Pharmacology Discovery Services

A Eurofins Discovery Partner Lab

eurofins | DISCOVERY

Autoimmune and Inflammation Models for Preclinical Efficacy Studies

In Vivo Services to Advance Your Drug Candidates

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65+ Validated *In Vivo* Autoimmune and Inflammation Models

Pharmacology Discovery Services (PDS), a partner lab of Eurofins Discovery, offers preclinical CRO services and has over 65+ validated *in vivo* animal models for autoimmune and inflammatory diseases. These models range from basic models of immune modulation, restoration, suppression, and stimulation to specific models of inflammation-induced organ damage. All experimental models are validated with approved benchmark positive controls. We routinely measure relevant biomarkers (e.g., cytokines) and physiologic outcomes like airway hyperresponsiveness and swelling. More complex behavioral outcomes, such as scratching, can also be measured, as well as other *ex vivo* analyses, such as flow cytometry, RT-qPCR, or histopathology. To meet the needs of your specific Inflammation/Allergy drug discovery projects, we have the flexibility and expertise to develop custom *in vivo* models.

AUTOIMMUNE DISEASES

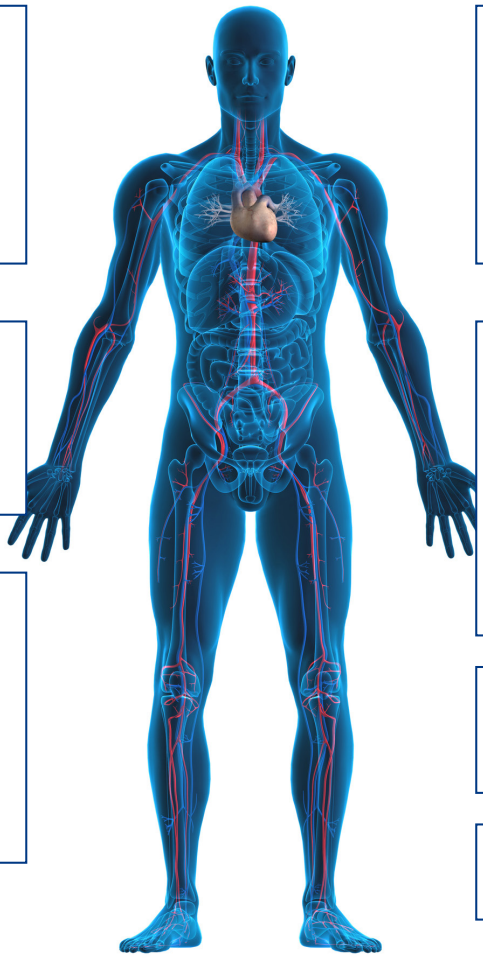
- Rheumatoid Arthritis (RA)
- Inflammatory Bowel Disease (IBD)
- Psoriasis
- Diabetes, Type I
- Systemic Lupus Erythematosus (SLE)
- Multiple Sclerosis (MS)

METABOLIC DISEASES

- Diet-induced Obesity (DIO)
- Diabetes, Type II
- Diabetes, Type I
- Hyperuricemia

DERMAL INFLAMMATION

- Allergy
- Dermatitis (Atopic or Contact)
- Pruritus
- Psoriasis
- Delayed-Type Hypersensitivity
- Passive Cutaneous Anaphylaxis (PCA)
- Wound Healing



RESPIRATORY SYSTEM

- Asthma
- Cough
- Lung Fibrosis
- Neutrophilia
- Chronic Obstructive Pulmonary Disease (COPD)

DIGESTIVE SYSTEM

- Gastric Irritation
- Gastric Ulcer
- Gastrointestinal Motility
- Hepatic Injury
- Liver Fibrosis
- NASH
- Inflammatory Bowel Disease (IBD)
- Pancreatitis

JOINT

- Rheumatoid Arthritis (RA)
- Gout

SYSTEMIC INFLAMMATION

- Septic Shock

Return to TOC

PK and Safety Assessment

Prior to efficacy testing, evaluation of test articles may start with safety/tolerability and PK studies. A recommended strategy typically looks like this:

- **Plasma Stability** – to confirm the in-life plasma stability of a test article
- **PK Testing** – to evaluate PK profiles using the same route of administration as the efficacy model
- **Maximum Tolerated Dose (MTD)** – to identify the maximum dose that does not display toxicity
- **Side Effect Profiling**
  - Modified Irwin
  - Locomotor activity
  - Roto-rod test of coordination

Optional Services

- **In-life PK and bio-analysis** from plasma or tissues
- **Tissue harvest:** brain, spinal cord, paw, skin, etc.
- **Biomarker analysis:** cytokines, chemokines, and other biomarkers assayed in protein or mRNA levels
- **Flow cytometry**
- **Histopathology**

Facility and Accreditations

- **AAALAC accredited**
- **Compliant with the Office of Laboratory Welfare (OLAW)**
- **BSL-2 facility**

Experiments are performed under specific-pathogen-free (SPF) conditions in our AAALAC-accredited vivarium with the oversight of veterinarians to assure compliance with the Pharmacology Discovery Services IACUC regulations and the humane treatment of laboratory animals.

Your Best *In Vivo* Partner to Establish Pre-Clinical Proof-of-Concept

We provide therapeutically focused disease efficacy models that incorporate biomarkers and outcome measures to enable greater prediction of success in the clinic.

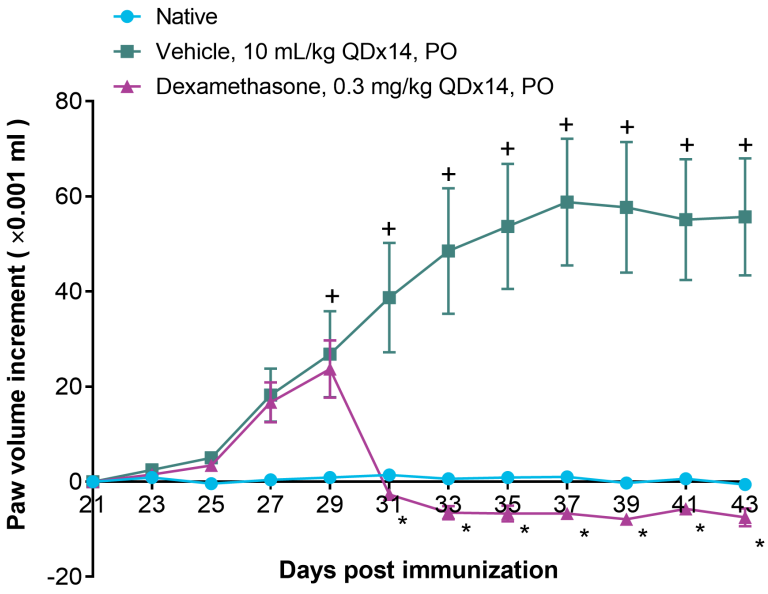
Autoimmune Diseases

Collagen-Induced Arthritis (CIA) Model

Rheumatoid arthritis (RA) is a chronic inflammatory disorder that causes pain, swelling, stiffness, and loss of function in joints. Collagen-induced arthritis (CIA) is commonly used to study the mechanisms of inflammatory joint disease and evaluate the therapeutic efficacy of test articles.

In the CIA mouse model (#553680), DBA/1 mice at 8-12 weeks are challenged with bovine type-II collagen emulsified with complete Freund's adjuvant (CFA) on Day 0 (0.1 mg/ 0.1 mL/mouse, intradermally (ID) at the base of the tail) and boosted on Day 21 with collagen emulsified with IFA (0.1 mg/ 0.1 mL/ mouse). Animals are stratified into groups based on the volume of two hind paws on Day 29. Test article and vehicle are administered orally (PO) once daily for 14 consecutive days from Day 29 to Day 42. Arthritis is assessed using a qualitative severity score system and hind paw volume.

CIA rat model (#553700) is also available.



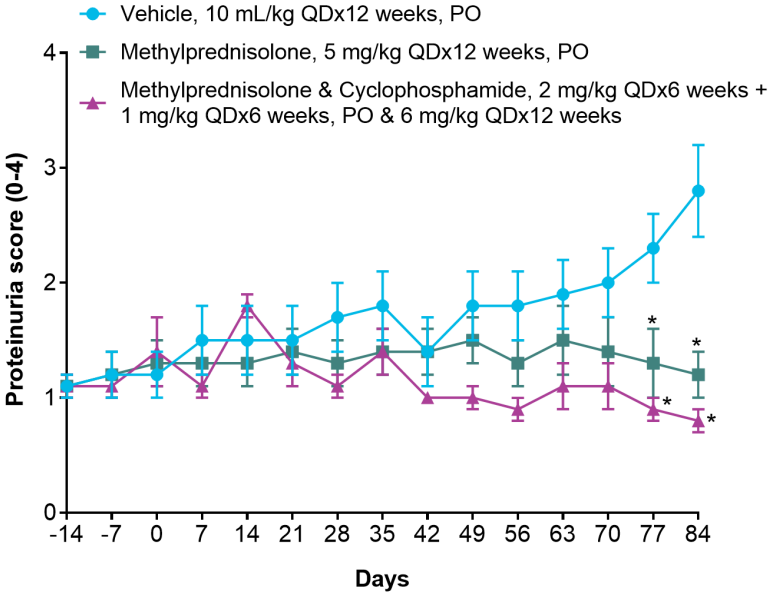
+ $p < 0.05$, vs. sham control; *$p < 0.05$, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 1. Hind paw volume in the collagen-induced arthritis model (#553680).

Systemic Lupus Erythematosus (SLE) Models

Systemic lupus erythematosus (SLE) is an autoimmune disease that is characterized by autoantibody production and involves many organs such as skin, joints, kidneys, and the central nervous system (CNS), and the renal disease (lupus nephritis) is considered the most severe manifestation of SLE with an increased risk of morbidity and mortality. The two most used spontaneous mouse models are NZBWF1/J mice and MRL/lpr mice.

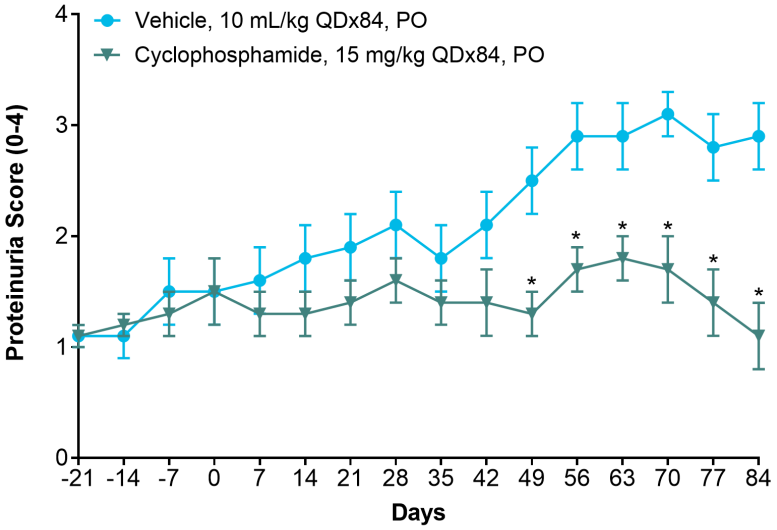
In the NZBWF1/J mouse model (#558000), female NZBWF1/J mice of 24-26 weeks of age are used. Mice are randomly assigned to different treatment groups after kidney damage around 26-28 weeks of age. Vehicle and test articles are administered orally for 12 weeks. The animals are sacrificed at the end of Week 38 or 40, and kidneys, spleen, and draining lymph nodes are collected and weighed. Readouts include body weight, proteinuria, serum blood urea nitrogen (BUN), creatinine, total IgG, histopathology analysis, etc.



*$p < 0.05$, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 2. Proteinuria score in NZBWF1/J mouse SLE model (#558000).

In the MRL/lpr mouse model (#558050), female MRL/lpr mice of 10-12 weeks of age are used. Mice are randomly assigned to different treatment groups after kidney damage around 12-14 weeks of age. Vehicle and test articles are administered orally for 12 weeks. The animals are sacrificed at the end of Week 24 or 26, and kidneys, spleen, and mesenteric lymph nodes are collected and weighed. Readouts include body weight, proteinuria, macroscopic skin lesions, serum blood urea nitrogen (BUN), creatinine, total IgG, and histopathology analysis, etc.



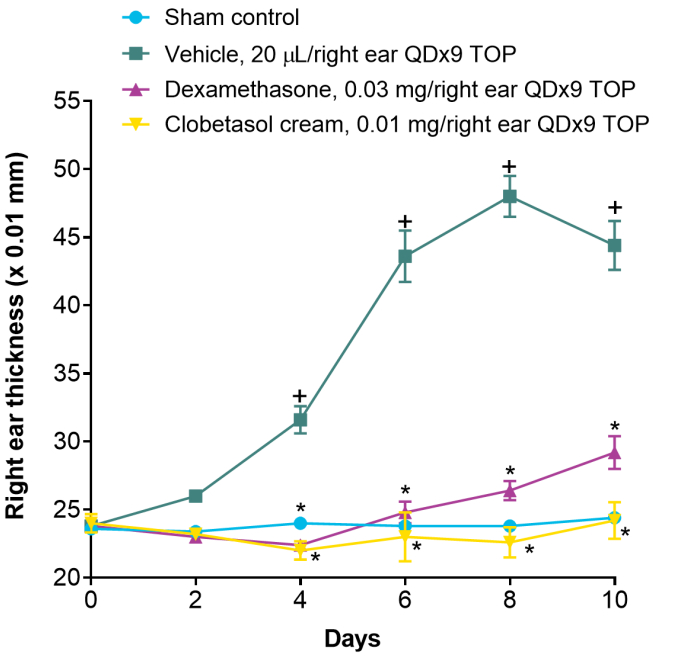
*p < 0.05, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 3. Proteinuria score in MRL/lpr mouse SLE model (#558050).

Imiquimod (IMQ)-Induced Psoriasis Mouse Model

Psoriasis is a chronic autoimmune skin disease characterized by the focal formation of plaque psoriasis, erythema, skin thickening, epidermal alterations, and T cell and dendritic cell infiltration. Topical application of Imiquimod (IMQ) on the ear of mice induces skin lesions closely resembling human plaque-type psoriasis. IMQ-induced psoriasis is commonly used to study the mechanisms of skin inflammation and evaluate the therapeutic efficacy of test articles.

Male BALB/c mice were applied with a daily topical dose (TOP) (#555650) of commercially available IMQ cream (5%) on the right ear for 9 consecutive days. Vehicle, Dexamethasone, and test articles are administered by TOP once daily for 9 consecutive days 1 hour before the IMQ challenge. Ear swelling is measured with a dial thickness micrometer gauge as an index of inflammation. Ear swelling is measured 24 hours after the last dosing. The animals are sacrificed, and then the ears are harvested and weighed.



+p < 0.05, vs. sham control; *p <0.05, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 4. Ear thickness in IMQ-induced psoriasis model (#555650).

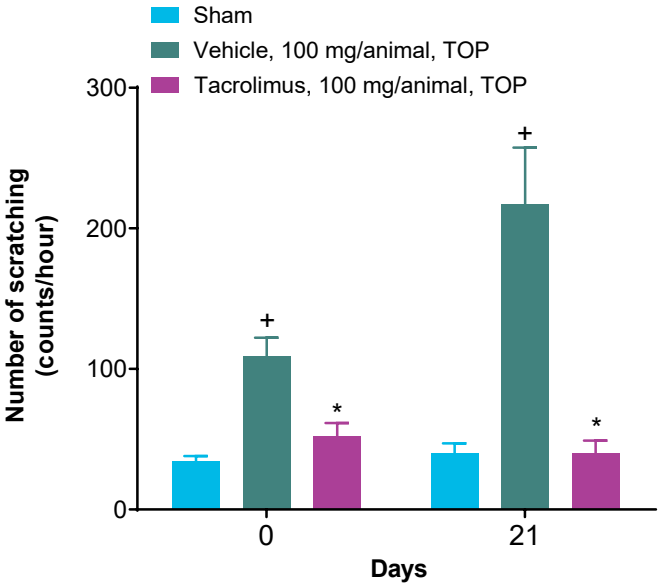
Validated Autoimmune Disease Models			
Model Name	**Item Number**	**Species**	**Turnaround Time**
Arthritis, Collagen-Induced (CIA), Mouse	553680	Mouse	60 Days
Arthritis, Collagen-Induced (CIA), Rat	553700	Rat	40 Days
Lupus, Systemic Lupus Erythematosus (SLE), NZB/W F1 Mouse	558000	Mouse	120 Days
Lupus, Systemic Lupus Erythematosus (SLE), MRL/lpr Mouse	558050	Mouse	120 Days
Psoriasis, Topical, Imiquimod (IMQ)-Induced	555650	Mouse	40 Days

Dermal Inflammation

House Dust Mite (HDM)-Induced Atopic Dermatitis Mouse Model

Atopic dermatitis (AD) is characterized by chronic, highly pruritic, and relapsing inflammatory skin lesions. It is reported that mite allergen from *Dermatophagoides farinae* induces stable clinical AD-like skin diseases in female NC/Nga mice. Skin changes in NC/Nga mice are evidenced by scratching behavior, followed by the rapid development of erythema, lichenification with edema, and hemorrhage. In addition to these skin changes, NC/Nga mice exhibit elevated levels of total serum IgE.

In this model (#555710), female 8 to 10-week-old NC/Nga mice are treated with Biostir®-AD twice a week for three weeks. Test articles and vehicle are administered daily by gavage for 21 days. The dosing patterns may change per client's requests. Scratching assay, evaluation of skin lesions, and ear thickness are performed on Days 0 (baseline) and 21; these can be extended to weekly observations. The severity of skin lesions is characterized by the presence of erythema/hemorrhage, edema, excoriation/erosion, and dryness/scaling.



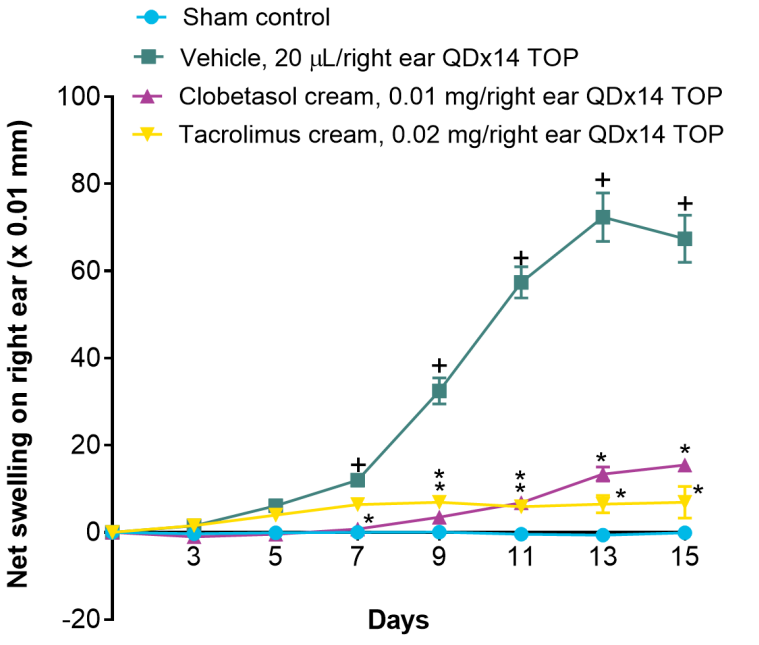
+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; unpaired Student's t-test.

Figure 5. Number of scratching in house dust mite (HDM)-induced atopic dermatitis mouse model (#555710).

MC903-Induced Atopic Dermatitis Mouse Model

The vitamin D3 analog MC903 (calcipotriol), a psoriasis therapeutic drug, is used to induce atopic dermatitis (eczema)-like symptoms, including Th2 type inflammation and eosinophilia. The MC903-induced atopic dermatitis (eczema) mouse model is commonly used to study the mechanisms of skin inflammation and evaluate its therapeutic efficacy.

In this MC903 mouse model (#555740), female C57BL/6 mice at 8 weeks old are treated with MC903 (2 nmole/20 µL, dissolved in 100% ethanol) topically (TOP) daily on the right ear one hour after treatment from Day 1 to Day 14 for 14 consecutive days. Control mice receive the same volume of ethanol during the same study period. The dosing regimen may change per client's requests. Ear swelling is measured by an experimenter blinded to treatment group, with a dial thickness micrometer gauge as an index of inflammation 30 min before dosing on Days 1, 3, 5, 7, 9, 11, and 13. On Day 15, ear swelling is measured 24 hours after the last dosing. The animals are sacrificed, and then the ears are harvested and weighed.



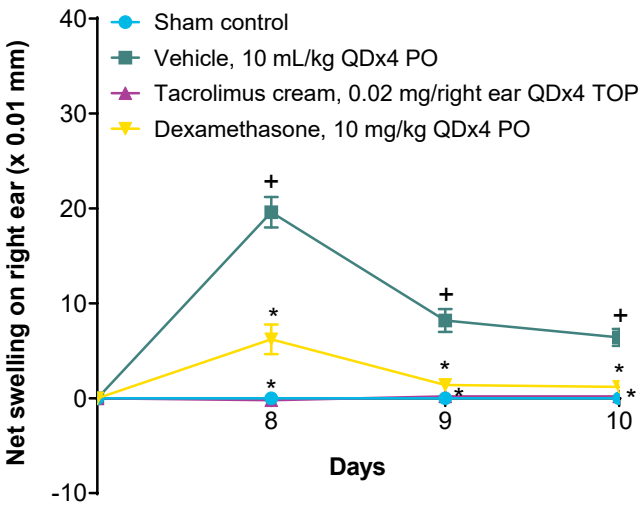
+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 6. Ear swelling in MC903-induced atopic dermatitis mouse model (#555740).

Fluorescein Isothiocyanate (FITC)-Induced Contact Hypersensitivity (CHS) Mouse Models

Allergic contact dermatitis (ACD), which is caused by allergens, is a type of delayed hypersensitivity. Contact hypersensitivity (CHS) is a T cell-mediated immune response in the epidermis. The fluorescein isothiocyanate (FITC)-induced CHS models in mice are commonly used to study the mechanisms of skin inflammation and evaluate the therapeutic efficacy.

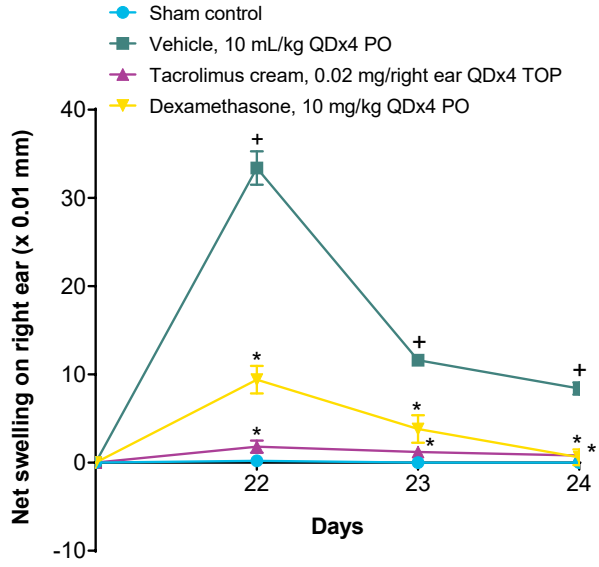
In acute CHS mouse model (#555720), male BALB/c mice at 8 weeks of age are treated with two hundred microliter (200 µL) of 0.5% Fluorescein Isothiocyanate (FITC) topically (TOP) onto the shaved abdominal skin on Days 1 and 2, respectively. On Day 7, mice are challenged by applying 20 µL of 0.5% FITC solution onto both sides of the right ear. The dosing regimen may change per the client's requests. Ear swelling is measured by an experimenter blinded to treatment group, with a dial thickness micrometer gauge as an index of inflammation 30 min before dosing on Days 7, 8, 9, and 10. On Day 10, ear swelling is measured at 24 hours after the last dosing. The animals are sacrificed, and the ears are then harvested and weighed.



+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 7. Ear swelling in FITC-induced acute AD model (#555720).

In chronic CHS mouse model (#555725), male BALB/c mice at 8 weeks of age are treated with two hundred microliter (200 µL) of 0.5% Fluorescein Isothiocyanate (FITC) topically (TOP) onto the shaved abdominal skin on Days 1, 2, 15, and 16, respectively. On Day 21, mice are challenged by applying 20 µL of 0.5% FITC solution onto both sides of the right ear. The dosing regimen may change per the client's requests. Ear swelling is measured by an experimenter blinded to treatment group, with a dial thickness micrometer gauge as an index of inflammation 30 min before dosing on Days 21, 22, 23, and 24. On Day 24, ear swelling is measured at 24 hours after the last dosing. The animals are sacrificed, and then the ears are harvested and weighed.



+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 8. Ear welling in FITC-induced chronic AD model (#555725).

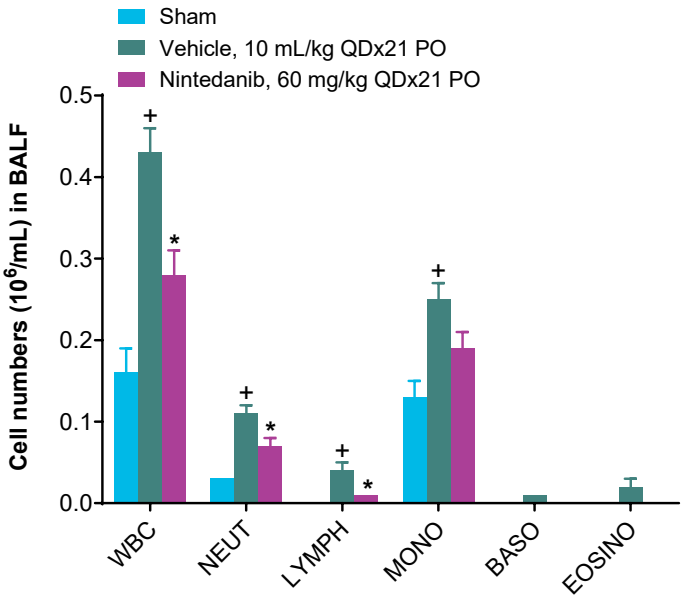
Validated Dermal Inflammation Disease Models			
Model Name	**Item Number**	**Species**	**Turnaround Time**
Dermatitis, Atopic, Mite-Induced	555710	Mouse	45 Days
Dermatitis, Atopic, MC903-Induced	555740	Mouse	20 Days
Contact Hypersensitivity (CHS), Fluorescein Isothiocyanate (FITC)-Induced, Acute	555720	Mouse	20 Days
Contact Hypersensitivity (CHS), Fluorescein Isothiocyanate (FITC)-Induced, Chronic	555725	Mouse	60 Days

Fibrosis

Bleomycin-Induced Lung Fibrosis Mouse Model

Pulmonary fibrosis is characterized by alveolar epithelial cell injury, areas of type II cell hyperplasia, accumulation of fibroblasts and myofibroblasts, and the deposition of extracellular matrix proteins. Intratracheal instillation (IT) of bleomycin is a widely used experimental model for lung fibrosis and assessment of anti-fibrotic agents.

Male C57BL/6 mice weighing 24 ± 2 g are used. The animals are intratracheally treated with a single dose of bleomycin (1.5 IU/kg) on Day 1. Dosing of vehicle and test articles starts immediately post bleomycin administration through Day 21. The animals are sacrificed on Day 22, and bronchoalveolar lavage fluid (BALF) as well as the lung sample are collected. Readouts include total and differential cell counts in BALF, level of TGF-β1 in BALF, level of lung hydroxyproline, and histopathological analysis, etc.



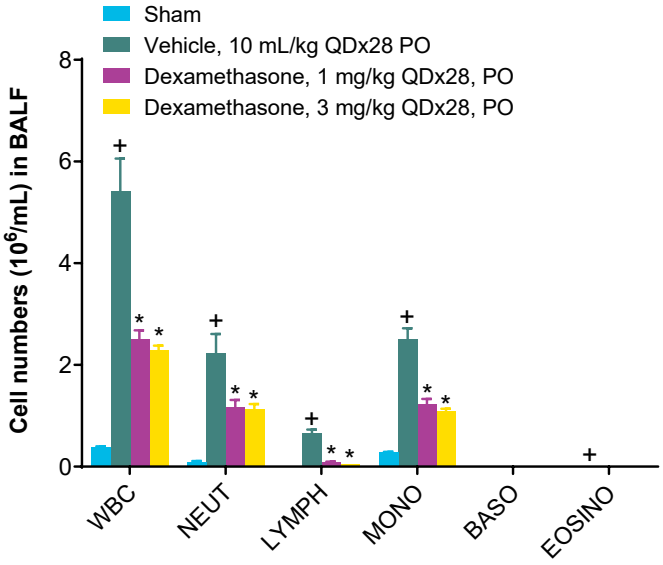
+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

Figure 9. Cell numbers in BALF in bleomycin-induced lung fibrosis mouse model (#568070).

Porcine Pancreatic Elastase (PPE)-Induced Chronic Obstructive Pulmonary Disease (COPD) Mouse Model

Chronic obstructive pulmonary disease (COPD) is a serious health problem with high morbidity and mortality rates. It is characterized by lung parenchyma destruction, emphysema, and chronic lung inflammation. The pathophysiology of airways in COPD involves oxidative stress, neutrophilic airway inflammation, and protease–anti-protease imbalance. Porcine pancreatic elastase (PPE) is a protease that can induce the breakdown of alveolar tissue and emphysema and has been commonly used as an animal model for COPD.

Male BALB/c mice at age of 7-8 weeks old are used. The animals are intratracheally treated with porcine pancreatic elastase (PPE, 1.2 U/20 µL/mouse) on Days 0, 7, 14, and 21 and E. Coli lipopolysaccharide (LPS, 7 µg/20 µL/mouse) on Days 4, 11, 18, and 25. Vehicle and test articles will be administered by oral gavage once daily starting immediately post-PPE administration through Day 27. The animals are sacrificed on Day 28, and bronchoalveolar lavage fluid (BALF) as well as the lung sample are collected. Readouts include total and differential cell counts in BALF, histopathological analysis etc.



+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

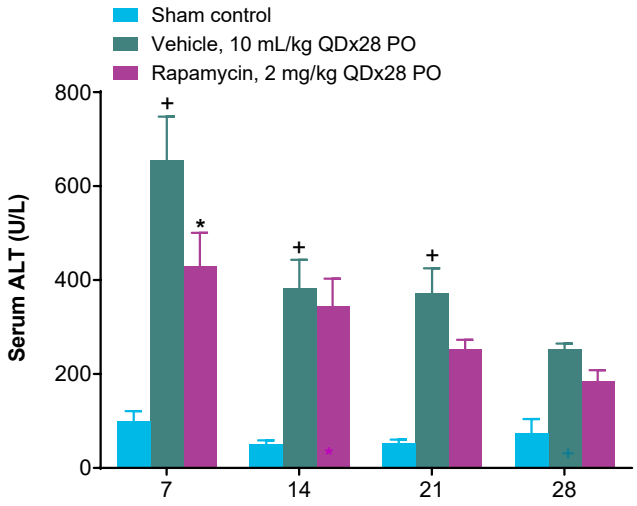
Figure 10. Cell numbers in BALF in PPE-induced COPD mouse model (#568080).

Bile Duct Ligation (BDL)-Induced Liver Fibrosis Mouse Model

Bile Duct Ligation (BDL) is widely used to induce liver cholestasis and fibrosis. In the ligation protocol, the mice are subjected to double ligation of the common bile duct with dissection of the bile duct between the ligatures. This model is applied to investigate the anti-inflammatory and anti-fibrotic effects of test articles for hepatic inflammation and fibrosis in mice.

In the BDL-induced liver fibrosis mouse model, laparotomy is performed in male C57BL/6 mice at 8 weeks of age. The exposed bile duct is ligated and secured with two double ligatures around the proximal and distal parts of the bile duct. Administrations of the vehicle and test articles start at 2 hours after BDL surgery (Day 0) and once daily for 4 weeks. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin (T-BIL) levels are measured on Days 7, 14, 21 and 28. Body weight is recorded three times a week. The animals are sacrificed 24 hours after the final treatment (Day 28), and the liver is harvested and weighed. Liver-to-body weight ratio is calculated for each animal.

(BDL)-induced liver fibrosis rat model (#546090) is also available.



+$p < 0.05$, vs. sham control; *$p < 0.05$, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 11. Serum ALT level in BDL-induced liver fibrosis mouse model (#546095).

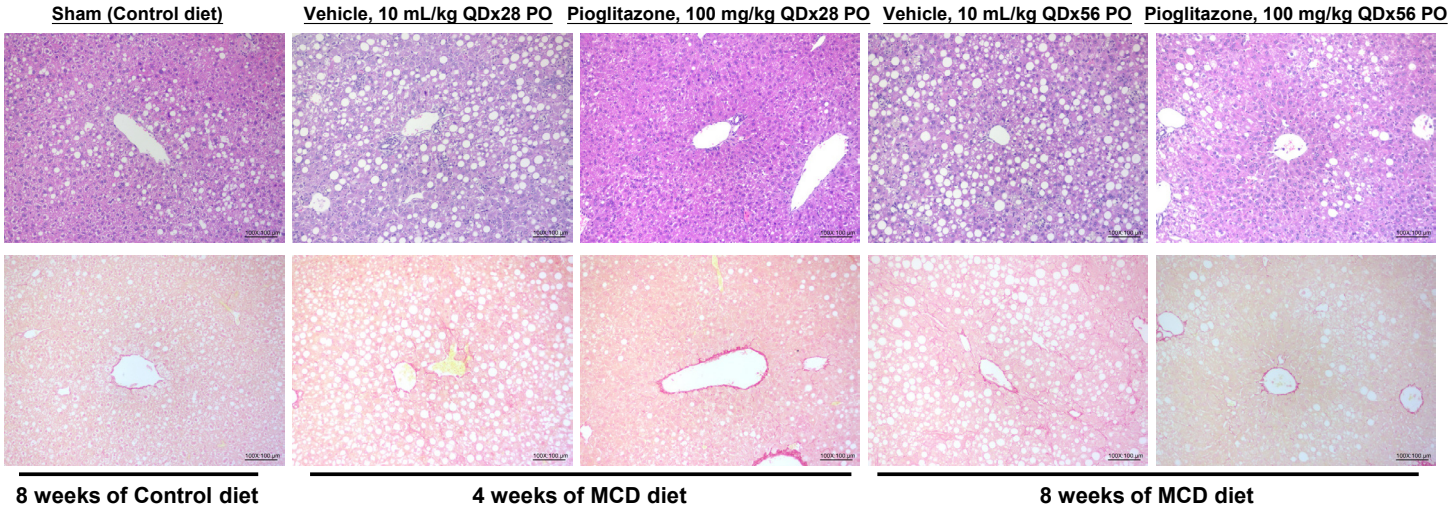
Validated Fibrosis *In Vivo* Models			
Model Name	**Item Number**	**Species**	**Turnaround Time**
Fibrosis, Lung, Bleomycin-Induced	568070	Mouse	60 Days
Chronic Obstructive Pulmonary Disease (COPD), Elastase-Induced	568080	Mouse	50 Days
Hepatic Injury, Liver Fibrosis, Bile Duct Ligation (BDL)-Induced, Mouse	546095	Mouse	60 Days
Hepatic Injury, Liver Fibrosis, Bile Duct Ligation (BDL)-Induced, Rat	546090	Rat	60 Days

Non-Alcoholic Steatohepatitis (NASH)

Pharmacology Discovery Services (PDS) offers two types of diet-induced rodent models of NASH, using either a Methionine and Choline-deficient (MCD) diet or a Choline-deficient, L-amino acid-defined, High-fat Diet (CDAHFD). For the CDAHFD model, either C57BL/6 mice or humanized liver chimeric mice can be used. Both diet-induced models rely upon lipotropic deficiency (methionine and/or choline) that impedes normal intrahepatic triglyceride metabolism. This leads to steatosis, oxidative stress, and liver cell death. Readouts include but are not limited to body weight, liver/body weight ratio, histological changes, and biochemical analysis etc.

Methionine and Choline Deficient (MCD) Diet-Induced NASH Mouse Model

The mouse MCD diet-induced NASH model (#546080) rapidly elicits pathogenesis in the liver (e.g., 4-8 weeks) that is similar to NASH in humans. In this model, male C57BL/6 mice at 8-10 weeks of age are used. Mice are fed with MCD or a control diet for 4 or 8 weeks. Vehicle and test articles are administered orally by gavage to mice daily during the 4 or 8 weeks of diet feeding. The animals are sacrificed 24 hours after the final treatment, and the liver is harvested and weighed.



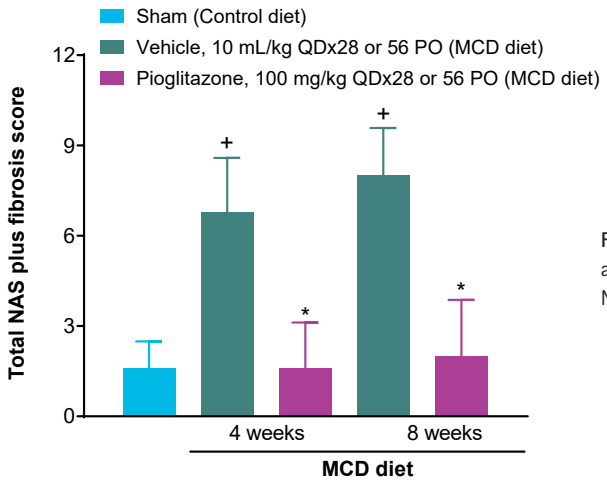
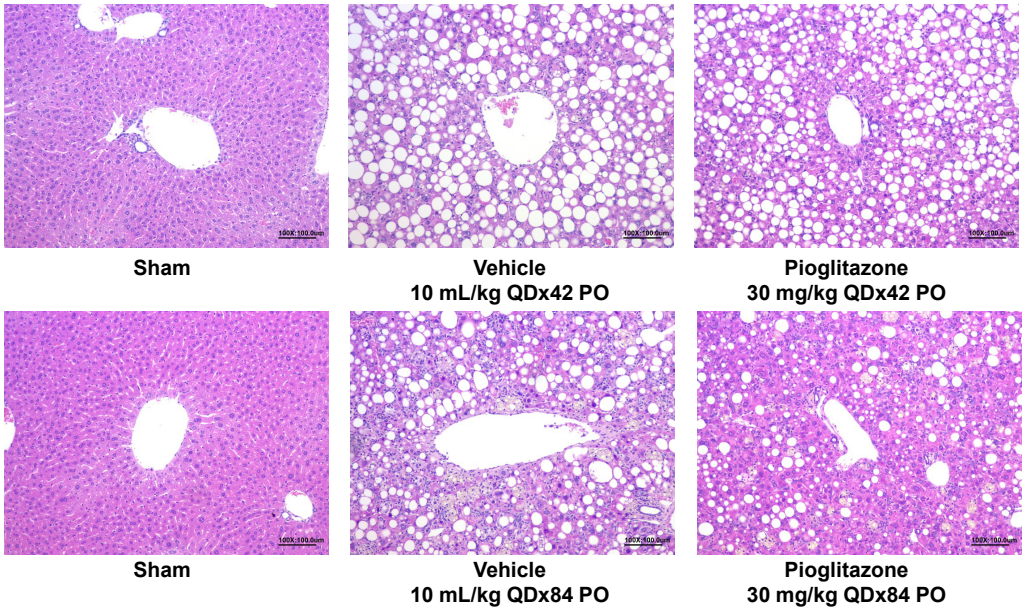


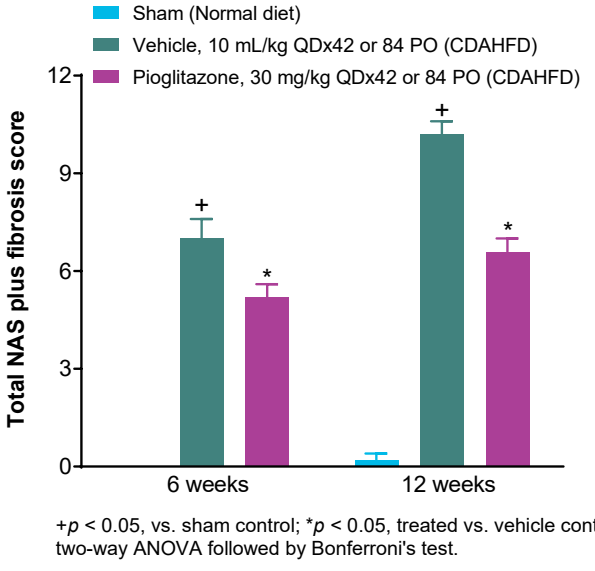
Figure 12. (Top to bottom) Liver histopathology and total NAS plus fibrosis score in MCD diet-induced NASH model (#546080).

+$p < 0.05$, vs. sham control; *$p < 0.05$, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

Choline-Deficient and High-Fat Diet (CDAHFD)-Induced NASH Mouse Model

Male C57BL/6 mice at 8-10 weeks of age are used. Mice fed with a choline-deficient, amino acid-defined high-fat diet (CDAHFD) show a histopathological progression from steatosis, NASH, and fibrosis over a 12-week study period, which nicely resembles the human NASH phenotype. In this model (#546082), mice are fed with CDAHFD or a normal diet for 12 weeks. Vehicle and test articles are administered by oral gavage once daily during the 12 weeks of diet feeding. At termination (Day 84), animals are sacrificed 24 hours after the final treatment, and the livers are harvested and weighed.





+$p < 0.05$, vs. sham control; *$p < 0.05$, treated vs. vehicle control; two-way ANOVA followed by Bonferroni's test.

Figure 13. (Top to bottom) Liver histopathology and total NAS plus fibrosis score in CDAHFD-induced NASH model (#546082).

CDAHFD-Induced NASH Model in Humanized Liver Chimeric Mice

PDS has recently launched a NASH model in humanized liver chimeric mice (HLCM)(#546086). These chimeric mice, called PXB-mice, have been created in which mouse hepatocytes are largely replaced by human hepatocytes and have been used for drug metabolism, pharmacokinetic studies, liver toxicity testing, drug transport, and drug-drug interactions. PXB-mice are fed a choline-deficient, amino acid-defined high-fat diet (CDAHFD), or control diet (CRF-1 diet) for 12 weeks. Vehicle and test articles are administered by oral gavage once daily during the 12 weeks of diet feeding. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels are determined for evaluation of hepatic impairment on Weeks 2, 4, 6, 8, 10, and 12. Animals are sacrificed at Week 12, and the livers are harvested and weighed.

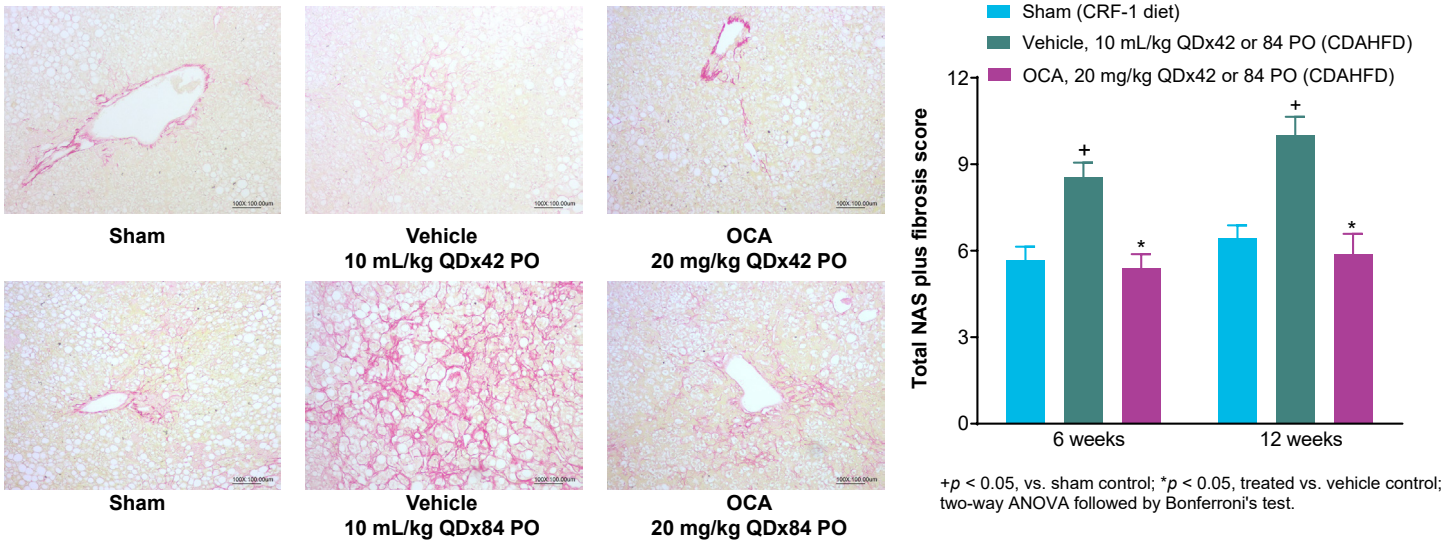


Figure 14. (Left to right) Liver histopathology and total NAS plus fibrosis score in CDAHFD-induced NASH model in humanized liver chimeric mice (#546086).

Validated NASH Models

Model Name	Item Number	Species	Turnaround Time
Nonalcoholic Steatohepatitis (NASH), MCD Diet-Induced	546080	Mouse	40 Days
Nonalcoholic Steatohepatitis (NASH), CDAHFD Diet-Induced	546082	Mouse	120 Days
Nonalcoholic Steatohepatitis (NASH), CDAHFD Diet-Induced, Humanized Liver Chimeric Mouse	546086	Mouse	120 Days

Inflammatory Bowel Disease (IBD)

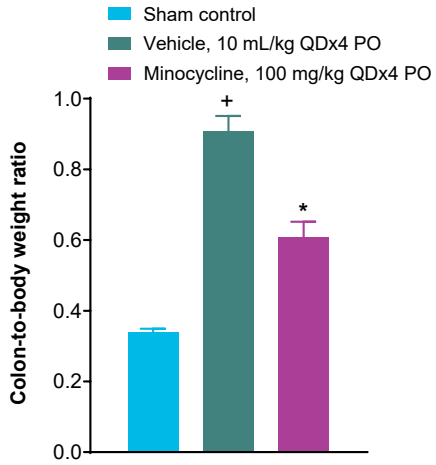
Seven different chemically induced models of IBD (DNBS, DSS, Oxazolone, or TNBS) are available from Pharmacology Discovery Services. Some models are available in both mice and rats. Catheters can be surgically implanted into the colon for test article delivery to achieve maximal local drug concentration and minimize systemic exposure. Available readouts include but are not limited to colon-to-body weight ratio, fecal occult blood, stool consistency, body weight, and biomarker analysis.

Acute DSS-Induced Colitis Mouse Model

In the Dextran Sulphate Sodium (DSS)-induced colitis model, DSS acts to disrupt the gut epithelial cells of the basal crypts and affect the integrity of the mucosal barrier, allowing the exposure of the lamina propria to bacterial antigens to trigger inflammatory responses. A key benefit of the DSS-induced colitis model is that it can be run in an acute or chronic setting depending on the purpose of the study.

In the acute mouse model (#553420), DSS at 2.5% or 5% was given in autoclaved drinking water for 5 days to C57BL/6 or BALB/c mice, respectively. Dose administrations of the test articles, vehicle, and reference agents are initiated on Day 6 and continued for 4 days.

Acute DSS-induced colitis rat model (#553425) is also available.

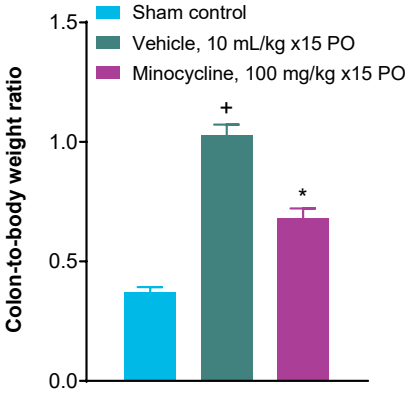


+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

Figure 15. Colon-to-body weight ratio in acute DSS-induced colitis mouse model (#553420).

Chronic DSS-Induced Colitis Mouse Model

In the chronic mouse model (#553440), 2.5% DSS is given in autoclaved drinking water for 5 days in each cycle, followed by a recovery period of 7 days with normal drinking water. Animals are exposed to three cycles in total. The mice in Sham group are given drinking water only. Test articles, vehicle, and the standard minocycline are administered during the DSS challenge periods for a total 15 treatments. During the study period, body weight, fecal occult blood, and stool consistency will be recorded every other day. On Day 30, the mice are euthanized by CO_2 asphyxiation, colon is weighed, and its length is recorded.



+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

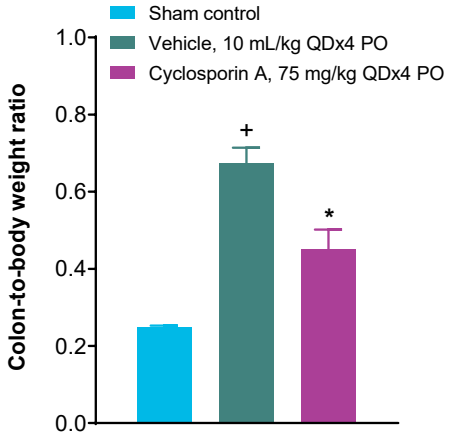
Figure 16. Colon-to-body weight ratio in chronic DSS-induced colitis mouse model (#553440).

TNBS-Induced Colitis Mouse Model

TNBS is a hapten agent that elicits a strong Th1 immunologic response in the mucosal layer by attaching to autologous or microbial proteins in the colon that make them immunogenic to the host immune system.

Distal colitis is induced in male BALB/c mice by intracolonic instillation of TNBS (1 mg in 0.1 mL 50% ethanol). Test articles, vehicle, and the standard cyclosporine A are administered by oral gavage 24 hours and 2 hours before TNBS administration, followed by daily dosing for 2 days.

TNBS-induced colitis rat model (#553410) is also available.



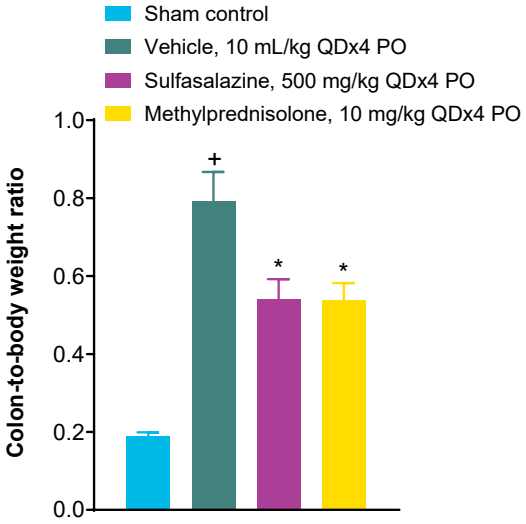
+p< 0.05, vs. sham control; *p < 0.05, treated vs. vehicle contro one-way ANOVA and Dunnett's test.

Figure 17. Colon-to-body weight ratio in TNBS-induced colitis mouse model (#553405).

Oxazolone-Induced Colitis Mouse Model

Oxazolone (4-ethoxymethylene-2-phenyl-2-oxazolin-5-one, OXA)-induced colitis model (#553430) has become to be accepted as a T helper-2 (Th-2) type colitis model for human ulcerative colitis (UC) and is commonly used to study the mechanisms of gastrointestinal inflammation and evaluate the therapeutic efficacy.

Male BALB/c mice are sensitized by applying oxazolone (150 µL, 3% in acetone/olive oil, 4:1 v/v) to their pre-shaved rostral back on Day 0. The animals are re-sensitized with oxazolone on Day 5. Distal colitis is induced by intracolonic instillation of oxazolone solution (100 µL, 1% in 40% ethanol). Test articles, vehicle, and the standard Sulfasalazine are administered by oral gavage 24 hours and 2 hours before oxazolone administration, followed by daily dosing for 2 days.



+p < 0.05, vs. sham control; *p < 0.05, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

Figure 18. Colon-to-body weight ratio in Oxazolone-induced colitis mouse model (#553430).

Validated Inflammatory Bowel Disease (IBD) Models

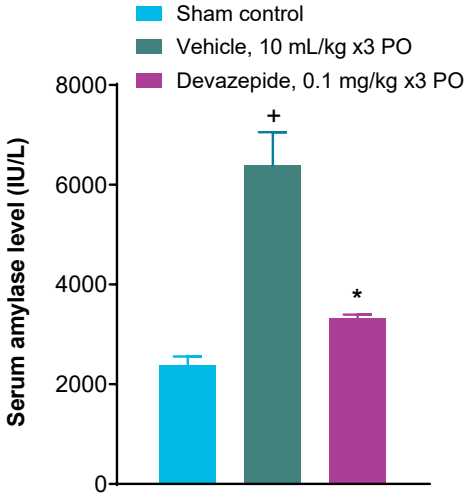
Model Name	Item Number	Species	Turnaround Time
Inflammatory Bowel Disease (IBD), DSS-Induced Colitis, Mouse	553420	Mouse	30 Days
Inflammatory Bowel Disease (IBD), DSS-Induced Colitis, Rat	553425	Rat	20 Days
Inflammatory Bowel Disease (IBD), DSS-Induced Colitis, Chronic	553440	Mouse	60 Days
Inflammatory Bowel Disease (IBD), TNBS-Induced Colitis, Mouse	553405	Mouse	20 Days
Inflammatory Bowel Disease (IBD), TNBS-Induced Colitis, Rat	553410	Rat	20 Days
Inflammatory Bowel Disease (IBD), Oxazolone-Induced Colitis	553430	Mouse	30 Days

Pancreatitis

Caerulein-induced pancreatitis in mice is a well-studied model of gastrointestinal disorders, including acute pancreatitis and chronic pancreatitis. The initiation of this disorder is mediated by the activation of a cascade of digestive zymogens that results in acinar cell necrosis and pancreatic edema followed by an inflammatory response. The caerulein-induced pancreatitis is a useful mouse model to examine mechanisms of pathogenesis as well as therapeutic and prophylactic efficacy.

Caerulein-Induced Acute Pancreatitis Mouse Model

In the acute caerulein-induced pancreatitis model (#566100), male ICR mice with overnight fasting received three IP injections of caerulein (100 µg/kg) with 2 hours intervals. The test article is administered 1 hour after each injection. Animals are sacrificed at 9 hours after the first caerulein injection, and serum alpha-amylase concentration from each animal is determined. Additional analyses that can be requested include but are not limited to serum lipase levels, MPO activity, pancreas weight, biomarker analysis (protein and/or mRNA), and histopathology.

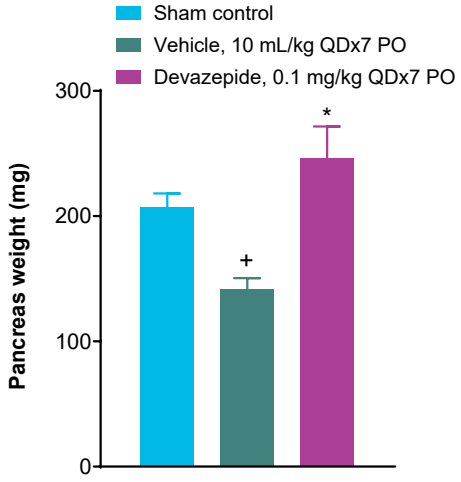


+$p < 0.05$, vs. sham control; *$p < 0.05$, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

Figure 19. Serum amylase level in caerulein-induced acute pancreatitis mouse model (#566000).

Caerulein-Induced Chronic Pancreatitis Mouse Model

In the chronic caerulein-induced pancreatitis model, male ICR mice are treated with six repeated hourly IP injections of caerulein (50 µg/kg) every other day for three days (Days 1, 3, and 5), for a total of 18 injections. The test article is administered once daily for 7 days, 1 hour before caerulein injection on Days 1, 3, and 5. Animals are sacrificed on Day 8, three days after the final caerulein treatment. Serum α-amylase concentration and pancreas weight are determined. Additional analyses that can be requested include MPO, biomarkers (protein and/or mRNA), and histopathology.



+$p < 0.05$, vs. sham control; *$p < 0.05$, treated vs. vehicle control; one-way ANOVA and Dunnett's test.

Figure 20. Pancreas weight in caerulein-induced chronic pancreatitis mouse model (#566100).

Validated Pancreatitis Disease Models

Model Name	Item Number	Species	Turnaround Time
Pancreatitis, Caerulein-Induced, Acute	566000	Mouse	20 Days
Pancreatitis, Caerulein-Induced, Chronic	566100	Mouse	40 Days

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