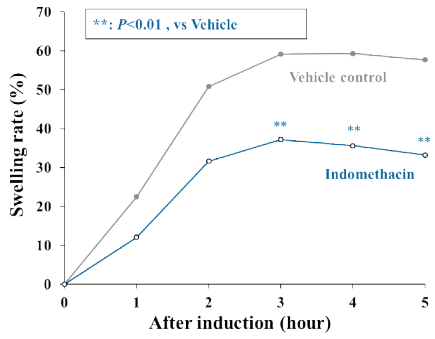
Oxazolone-induced ear edema model

- **Rat, Mouse**
- **Evaluation**
  Ear weight, ear thickness



Carrageenin-induced limb edema model

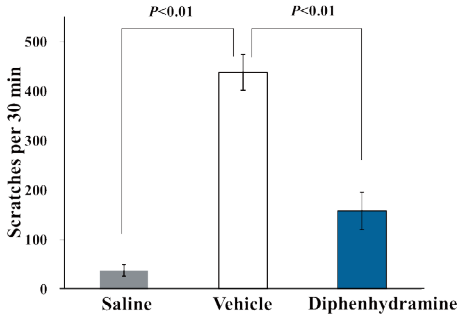
- **Rat**
- **Evaluation**
  Edema rate



Itchiness

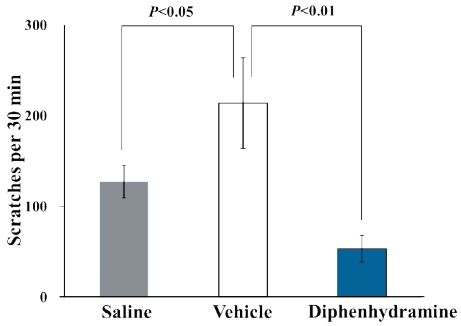
Compound 40/80-induced itch model

- **Mouse**
- **Evaluation**
  Scratching behavior



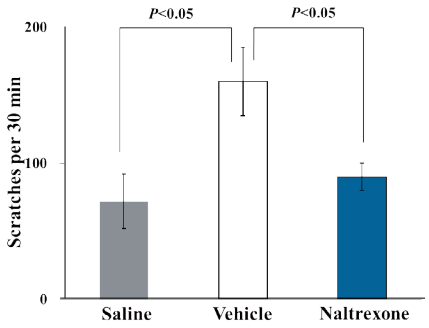
Histamine-induced itch model

- **Mouse**
- **Evaluation**
  Scratching behavior



Substance P-induced itch model

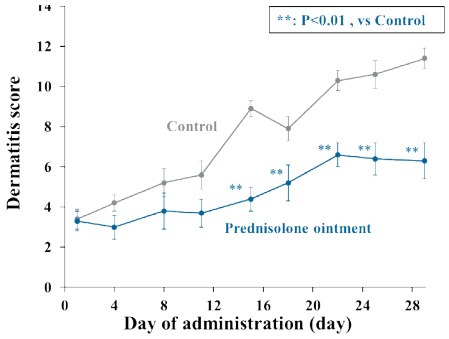
- **Mouse**
- **Evaluation**
  Scratching behavior



Atopic dermatitis

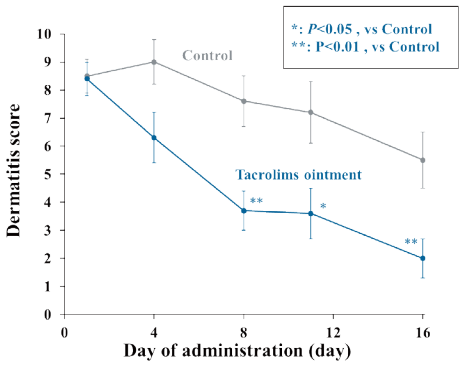
PiCl-induced atopic dermatitis model

- **Mouse**
- **Evaluation**
  Dermatitis score, histopathological examination, blood chemical analysis (IgE), scratching behavior



Mite antigen-induced atopic dermatitis model

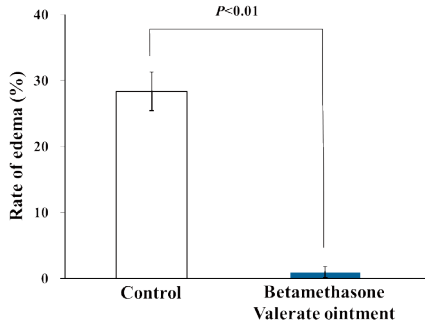
- **Mouse**
- **Evaluation**
  Dermatitis score, histopathological examination, blood chemical analysis (IgE), scratching behavior



Allergic dermatitis

PiCl-induced type IV allergic dermatitis model

- **Mouse**
- **Evaluation**
  Ear thickness



DNFB-induced allergic dermatitis model

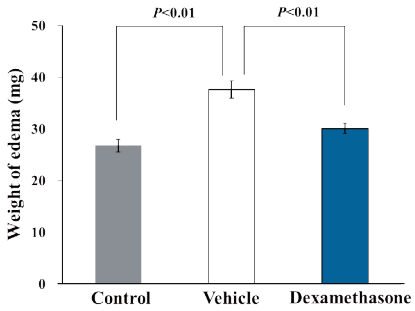
- **Minipig**
- **Evaluation**
  Dermatitis score, histopathological examination, erythema meter

1	2	3	4	5
Non-treated	White petrolatum ointment	Tacrolimus ointment	Betamethasone valerate ointment	Normal

Allergic conjunctivitis

Croton oil-induced allergic conjunctivitis model

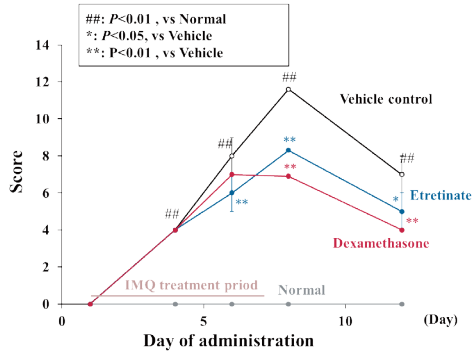
- **Rat**
- **Evaluation**
  Eyelid weight



Psoriasis

Imiquimod-induced psoriasis model

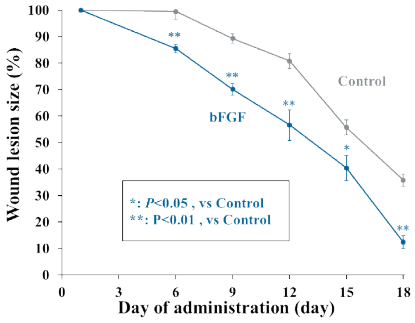
- **Mouse**
- **Evaluation**
  Dermatitis score,histopathological examination, blood chemical analysis



Wound

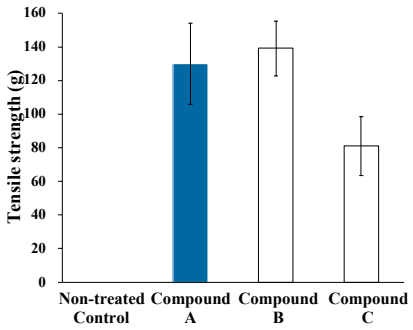
Wound healing model

- **Rat, Mouse**
- **Evaluation**
  Defect area, healing period, histopathological examination



Skin incision model

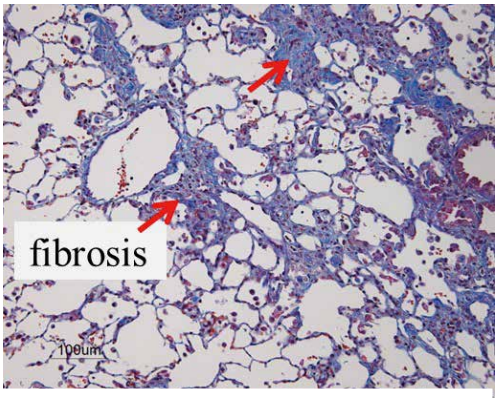
- **Rat**
- **Evaluation**
  Wound tension strength



Pulmonary fibrosis

Bleomycin-induced pulmonary fibrosis model

- **Rat, Mouse**
- **Evaluation**
  Histopathological examination, hydroxyproline

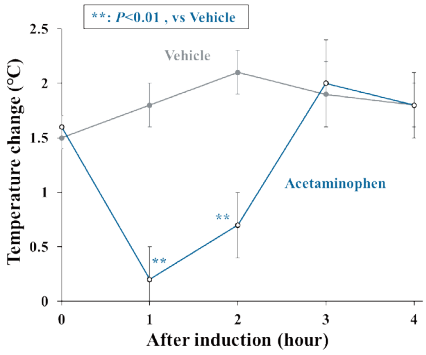


Masson trichrome stain

High fever

Yeast-induced fever model

- **Rat**
- **Evaluation**
  Body temperature

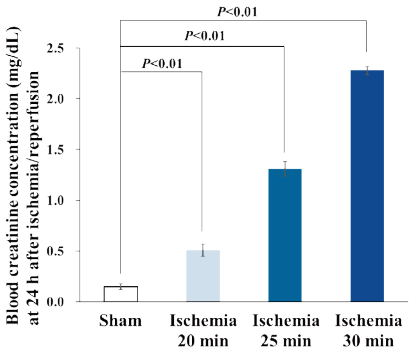


3. Kidney/Urinary Systems

Acute kidney injury

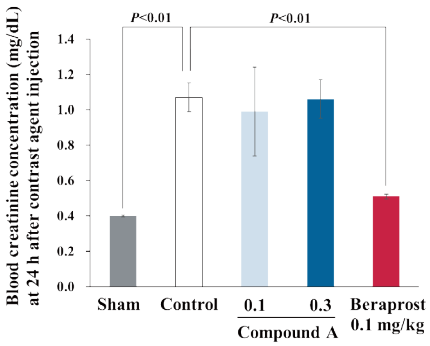
Ischemic acute kidney injury model

- **Rat, Mouse, Minipig**
- **Evaluation**
  Blood chemical analysis, histopathological examination, urinalysis (rat and minipig)



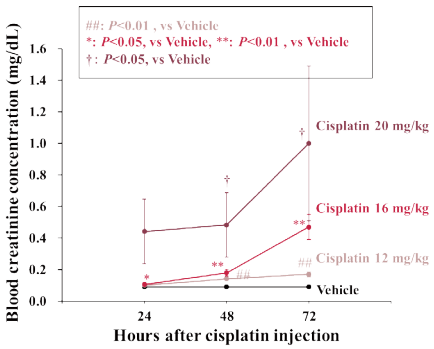
Contrast agent-induced acute kidney injury model

- **Rat**
- **Evaluation**
  Blood chemical analysis, urinalysis, histopathological examination



Cisplatin-induced acute kidney injury model

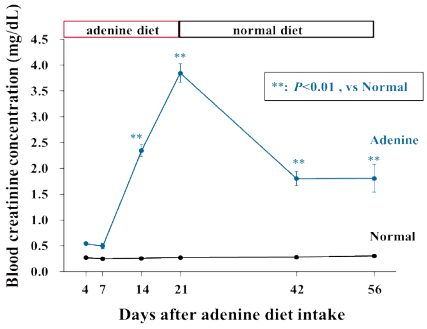
- **Mouse**
- **Evaluation**
  Blood chemical analysis, histopathological examination



Chronic kidney disease

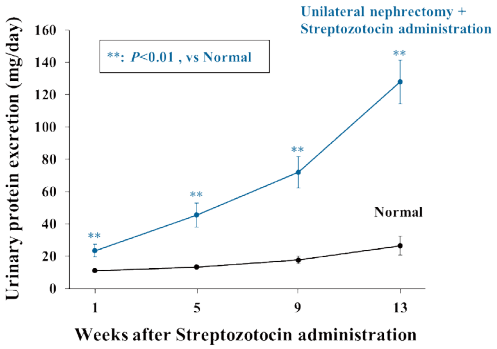
Adenine nephropathy model

- **Rat**
- **Evaluation**
  Blood chemical analysis, histopathological examination, calcium and phosphorus in tissues



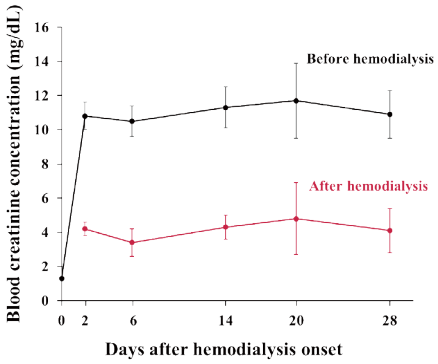
Streptozotocin-induced diabetic nephropathy model

- **Rat**
- **Evaluation**
  Blood chemical analysis, urinalysis, histopathological examination



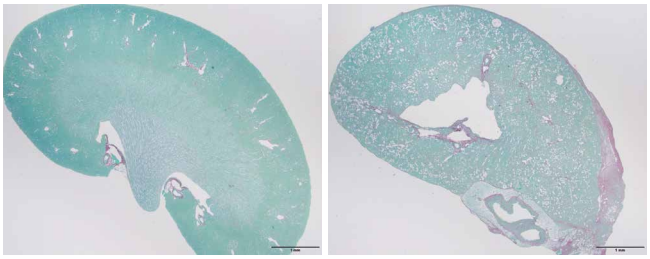
Bilateral nephrectomy dialysis model

- **Minipig**
- **Evaluation**
  Blood chemical analysis, urinalysis



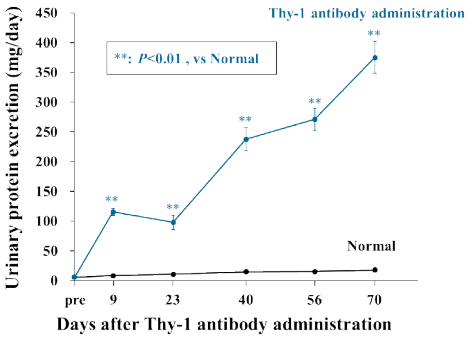
Unilateral ureteral ligation (UUO) model

- **Rat, Mouse**
- **Evaluation**
  Hydroxyproline, histopathological examination



Thy-1 nephritis model

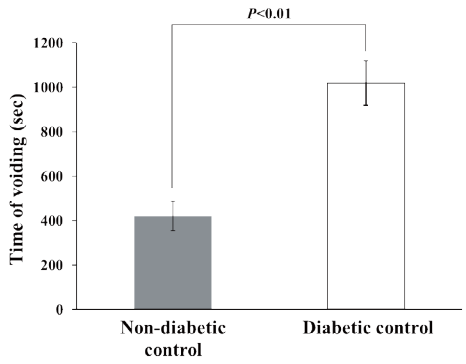
- **Rat**
- **Evaluation**
  Blood chemical analysis, urinalysis, histopathological examination



Frequent urination

Bladder function evaluation model

- **Rat, Dog, Minipig**
- **Evaluation**
  Cystometry



Prostatic hypertrophy

Urethral function evaluation model

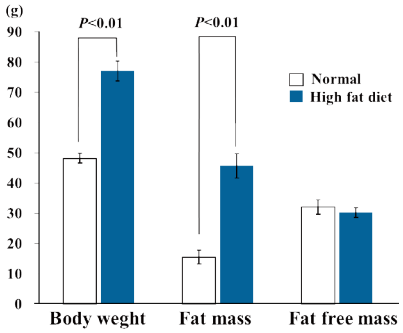
- **Rat, Dog**
- **Evaluation**
  Urethral manometry

4. Metabolic System

Obesity

High-fat diet-induced obesity model

- **Mouse**
- **Evaluation**
  Blood chemical analysis (neutral fat, leptin, adiponectin), visceral fat weight



Obese model (Zucker Fatty)

- **Rat**
- **Evaluation**
  Blood chemical analysis (neutral fat, leptin, adiponectin), visceral fat weight

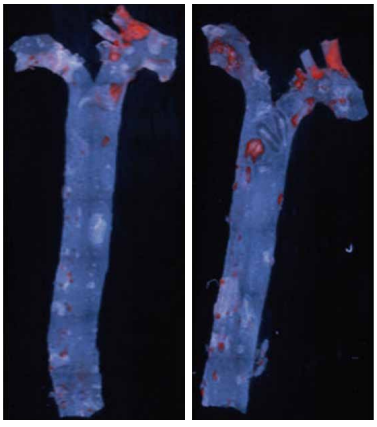
Arteriosclerosis

Cholesterol loading model

- **Rabbit**
- **Evaluation**
  Blood chemical analysis, aortic lesion area, histopathological examination (aorta, coronary artery)

Genetically modified arteriosclerosis model (apoEKO mouse)

- **Mouse**
- **Evaluation**
  Blood chemical analysis, aortic lesion area, histopathological examination (aorta, coronary artery)



Spontaneous arteriosclerosis model (WHHL)

- **Rabbit**
- **Evaluation**
  Blood chemical analysis, aortic lesion area, histopathological examination (aorta, coronary artery)

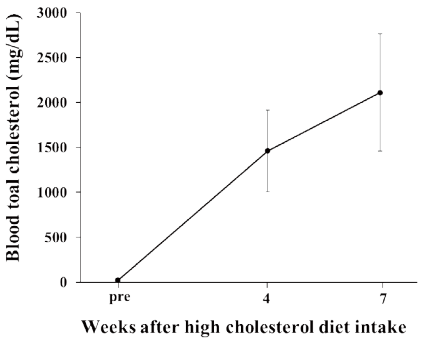
Hyperlipidemia

High fat feed loading model

- **Rabbit**
- **Evaluation**
  Blood chemical analysis (neutral fat, etc.)

High cholesterol feed loading model

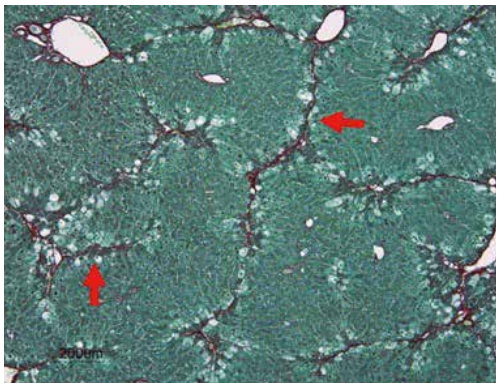
- **Rabbit**
- **Evaluation**
  Blood chemical analysis (neutral fat, etc.)



Liver damage

Carbon tetrachloride-induced liver injury model

- **Rat, Mouse**
- **Evaluation**
  Blood chemical analysis (liver enzymes), histopathological examination (liver)



Sirius Red-Fast Green stain ↑ : fibrosis

Galactosamine-induced acute liver failure model

- **Rat**
- **Evaluation**
  Blood chemical analysis (liver enzymes), histopathological examination (liver)

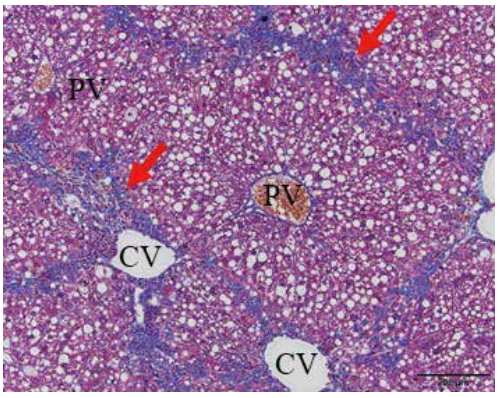
Acetaminophen-induced liver injury model

- **Mouse**
- **Evaluation**
  Blood chemical analysis (liver enzymes), histopathological examination (liver)

Steatohepatitis

Nonalcoholic steatohepatitis (NASH) model

- **Rat, Mouse**
- **Evaluation**
  Histopathological examination (liver), blood chemical analysis (liver enzymes)

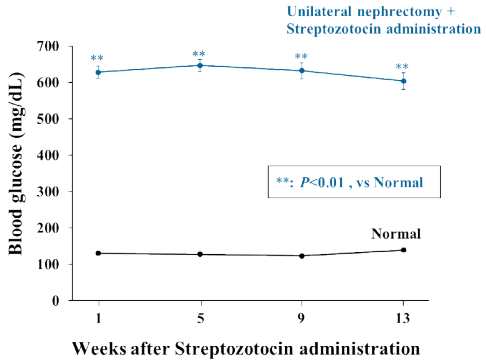


MT stain ↑ : fibrosis

Diabetes

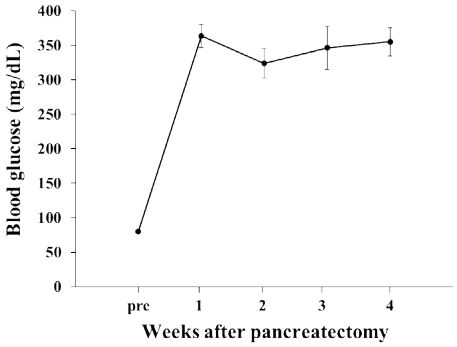
Streptozotocin-induced diabetes model (type 1 diabetes)

- **Rat**
- **Evaluation**
  Blood chemical analysis (blood glucose, insulin, glycated hemoglobin), nerve conduction velocity, glucose tolerance test, histopathological examination, retinal evoked potential (ERG), cystometry



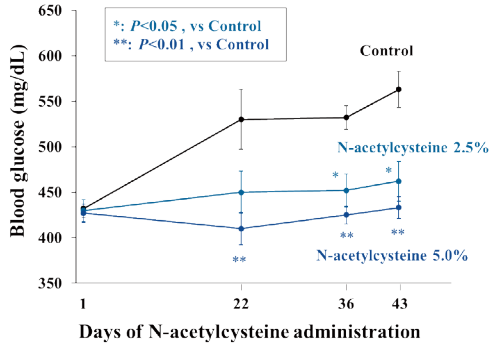
Pancreatectomy diabetes model (type 1 diabetes)

- **Minipig**
- **Evaluation**
  Blood chemical analysis (blood glucose, insulin), glucose tolerance test, histopathological examination



Type 2 diabetes model (KK-A^{y})

- **Mouse**
- **Evaluation**
  Blood chemical analysis (blood glucose, insulin, glycated hemoglobin), glucose tolerance test, retinal evoked potential (ERG)

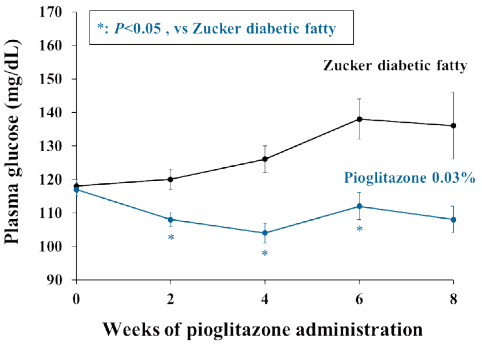


Obese type 2 diabetes model (*db/db*)

- **Mouse**
- **Evaluation**
  Blood chemical analysis (blood glucose, insulin, glycated hemoglobin), glucose tolerance test, retinal evoked potential (ERG)

Obese type 2 diabetes model (Zucker Diabetic Fatty)

- **Rat**
- **Evaluation**
  Blood chemical analysis (blood glucose, insulin, glycated hemoglobin), glucose tolerance test, retinal evoked potential (ERG), histopathological examination

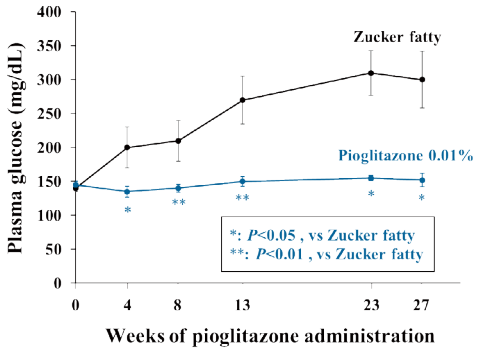


Non-obese type 2 diabetes model (GK)

- **Rat**
- **Evaluation**
  Blood chemical analysis (blood glucose, insulin, glycated hemoglobin), glucose tolerance test, retinal evoked potential (ERG), histopathological examination

Obese model (Zucker Fatty)

- **Rat**
- **Evaluation**
  Blood chemical analysis (blood glucose, insulin, glycated hemoglobin), glucose tolerance test, retinal evoked potential (ERG), histopathological examination



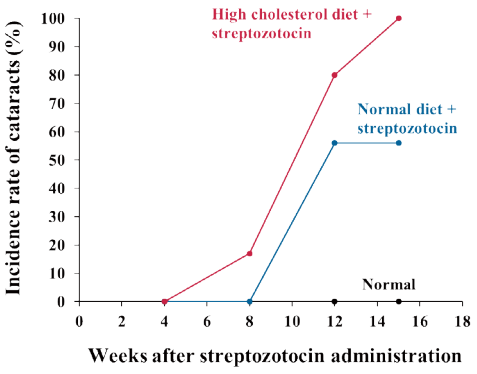
Sodium laurate-induced peripheral artery occlusion model

- **Rat**
- **Evaluation**
  Blood flow

Cataract

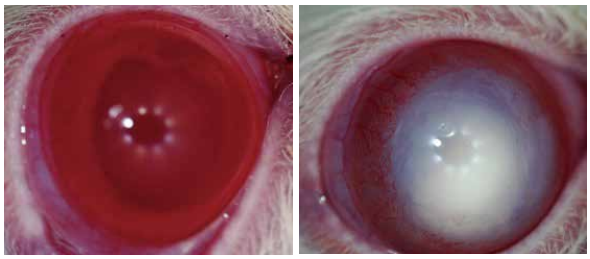
Streptozotocin-induced diabetic cataract model

- **Rat**
- **Evaluation**
  Cataract incidence rate



Galactose-induced cataract model

- **Rat**
- **Evaluation**
  Cataract incidence rate



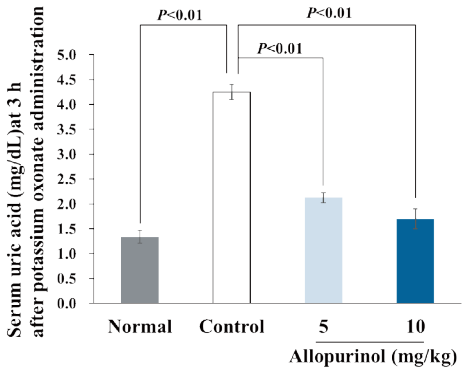
Sodium selenite-induced cataract model

- **Rat**
- **Evaluation**
  Cataract incidence rate

Hyperuricemia

Potassium oxonate-induced hyperuricemia model

- **Rat**
- **Evaluation**
  Blood chemical analysis (uric acid)

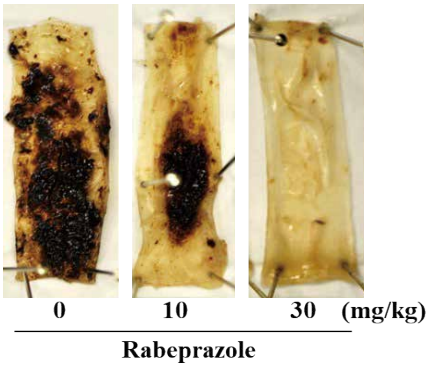


5. Digestive System

Reflux esophagitis

Pylorus ligation reflux esophagitis model

- **Rat**
- **Evaluation**
  Score



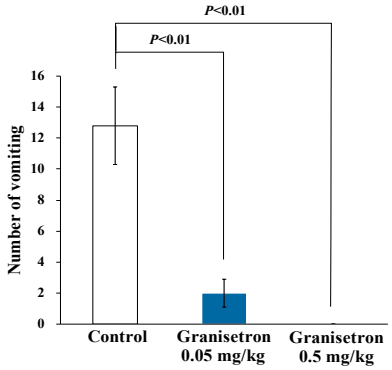
Vomiting

Anticancer drug-induced delayed emesis model

- **Minipig, Dog, Ferret**
- **Evaluation**
  Frequency of vomiting (minipig, ferret and dog), vagal nerve action potential (minipig), vomiting duration (dog and ferret), gastrointestinal motility (dog)

Drug-induced acute emesis model

- **Ferret**
- **Evaluation**
  Frequency of vomiting, vomiting duration



Stomach ulcer

Water immersion stress-induced gastric ulcer model

- **Rat**
- **Evaluation**
  Length of gastric mucosal lesion

Hydrochloric acid/ethanol-induced gastric ulcer model

- **Rat**
- **Evaluation**
  Length of gastric mucosal lesion

Ethanol-induced gastric ulcer model

- **Rat**
- **Evaluation**
  Length of gastric mucosal lesion

Indomethacin-induced gastric ulcer model

- **Rat**
- **Evaluation**
  Length of gastric mucosal lesion

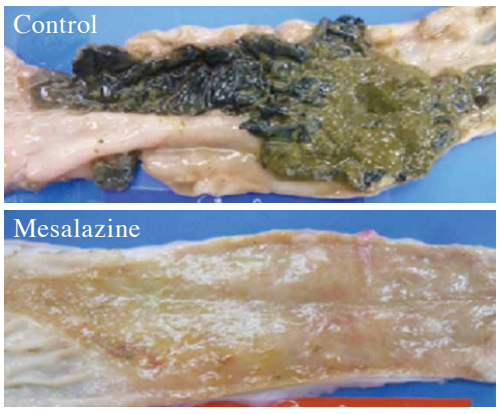
Aspirin-induced gastric ulcer model

- **Rat**
- **Evaluation**
  Length of gastric mucosal lesion

Ulcerative colitis

TNBS-induced colitis model

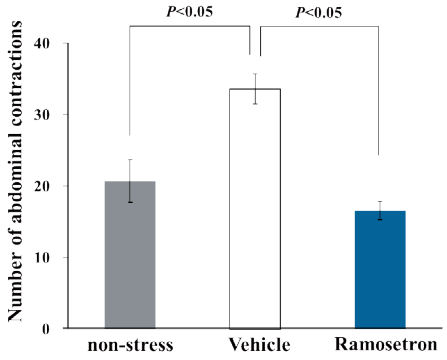
- **Minipig**
- **Evaluation**
  Bleeding score, diarrhea score, large intestine weight, histopathological examination



Irritable bowel syndrome

Restraint stress-induced irritable bowel syndrome model

- **Rat**
- **Evaluation**
  Frequency of defecation, number of abdominal muscle contractions



Diarrhea

Castor oil-induced diarrhea model

- **Rat**
- **Evaluation**
  Stool weight, fecal properties

Picosulfate Na-induced diarrhea model

- **Rat**
- **Evaluation**
  Stool weight, fecal properties

Sennoside-induced diarrhea model

- **Rat**
- **Evaluation**
  Stool weight, fecal properties

Constipation

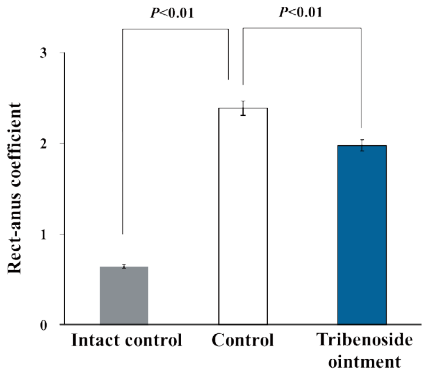
Loperamide-induced constipation model

- **Rat, Mouse**
- **Evaluation**
  Stool weight, fecal properties

Hemorrhoids

Croton oil-induced hemorrhoids model

- **Rat**
- **Evaluation**
  Rectal weight, histopathological examination



Others

Restraint stress-induced gastric emptying dysfunction model

- **Rat**
- **Evaluation**
  Excretion rate

Heidenhain pouch model

- **Dog**
- **Evaluation**
  Gastric juice pH, gastric juice volume

Continuous intragastric pH measurement model

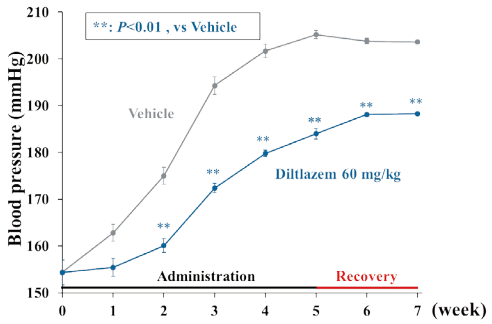
- **Dog**
- **Evaluation**
  Gastric pH

6. Circulatory/Respiratory Systems

High blood pressure

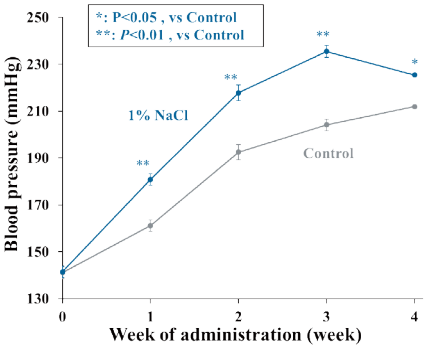
Spontaneously hypertensive rat model (SHR)

- **Rat**
- **Evaluation**
  Blood pressure, heart rate, blood chemical analysis



Stroke-prone spontaneously hypertensive rat model (SHRSP)

- **Rat**
- **Evaluation**
  Blood pressure, heart rate, blood chemical analysis



Deoxycorticosterone acetate hypertensive model

- **Rat**
- **Evaluation**
  Blood pressure, heart rate, blood chemical analysis

Dahl salt-sensitivity model

- **Rat**
- **Evaluation**
  Blood pressure, heart rate, blood chemical analysis

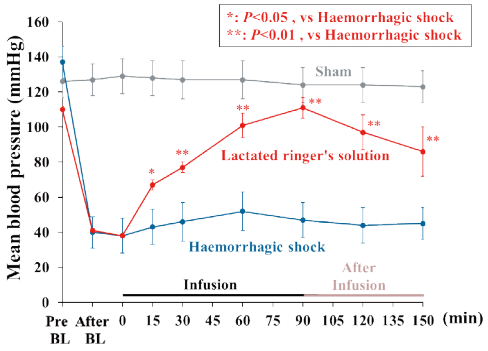
Two-kidney one-clip hypertensive model

- **Rat**
- **Evaluation**
  Blood pressure, heart rate, blood chemical analysis, histopathological examination

Hemorrhagic shock

Hemorrhagic shock model

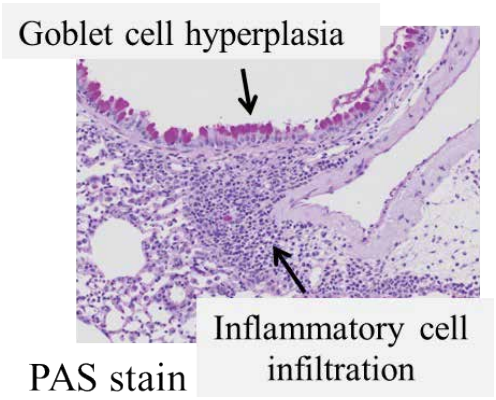
- **Dog**
- **Evaluation**
  Blood gas, blood pressure, heart rate, blood flow, blood chemical analysis



Asthma

Mite antigen-induced asthma model

- **Mouse**
- **Evaluation**
  Histopathological examination, number of inflammatory cells in bronchoalveolar lavage fluid

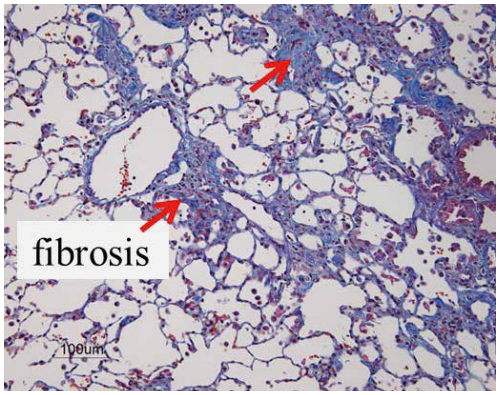


PAS stain

Pulmonary fibrosis

Bleomycin-induced pulmonary fibrosis model

- **Rat, Mouse**
- **Evaluation**
  Histopathological examination, hydroxyproline

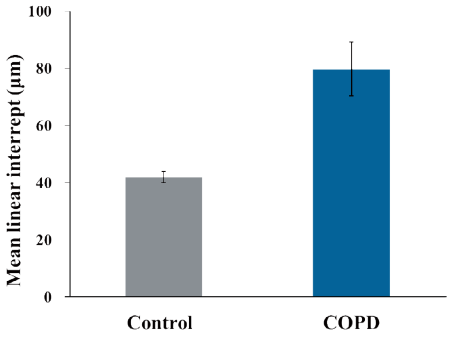


Masson trichrome stain

COPD

Elastase/LPS-induced COPD model

- **Mouse**
- **Evaluation**
  Histopathological examination



Others

Spinal cord injury model

- **Rat**
- **Evaluation**
  Blood pressure

Vascular transplantation model

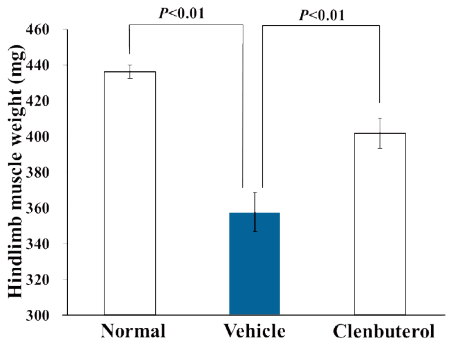
- **Minipig**
- **Evaluation**
  Histopathological examination, blood flow

7. Muscles/Bones

Sarcopenia

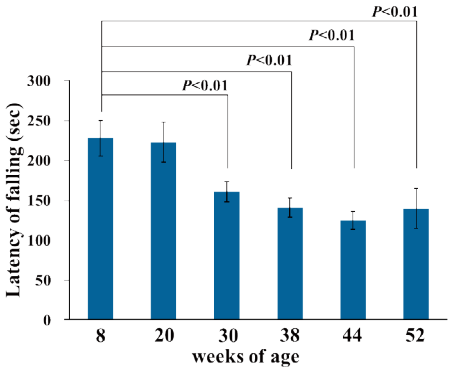
Hindlimb suspension model

- **Rat, Mouse**
- **Evaluation**
  Muscle weight, treadmill test



Natural aging model (B6J-Aged)

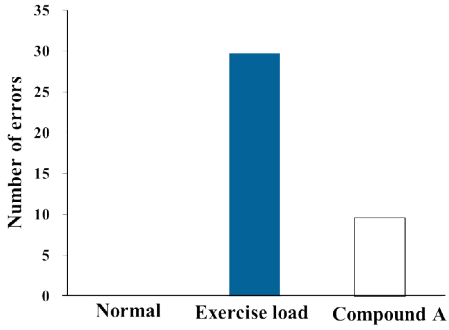
- **Mouse**
- **Evaluation**
  Rotarod test, muscle weight



Exercise fatigue

Exercise load model

- **Rat**
- **Evaluation**
  Blood chemical analysis (lactic acid level), muscle lactic acid level



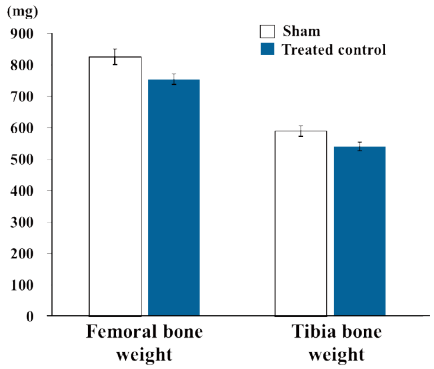
Osteoporosis

RANKL-induced osteoporosis model

- **Mouse**
- **Evaluation**
  Blood chemical analysis, bone density, bone mineral

Ovariectomized osteoporosis model

- **Rat, Mouse**
- **Evaluation**
  Blood chemical analysis, bone density, bone mineral



Others

Muscle implantation test

- **Rabbit**
- **Evaluation**
  Histopathological examination

Bone implantation test

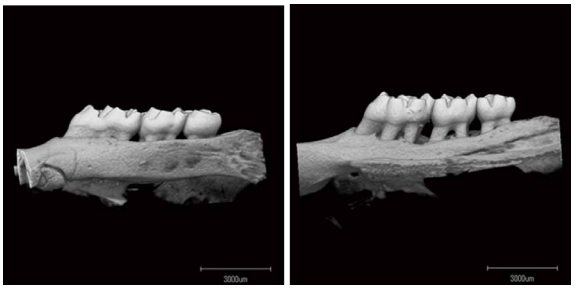
- **Rabbit, Minipig, Dog**
- **Evaluation**
  Pull-out test (rabbit and minipig), histopathological examination

8. Dentistry/Oral Surgery

Periodontal disease

Periodontal disease model

- **Rat, Dog**
- **Evaluation**
  X-ray, histopathological examination



Use simulation test

Dental pulp/dentin use simulation test

- **Dog**
- **Evaluation**
  X-ray (reference data), histopathological examination

Root filling use simulation test

- **Dog**
- **Evaluation**
  X-ray (reference data), histopathological examination

Pulp capping test

- **Dog**
- **Evaluation**
  X-ray (reference data), histopathological examination

Oral surgery

GBR method (guided bone regeneration)

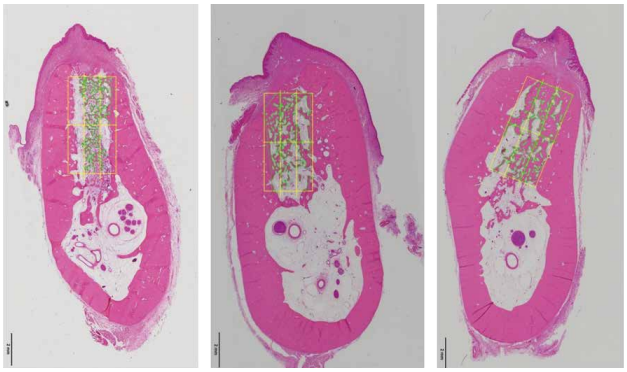
- **Dog**
- **Evaluation**
  Histopathological examination

GTR method (guided tissue regeneration)

- **Dog**
- **Evaluation**
  Histopathological examination

Socket preservation

- **Dog**
- **Evaluation**
  Histopathological examination



Implant

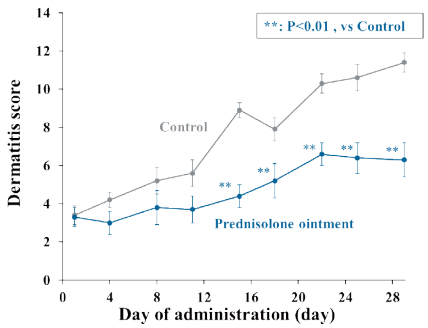
- **Dog**
- **Evaluation**
  Histopathological examination

9. Skin

Atopic dermatitis

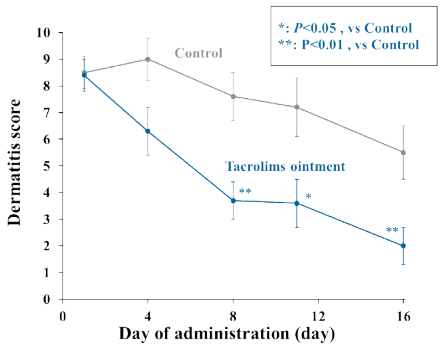
PiCl-induced atopic dermatitis model

- **Mouse**
- **Evaluation**
  Dermatitis score, histopathological examination, blood chemical analysis (IgE), scratching behavior



Mite antigen-induced atopic dermatitis model

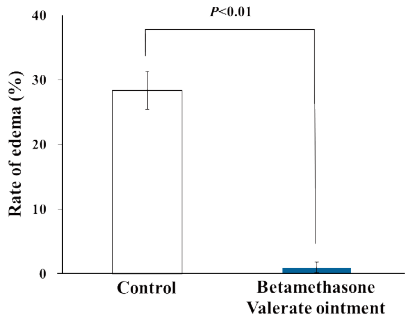
- **Rat, Mouse**
- **Evaluation**
  Dermatitis score, histopathological examination, blood chemical analysis (IgE), scratching behavior



Allergic dermatitis

PiCl-induced type IV allergic dermatitis model

- **Mouse**
- **Evaluation**
  Auricular thickness



DNFB-induced allergic dermatitis model

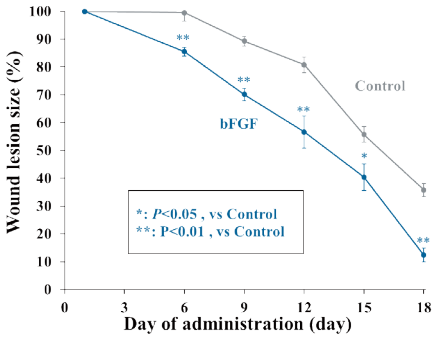
- **Minipig**
- **Evaluation**
  Dermatitis score, histopathological examination, erythema meter

1	2	3	4	5
Non-treated	White petrolatum ointment	Tacrolimus ointment	Betamethasone valerate ointment	Normal

Wound

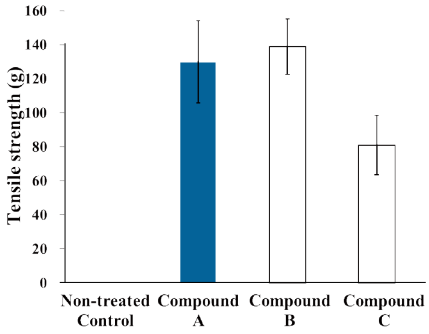
Wound healing model

- **Rat, Mouse**
- **Evaluation**
  Wound area, healing period, histopathological examination



Skin incision model

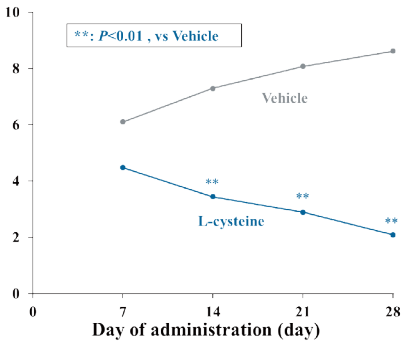
- **Rat**
- **Evaluation**
  Wound tension strength



Spots

UV irradiation-induced pigmentation model

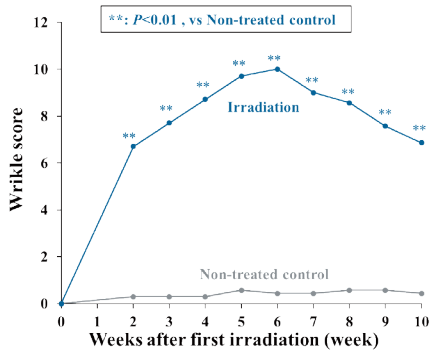
- **Mouse, Guinea pig**
- **Evaluation**
  L value



Wrinkles

UV irradiation-induced wrinkle model (hairless mouse)

- **Mouse**
- **Evaluation**
  Wrinkle analysis



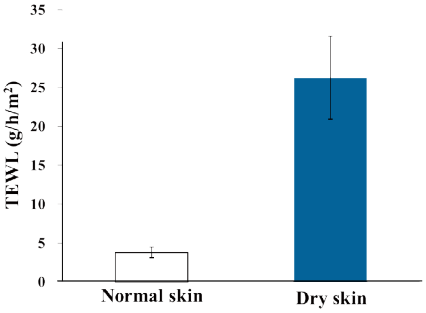
Rough skin

UV irradiation-induced rough skin model

- **Mouse, Guinea pig**
- **Evaluation**
  Skin moisture content, skin transpiration (guinea pig)

Lauryl sulfate application-induced rough skin model

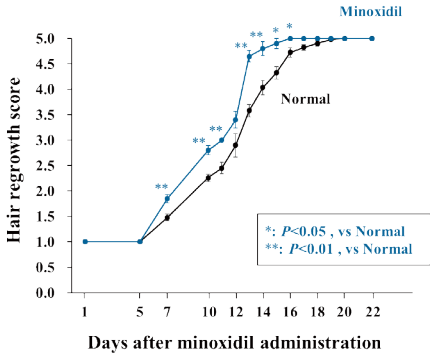
- **Mouse, Guinea pig**
- **Evaluation**
  Skin moisture content, skin transpiration



Alopecia

Hair growth test

- **Rat, Mouse**
- **Evaluation**
  Score

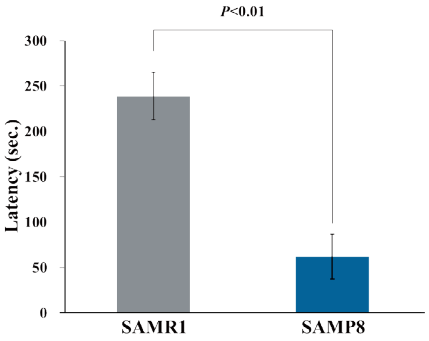


10. Age-Related Diseases

Dementia

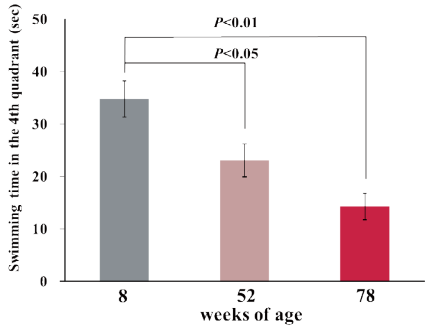
Senescence-Accelerated Mouse (SAM)

- **Mouse**
- **Evaluation**
  Passive avoidance test



Natural aging model (B6J-Aged)

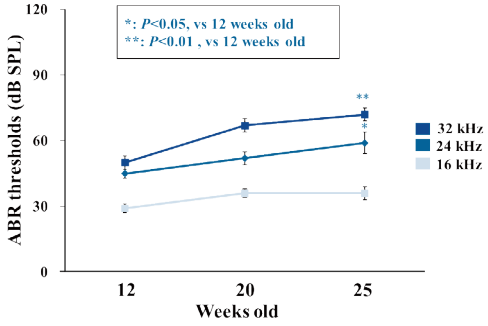
- **Mouse**
- **Evaluation**
  Morris water maze test



Hearing loss

Age-related hearing loss model

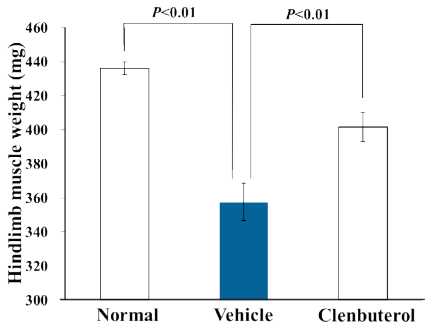
- **Mouse**
- **Evaluation**
  Auditory brainstem response (ABR)



Sarcopenia

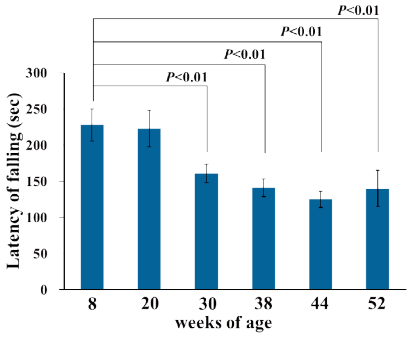
Hindlimb suspension model

- **Rat, Mouse**
- **Evaluation**
  Muscle weight, treadmill test



Natural aging model (B6J-Aged)

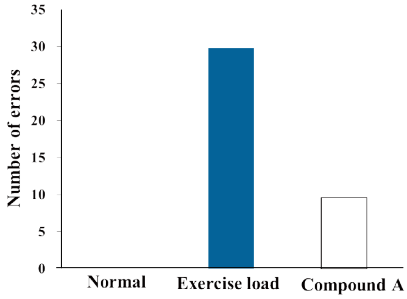
- **Mouse**
- **Evaluation**
  Rotarod test, muscle weight



Exercise fatigue

Exercise load model

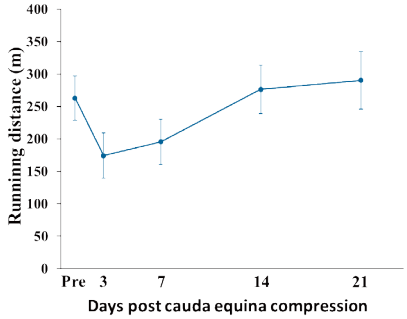
- **Rat**
- **Evaluation**
  Blood chemical analysis (lactic acid level), muscle lactic acid level



Cauda equina syndrome

Cauda equina compression model

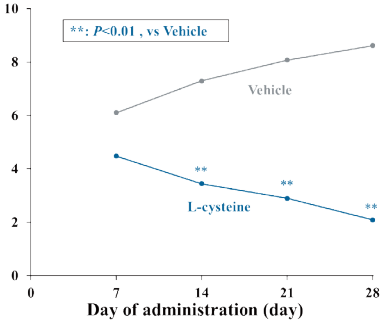
- **Rat**
- **Evaluation**
  Treadmill test, open field test



Spots

UV irradiation-induced pigmentation model

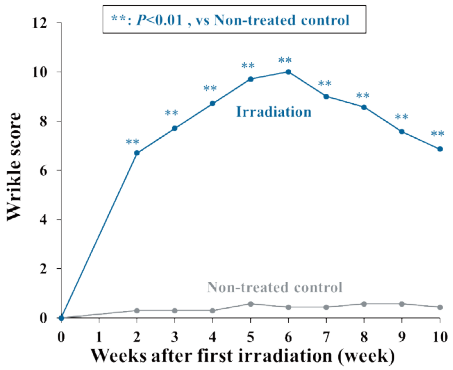
- **Mouse, Guinea pig**
- **Evaluation**
  L value



Wrinkles

UV irradiation-induced wrinkle model (hairless mouse)

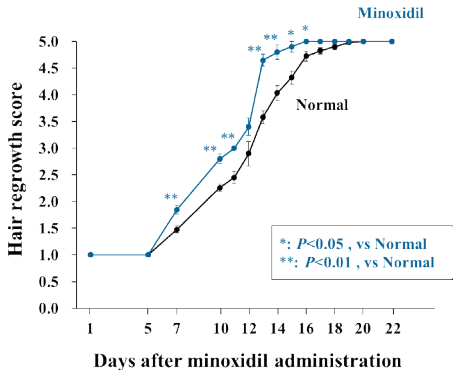
- **Mouse**
- **Evaluation**
  Wrinkle analysis



Alopecia

Hair growth test

- **Rat, Mouse**
- **Evaluation**
  Score

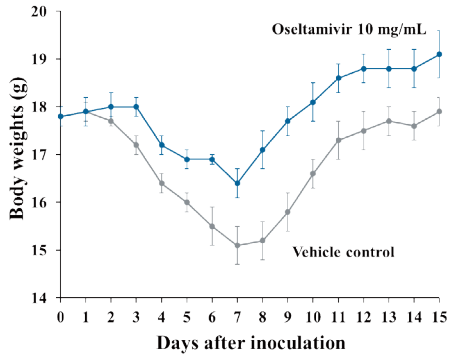


11. Infection

Influenza virus

Influenza virus lung infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, virological testing, NK activity



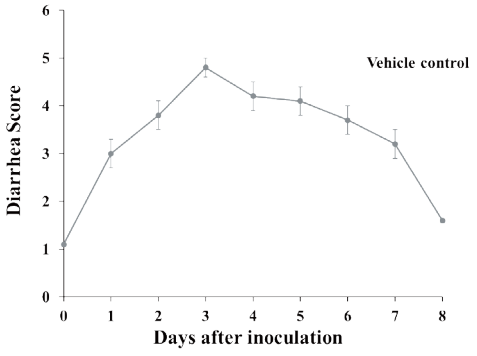
Drug susceptibility testing (influenza virus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Rotavirus

Rotavirus gastrointestinal infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, virological testing, NK activity



Drug susceptibility test (rotavirus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

MRSA

MRSA systemic infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination

Drug susceptibility testing (MRSA)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

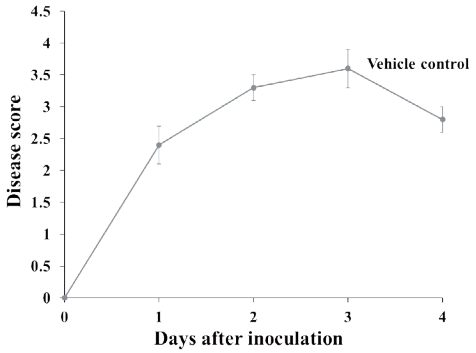
Staphylococcus aureus

Staphylococcus aureus systemic infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination

Staphylococcus aureus skin infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination



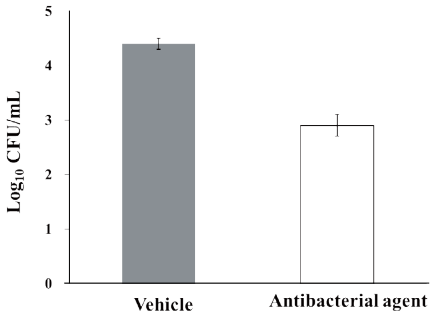
Drug susceptibility test (Staphylococcus aureus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Helicobacter pylori (H. pylori)

Pylori gastrointestinal infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination



Pseudomonas aeruginosa

Pseudomonas aeruginosa systemic infection

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination

Drug susceptibility test (Pseudomonas aeruginosa)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Multidrug-resistant Pseudomonas aeruginosa

Multidrug-resistant Pseudomonas aeruginosa systemic infection

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination

Drug susceptibility test (multidrug-resistant Pseudomonas aeruginosa)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Candida

Candida systemic infection

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination

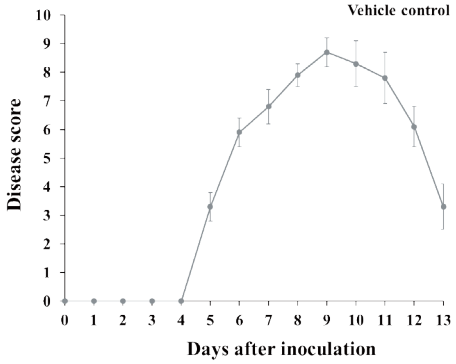
Drug sensitivity test (Candida)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Herpesvirus

Herpesvirus skin infection

- **Mouse**
- **Evaluation**
  Observation of lesion degree, virological testing

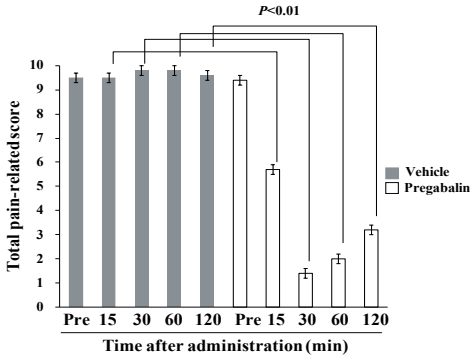


Drug susceptibility test (herpesvirus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Postherpetic neuralgia model

- **Mouse**
  Dermal inoculation of herpesvirus
- **Evaluation**
  Tactile stimulation (withdrawal threshold)



Coli

E. coli systemic infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination

Drug susceptibility test (E. coli)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Salmonella

Salmonella systemic infection model

- **Mouse**
- **Evaluation**
  Observation of lesion degree, bacteriological examination

Drug susceptibility test (Salmonella)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Clostridium difficile infection

Clostridium difficile gastrointestinal infection model

- **Hamster**
- **Evaluation**
  Observation of lesion degree, survival rate, stool quality

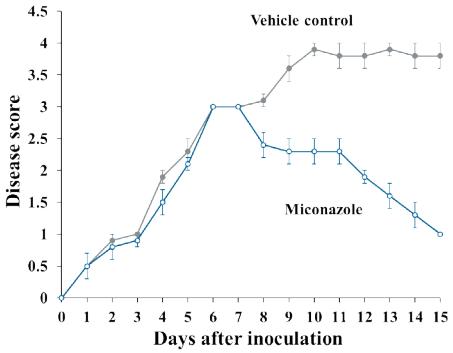
Trichophyton infection

Trichophyton nail infection model

- **Guinea pig**
- **Evaluation**
  Bacteriological examination

Trichophyton skin infection model

- **Guinea pig**
- **Evaluation**
  Observation of lesion degree, bacteriological examination



Drug susceptibility test (Trichophyton)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Feline calicivirus infection

Drug susceptibility test (feline calicivirus)

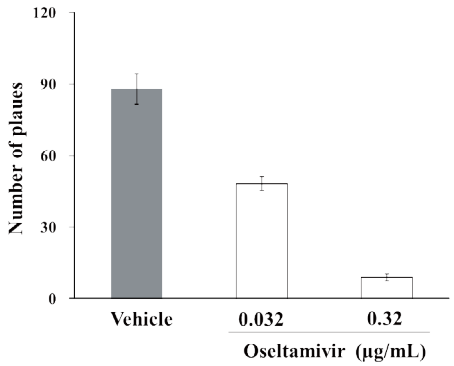
- ***In vitro***
- **Evaluation**
  Plaque reduction method

12. *In vitro*

Drug susceptibility test

Drug susceptibility test (influenza virus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method



Drug susceptibility test (rotavirus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (MRSA)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (Pseudomonas aeruginosa)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (Staphylococcus aureus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (multidrug-resistant Pseudomonas aeruginosa)

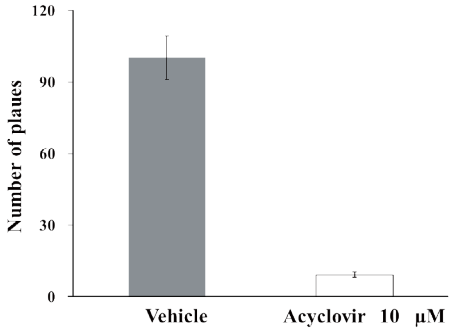
- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug sensitivity test (Candida)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (herpesvirus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method



Drug susceptibility test (E. coli)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (Salmonella)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (Trichophyton)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Drug susceptibility test (feline calicivirus)

- ***In vitro***
- **Evaluation**
  Plaque reduction method

Magnus method

Magnus method (intestinal tract)

- **Rat, Rabbit, Guinea pig**
- **Evaluation**
  Tension

Magnus method (aorta)

- **Rat, Dog, Minipig**
- **Evaluation**
  Tension

Magnus method (coronary artery)

- **Dog, Minipig**
- **Evaluation**
  Tension

Magnus method (trachea)

- **Rat, Guinea pig**
- **Evaluation**
  Tension

Magnus method (stomach)

- **Rat, Rabbit, Guinea pig**
- **Evaluation**
  Tension

Magnus method (pupil)

- **Rabbit, Dog**
- **Evaluation**
  Tension

Magnus method (urethra)

- **Rat, Minipig**
- **Evaluation**
  Tension

Magnus method (bladder)

- **Rat, Minipig**
- **Evaluation**
  Tension

Magnus method (vas deferens)

- **Rat**
- **Evaluation**
  Tension

Magnus method (uterus)

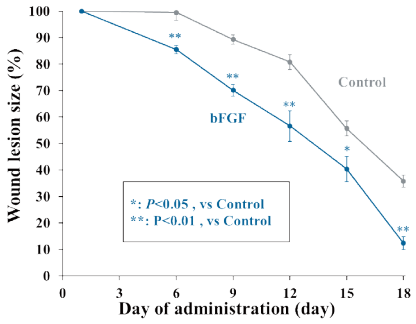
- **Rat**
- **Evaluation**
  Tension

13. Medical Devices

Wound

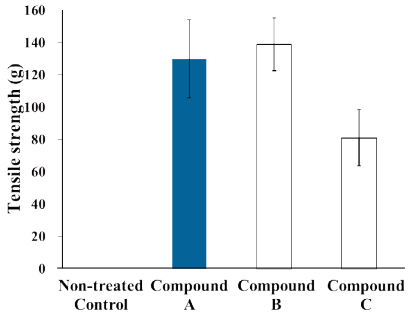
Wound healing model

- **Rat, Mouse**
- **Evaluation**
  Defect area, healing period, histopathological examination



Skin incision model

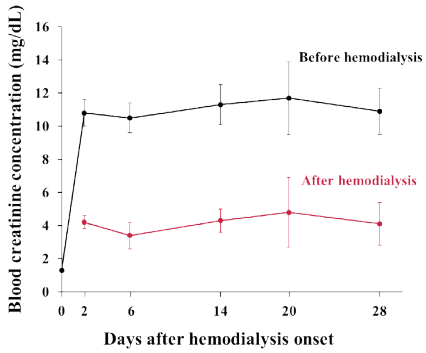
- **Rat**
- **Evaluation**
  Wound tension strength



Chronic kidney disease

Bilateral nephrectomy dialysis model

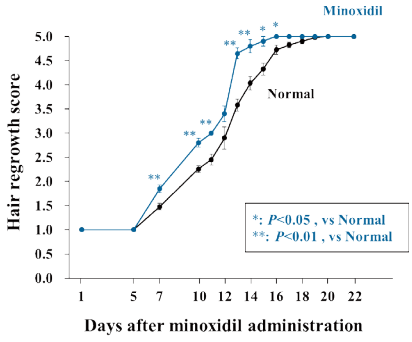
- **Minipig**
- **Evaluation**
  Blood chemical analysis, urinalysis



Alopecia

Hair growth test

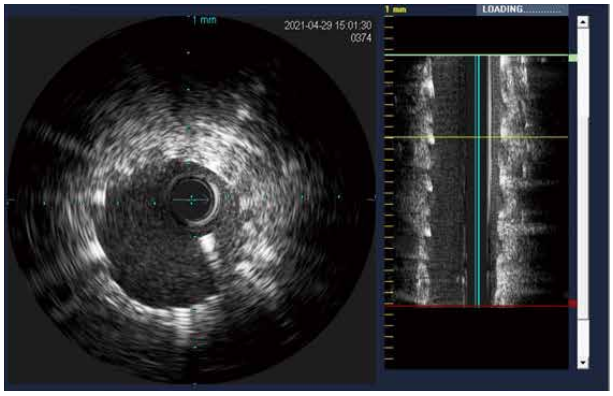
- **Rat, Mouse**
- **Evaluation**
  Score



Implantation

Stent implantation test

- **Minipig**
- **Evaluation**
  Blood flow, stenosis rate, histopathological examination



Others

Medical device performance testing

- **Rabbit, Dog, Minipig**
- **Evaluation**
  Histopathological examination

Muscle implantation test

- **Rabbit**
- **Evaluation**
  Histopathological examination

Bone implantation test

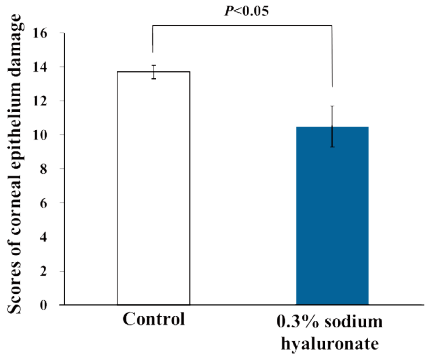
- **Rabbit, Dog, Minipig**
- **Evaluation**
  Pull-out test (rabbit and minipig), histopathological examination

14. Regenerative Medical Products

Corneal damage

Corneal epithelial disorder model

- **Rabbit**
- **Evaluation**
  Dye staining area



Hearing loss

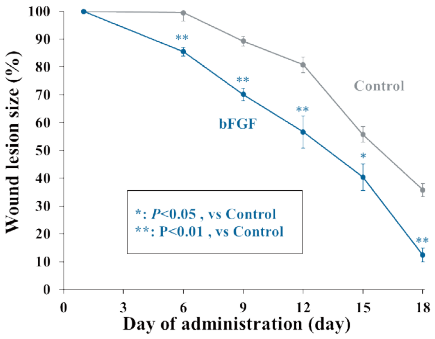
Tympanic membrane perforation model

- **Guinea pig**
- **Evaluation**
  Auditory brainstem response (ABR)

Wound

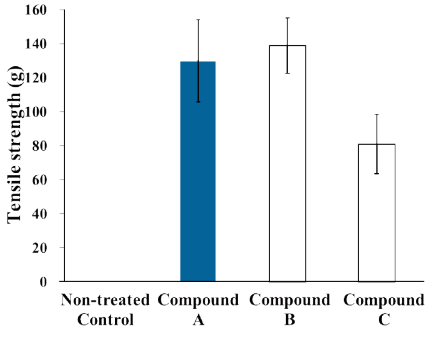
Wound healing model

- **Rat, Mouse**
- **Evaluation**
  Defect area, healing period, histopathological examination



Skin incision model

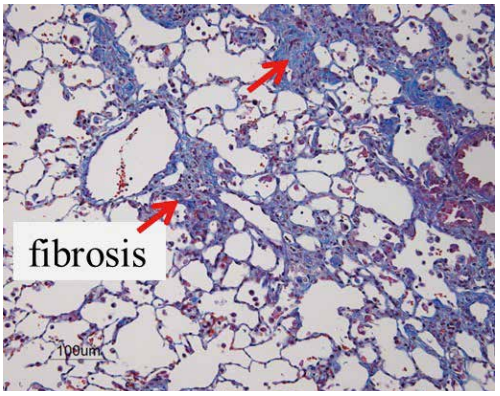
- **Rat**
- **Evaluation**
  Wound tension strength



Pulmonary fibrosis

Bleomycin-induced pulmonary fibrosis model

- **Rat, Mouse**
- **Evaluation**
  Histopathological examination, hydroxyproline

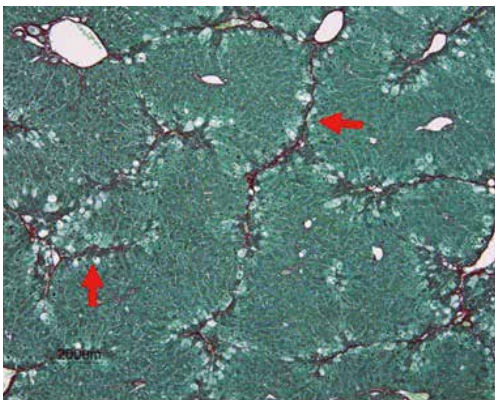


Masson trichrome stain

Hepatic fibrosis

Carbon tetrachloride-induced hepatic fibrosis model

- **Mouse**
- **Evaluation**
  Histopathological examination, hydroxyproline

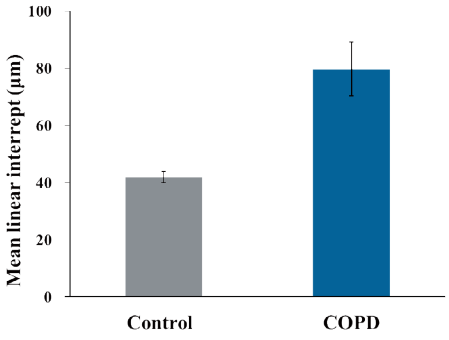


Sirius Red-Fast Green stain ↑ : fibrosis

COPD

Elastase/LPS-induced COPD model

- **Mouse**
- **Evaluation**
  Histopathological examination



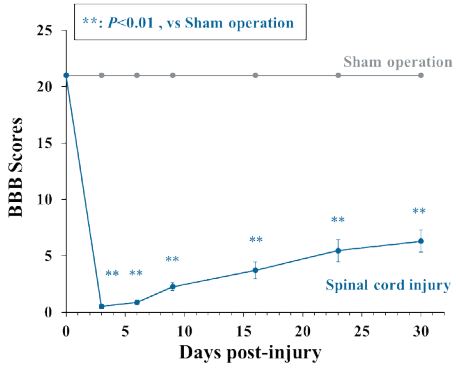
Nerve damage

Sciatic nerve injury

- **Rat**
- **Evaluation**
  Evaluation of sensation, nerve conduction velocity

Spinal cord injury

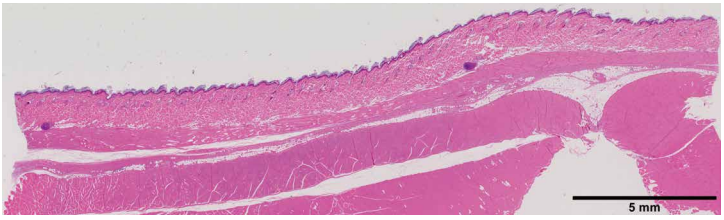
- **Rat, Mouse**
- **Evaluation**
  Motor function score, histopathological examination



Others

Local implantation test

- **Rat, Rabbit, Dog, Minipig**



Bone implantation test

- **Rabbit, Minipig, Dog**
- **Evaluation**
  Pull-out test (rabbit and minipig), histopathological examination

Vascular transplant study

- **Minipig**
- **Evaluation**
  Histopathological examination, blood flow

Osteoarthritis model

- **Minipig**
- **Evaluation**
  Histopathological examination

Safety Pharmacology Studies

Safety Pharmacology Studies

Core Battery/Confirmation Test of Adverse Reactions to Test Articles

1 Central nervous system

Title	Animal species	Evaluation item
Effects on clinical signs and behavior	Rat Mouse	Irwin's method

2 Cardiovascular system

Title	Animal species	Evaluation item
Effects on blood pressure, heart rate, and electrocardiogram	Dog Minipig	Blood pressure/heart rate and electrocardiogram (telemetry)

3 Respiratory system

Title	Animal species	Evaluation item
Effect on respiratory function	Rat	Respiration rate (plethysmography)

Follow-Up or Supplement/Confirmatory Study

1 Central nervous system

Title	Animal species	Evaluation item
Effect on locomotor activity	Rat Mouse	Locomotor activity
Effects of hexobarbital on sleep	Rat Mouse	Time of sleeping
Analgesic effect	Rat Mouse	Pain threshold
Effect on body temperature	Rat Mouse	Rectal temperature
Effect on spontaneous brain waves without anesthesia	Dog Rabbit Cat	Brain waves
Effect on conditioned avoidance response	Rat	
Effect on coordination	Rat Mouse	

2 Smooth muscle

Title	Animal species	Evaluation item
Effect on automatic movement of isolated ileum	Rabbit	Contraction response
Effects of agonists on contraction of isolated ileum (Ach, His, $BaCl_2$, 5-HT)	Guinea pig	Contraction response
Effect on isolated blood vessels	Rat Dog	Contraction response

Title	Animal species	Evaluation item
Effect on isolated trachea	Guinea pig	Contraction response
Effect on isolated vas deferens	Guinea pig	Contraction response
Effect on isolated uterus	Rat	Contraction response

3 Respiratory circulatory system

Title	Animal species	Evaluation item
Effects on cardiorespiratory system under anesthesia	Dog Minipig	Blood pressure, heart rate, and electrocardiogram
Effect on blood pressure response	Rat	Blood pressure, heart rate, and electrocardiogram
Effects on bradycardia caused by cervical vagus nerve stimulation and reflex pressor pressure caused by common carotid artery occlusion		
Effect on cervical vagus nerve stimulation	Rat	Blood pressure
Effect on reflex pressor pressure due to common carotid artery occlusion	Rat	Blood pressure
Effect on isolated atrium	Guinea pig	Contraction response
Effect on action potential duration (APD)	Guinea pig	*in vitro*(cardiac muscle cells)

4 Digestive system

Title	Animal species	Evaluation item
Effect on intestinal transport capacity (charcoal powder method)	Rat Mouse	Moving distance
Effect on gastric juice secretion	Rat	Gastric juice volume
Effect on gastric emptying capacity (dye method)	Rat	Number of beads
Effect on salivary secretion	Rat	Amount of saliva
Effect on bile secretion	Rat	Bile amount
Effect on pancreatic juice secretion	Rat	Pancreatic juice volume
Effect on gastrointestinal motility	Rat Dog	Contraction movement
Gastric mucosal damage effect	Rat	Ulcer prime
Small intestinal mucosal damage effect	Rat	Number of ulcers

5 Renal function

Title	Animal species	Evaluation item
Phenolsulfonephthalein test	Rat	Dye quantification
Osmotic clearance	Rat	Dye quantification
Urine volume and urinary electrolytes	Rat	Urine volume, urinary electrolyte concentration

6 Somatic nervous system

Title	Animal species	Evaluation item
Effect on tibialis anterior muscle specimen	Rat	Contractile response
Effect on diaphragm neuromuscular specimens	Rat	Contractile response
Muscle relaxing effect (suspension method)	Mouse	Time to hand the hind legs to wire
Local anesthetic effect		
Topical anesthetic effect	Guinea pig	Presence or absence of spasms during stimulation
Infiltration anesthesia effect	Guinea pig	Presence or absence of spasms during stimulation

7 Autonomic nervous system

Title	Animal species	Evaluation item
Effect on the pupil	Mouse	
Effect on nictitating membrane reflex	Cat	Palpebral tension

8 Blood system

Title	Animal species	Evaluation item
Effect on blood coagulation	Rabbit	Clotting time
Hemolytic effect	Rabbit	

9 Liver function

Title	Animal species	Evaluation item
Indocyanine green test	Rat	Dye quantification
Bromsulfarein test	Rat	Dye quantification

10 Others

Title	Animal species	Evaluation item
Anti-inflammatory effect (carrageenan footpad edema method)	Rat	Limb volume
Analgesic effect (acetic acid writhing method)	Mouse	Agony reaction
Analgesic effect (Randall-Selitto method)	Rat	Pain threshold

Safety Studies

Safety Studies

Safety Studies (Pharmaceuticals)

1 Single dose toxicity studies

Test	Animal species	Administration period	Group composition	Route of administration
Single dose toxicity study	Mouse Rat	Single	5 animals of each sex/group	Oral Percutaneous Intravenous Subcutaneous Intramuscular Intraperitoneal Intrarectal Oral mucosal
	Dog Minipig	Single	3 animals/group	

2 Repeated dose toxicity studies

Test	Animal species	Administration period	Group composition	Route of administration
Repeated dose toxicity study	Rat	4 weeks 13 weeks 26 weeks	10 animals of each sex/group	Oral Percutaneous Intravenous Subcutaneous Intramuscular Intraperitoneal Intrarectal Oral mucosal
		Recovery	6 animals of each sex/group	
	Dog	4 weeks	3 animals of each sex/group	
		13 weeks 39 weeks 52 weeks	4 animals of each sex/group	
		Recovery	2 animals of each sex/group	
	Minipig	4 weeks 13 weeks 39 weeks 52 weeks	3-4 animals of each sex/group	
		Recovery	2 animals of each sex/group	
	Rabbit	4 weeks	3 animals of each sex/group	Frequent eye drop test (6-12 times/day)

3 Reproductive and developmental toxicity studies

Test	Animal species	Group composition	Route of administration
FEED study	Rat	20 animals of each sex/group	Oral Transdermal Intravenous Subcutaneous Intramuscular Intraperitoneal Intrarectal Oral mucosal
	Mouse	22 animals of each sex/group	
PPND study	Rat	20 mated females/group	
	Mouse	25 mated females/group	
EFD study	Rat Rabbit	20 mated females/group	
	Mouse	22 mated females/group	

4 Local irritation tests

Test	Animal species, etc.	Group composition	Method
Primary skin irritation test	Guinea pig Rabbit Minipig	6 animals (intact skin, abraded skin)	
Eye irritation test	Rabbit	9 (3 with eyewash, 6 without eyewash)	
		5 animals/group	Frequent eye drops (6-12 times/day)

Test	Animal species, etc.	Group composition	Method
Cumulative skin irritation test	Guinea pig Rabbit Minipig	3 to 6 animals	14-day administration 28-day administration
Vascular irritation test	Rabbit	3 animals/group	
Perivascular irritation test	Rabbit	3 animals/group	
Hemolysis test	Rabbit blood Human blood		
Muscle irritation test	Rabbit	6 animals/group	
Subcutaneous irritation test	Rabbit	3 animals/group	
Rectal mucosal irritation test	Rabbit	6 animals/group	
Vaginal mucosal irritation test	Rabbit	3 animals/group	
Skin phototoxicity test	Guinea pig	10 animals	Morikawa's method
Other irritation tests	Guinea pig		Nasal mucosa irritation
	Rabbit etc.		Oral mucosa irritation
	3D cultured normal human epidermis (*in vitro*)		LabCyte EPI-MODEL 24 SIT (OECD TG 439)
	3D cultured human cornea-like epithelium (*in vitro*)		LabCyte CORNEA-MODEL (OECD TG 492)

5 Antigenicity tests

Test	Animal species	Group composition	Method
Skin sensitization test	Guinea pig	5 animals/negative control group 10 animals/test article group 5 animals/positive control group	Adjuvant and Patch test Maximization test Buehler test
Skin photosensitization test	Guinea pig	5 animals/negative control group 10 animals/test article group 5 animals/positive control group	Adjuvant and Strip test Harbor Test
Antigenicity test	Guinea pig	ASA PCA	

6 Genotoxicity tests

Test	Animal species, etc.	Bacterial species, etc.	
Reverse mutation (Ames test)	5 strains	TA98 TA100 TA1535 TA1537 WP2*uvrA*	
Chromosomal aberration test	Cell	CHL/IU	
Micronucleus test (*in vitro*)	Cell	CHL/IU	
Test	**Animal species**	**Group composition**	**Route of administration**
Micronucleus test (in vivo)	Mouse Rat	5 animals/group	Oral Percutaneous Intravenous Subcutaneous Intramuscular Intraperitoneal

Safety Studies (Health Foods)

1 Single dose toxicity studies

Test	Animal species	Administration period	Group composition	Route of administration
Single dose toxicity study	Mouse Rat	Single	5 animals of each sex/group	Oral

2 Repeated dose toxicity studies

Test	Animal species	Administration period	Group composition	Route of administration
Repeated dose toxicity study	Rat	4 weeks 13 weeks 26 weeks	6 animals of each sex/group	Oral Dietary

3 Reproductive and developmental toxicity studies

Test	Animal species	Group composition	Route of administration
FEED study	Rat	20 animals of each sex/group	Oral Dietary
PPND study	Rat	20 mated females/group	
EFD study	Rat Rabbit	20 mated females/group	
Breeding test	Rat	20 mated females/group	

4 Antigenicity tests

Test	Animal species	Group composition, etc.	Route of administration
Antigenicity test	Guinea pig	ASA PCA	Oral

5 Genotoxicity tests

Test	Animal species, etc.	Bacterial species, etc.
Reverse mutation test (Ames test)	5 strains	TA98 TA100 TA1535 TA1537 WP2*uvrA*
Umu test	Bacteria	NM2009
Chromosomal aberration test	Cell	CHL/IU
Micronucleus test (*in vitro*)	Cell	CHL/IU

Test	Animal species	Group composition	Route of administration
Micronucleus test (*in vivo*)	Mouse Rat	5 animals/group	Oral

Safety Studies (Medical Devices)

1 Cytotoxicity tests

Test	Animal species, etc.	Cell	Extraction method
Colony formation method	Cell	L929, V79	Extraction method Direct method
Elution test	Cell	L929	Extraction method

2 Skin sensitization tests

Test	Animal species	Group composition	Extraction method
Maximization Test	Guinea pig	10 animals/test group 5 animals/control group	Extraction with organic solvent Others
Adjuvant and Patch Test	Guinea pig	10 animals/test group 5 animals/control group	Extraction with organic solvent Others

3 Irritation tests/intradermal reaction tests

Test	Animal species	Group composition	Extraction method
Skin irritation test	Rabbit	6 animals/group	Extraction with physiological saline Extraction with vegetable oil
Intradermal reaction test	Rabbit	3 animals/group	Extraction with physiological saline Extraction with vegetable oil
Eye irritation test	Rabbit	6 animals/group	Extraction with physiological saline Extraction with vegetable oil
LabCyte EPI-MODEL 24 SIT	3D cultured normal human epidermis (*in vitro*)		Extraction with physiological saline Extraction with sesame oil

4 General toxicity tests

Test	Animal species	Group composition	Extraction method
Acute systemic toxicity test	Mouse	5 animals of each sex/ group	Extraction with physiological saline Extraction with sesame oil
Subacute toxicity test	Rat	5 animals of each sex/ group	Extraction with physiological saline
Subchronic toxicity test	Rat	10 animals of each sex/ group	Extraction with physiological saline
Chronic toxicity test	Rat	15 animals of each sex/ group	Extraction with physiological saline
Chronic toxicity test*	Dog Minipig		*Evaluation by implanting the test substance is also possible.

5 Genotoxicity tests

Test	Animal species, etc.	Bacterial species, etc.	
Reverse mutation test (Ames test)	5 strains	TA98 TA100 TA1535 TA1537 WP2*uvrA*	
Chromosomal aberration test	Cell	CHL/IU	
Micronucleus test (*in vitro*)	Cell	CHL/IU	
Test	**Animal species**	**Group composition**	**Route of administration**
Micronucleus test (*in vivo*)	Mouse Rat	5 animals/group	Oral

Safety Studies (Medical Devices)

6 Implantation tests

Test	Animal species	Implantation period	Group composition
Short-term intramuscular implantation	Rabbit	1 week 4 weeks	4 animals/group
Implantation in bone	Rabbit	4 weeks 13 weeks 26 weeks 39 weeks 52 weeks 104 weeks	
Implantation in organ	Dog Minipig	4 weeks 13 weeks 26 weeks 39 weeks 52 weeks 104 weeks	
Stent implantation	Minipig	4 weeks 13 weeks 26 weeks 39 weeks 52 weeks	
Subcutaneous implantation	Rat Rabbit	1 week 4 weeks 13 weeks	

7 Hemocompatibility tests

Test	Animal species
Hemolysis test	Rabbit

8 Others

Test	Animal species	Group composition	Others
Use simulation test	Rabbit Dog Minipig		Use simulation/chronic toxicity combination test
Reproductive and developmental toxicity test	Rat Rabbit		
Contact lens test	Rabbit	6 animals/group	ISO 9394
Extraction rate confirmation test using organic solvent			Acetone, methanol, cyclohexane and 2-propanol mixture

Safety Studies (Regenerative Medical Products)

1 General toxicity tests

Test	Animal species	Period	Group composition	Dosing route/remarks
General toxicity test	Immunodeficient animal *1 Immunosuppression *2	Single Repeat*3	5-10 animals of each sex	Clinical dosing route *1 Nude mouse, SKID mouse, NOG mouse, NSG mouse, etc. *2 Minipig, rabbit, beagle *3 See frequency of clinical administration

2 Safety pharmacology studies

Test	Animal species	Dosing route/remarks
Effects on clinical signs and behavior	Immunodeficient animal *1 Immunosuppression *2	Clinical dosing route *1 Nude mouse, SKID mouse, NOG mouse, NSG mouse, etc. *2 Minipig, rabbit, beagle
Effects on the cardiovascular system	Immunodeficient animal *1 Immunosuppression *2	Clinical dosing route *1 Nude mouse, SKID mouse, NOG mouse, NSG mouse, etc. *2 Minipig, rabbit, beagle
Effects on respiratory function	Immunodeficient animal *1 Immunosuppression *2	Clinical dosing route *1 Nude mouse, SKID mouse, NOG mouse, NSG mouse, etc. *2 Minipig, rabbit, beagle

3 Tumorigenicity tests

Test	Animal species	Group composition	Administration route/remarks
Tumorigenicity test (*in vivo*)	munodeficiency animal *1	10 animals/group	Clinical dosing route Subcutaneous administration *1 Nude mouse, SKID mouse, NOG mouse, NSG mouse, etc.

4 Soft agar colony formation tests

Test
Soft agar colony formation test (*in vivo*)

Nihon Bioresearch Inc.

Hashima Laboratory (Headquarters)
104, 6-chome, Majima, Fukuju-cho, Hashima, Gifu, 501-6251 Japan
Tel: +81-58-392-6222
Web: https://www.nbr.co.jp/en/ **e-mail:** nbrkikaku@nisshin.com

Shuzenji Branch (facilities for minipigs)
1868-23 Ohno, Izu, Shizuoka, 410-2402 Japan
Tel: +81-558-72-9091

Kisosansen Branch (facilities for infection studies)
676-2, Nakamukuri, Fukue, Kaizu-cho, Kaizu, Gifu, 503-0628 Japan
Tel: +81-584-51-2737

SCAN CODE

TO SEE WEBSITE

TO CONTACT US