

MSU-induced Gout Models



WuXi AppTec, WuXi Biology, Oncology & Immunology Unit



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OncoWuXi Newsletter

Outline

■ Background

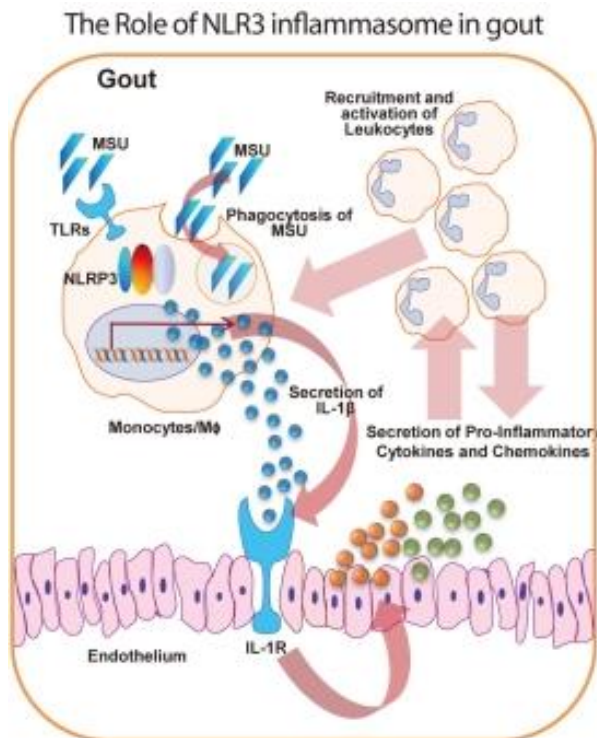
- Molecular mechanism of gout

■ MSU-induced gout models

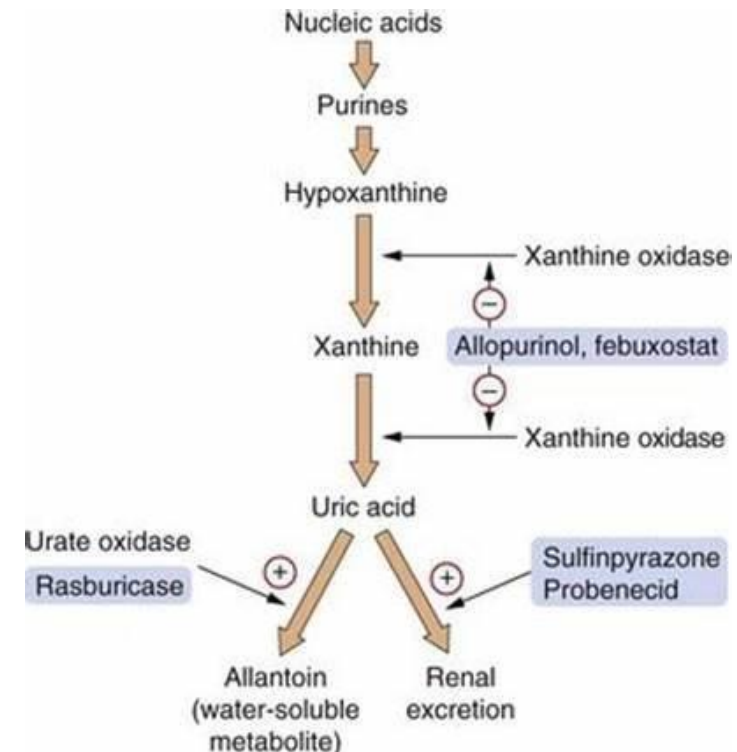
- Model summary
- Model development and validation

Molecular Mechanism of Gout

- Gout is a chronic inflammatory arthritis results from deposition of monosodium urate crystals (MSU), which activates the NLRP3 inflammasome and secretion of multiple cytokines like IL-1 β , IL-18, IL-6, TNF- α .
- The prevalence of gout is 3-6% in men and 1-2% in women around the world. Prevalence steadily increases with age, but plateaus after 70 years of age.
- Gout management includes rapid treatment of acute flares and effective long-term urate-lowering therapy. Clinical first-class drugs for gout includes NSAIDs, glucocorticoid, allopurinol, febuxostat and benzbromarone.



Gout seminar, Lancet, 10.1016/S0140-6736(16)00346-9



Doctorlib.info/Pharmacology/Medical Pharmacology and Therapeutics

MSU-induced Gout Models

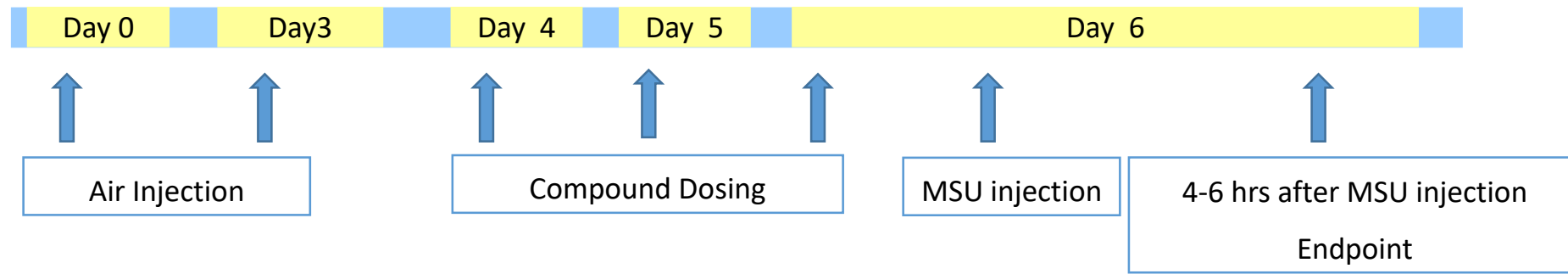
Model summary

Modeling method	Species	Duration	Common positive compound	Characteristics
Air pouch	Mouse	6 days	Colchicine (Clinical first-line)	Inflammatory cytokine measurement, WBC count and neutrophil analysis available; No histology change can be observed
	Rat			
Intra-articular injection	Mouse	3 days	MCC950 (NLRP3 inhibitor) Dexamethasone (Corticosteroid)	Histological data of joint cartilage available; Difficulty in testing cytokines due to limited sample volume
	Rat			
	Rabbit			Inflammatory cytokine measurement, WBC count and neutrophil analysis available; Histological data of joint cartilage available

MSU-induced air pouch gout model in mice

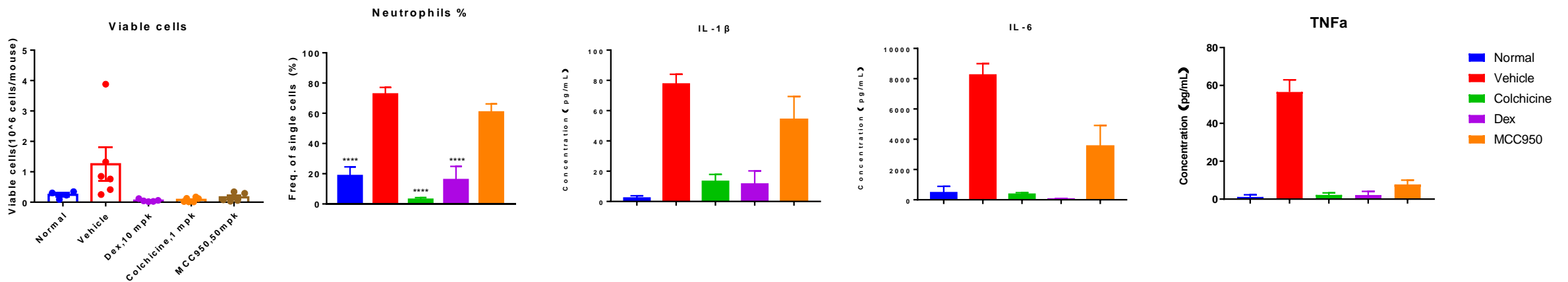
Model development and validation

Animals: Male BALB/c mice



Cells in air pouch lavage

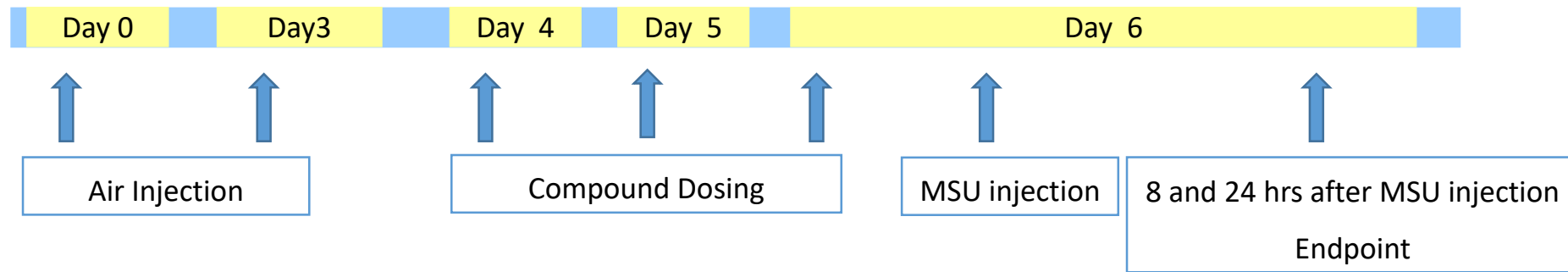
Cytokines in air pouch lavage



MSU-induced air pouch gout model in rats

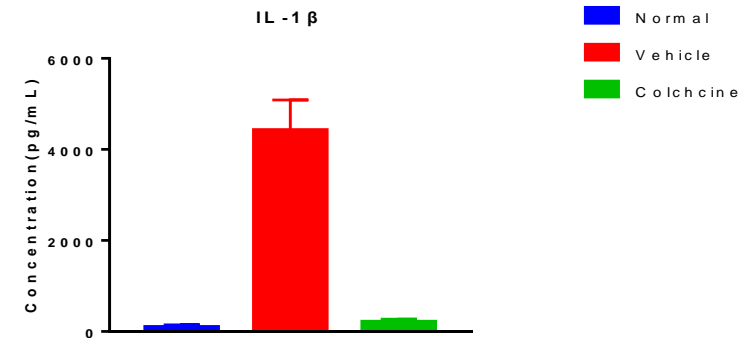
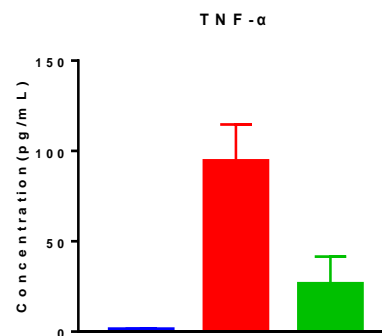
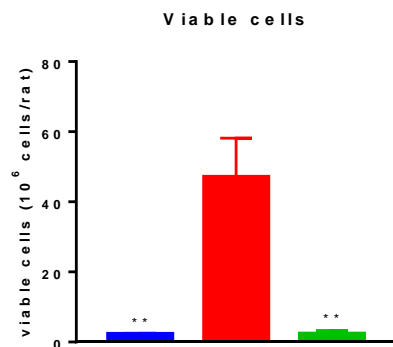
Model development and validation

Animals: Male SD rat



Cells in air pouch lavage at 24h

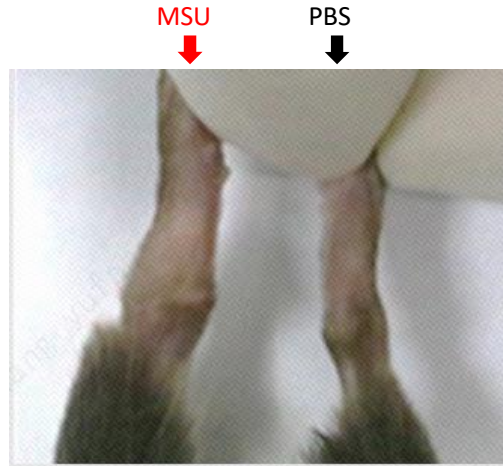
Cytokines in air pouch lavage at 8h



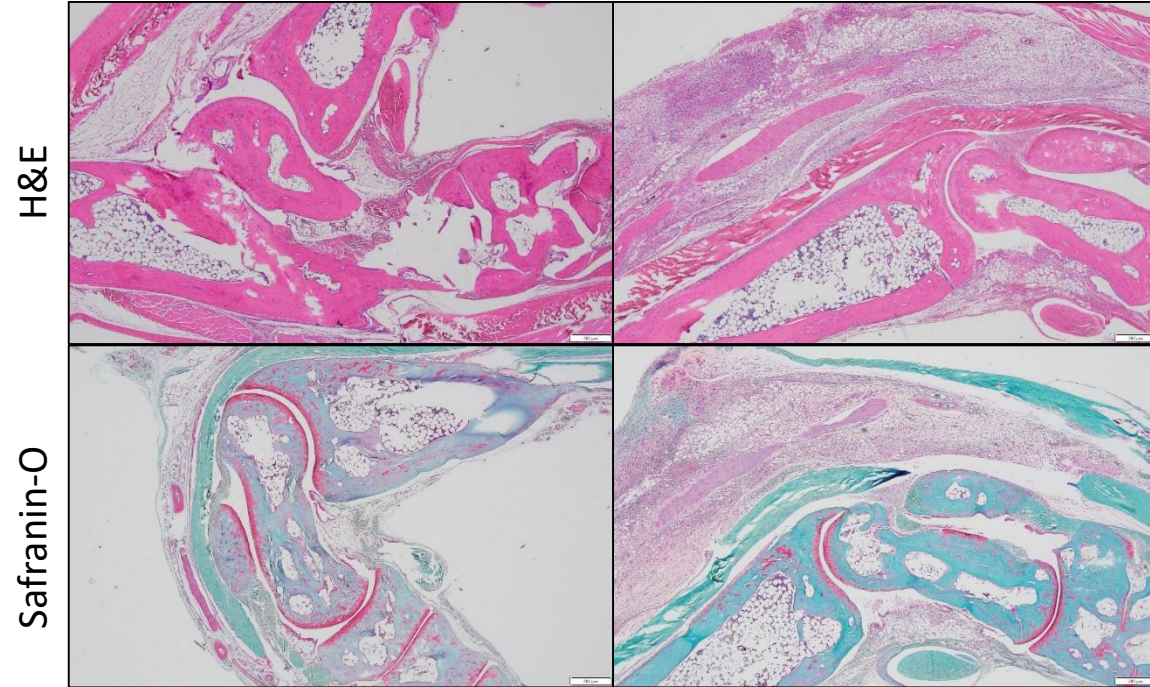
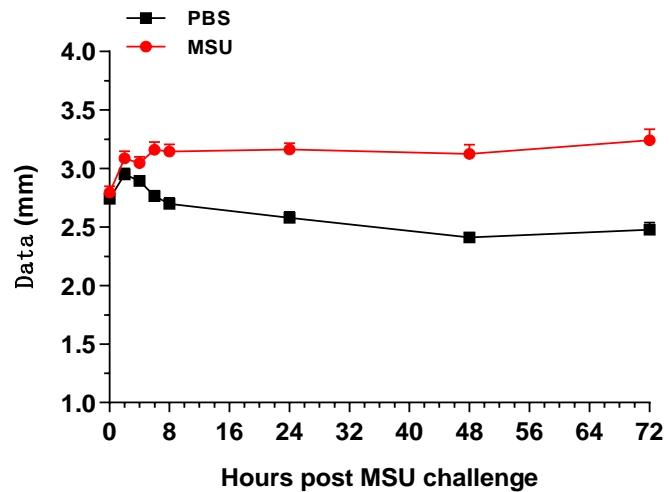
MSU articular injection in mouse ankle

Model development and validation

Animals: Female C57BL/6 mice



Diameter of ankle



PBS 40X

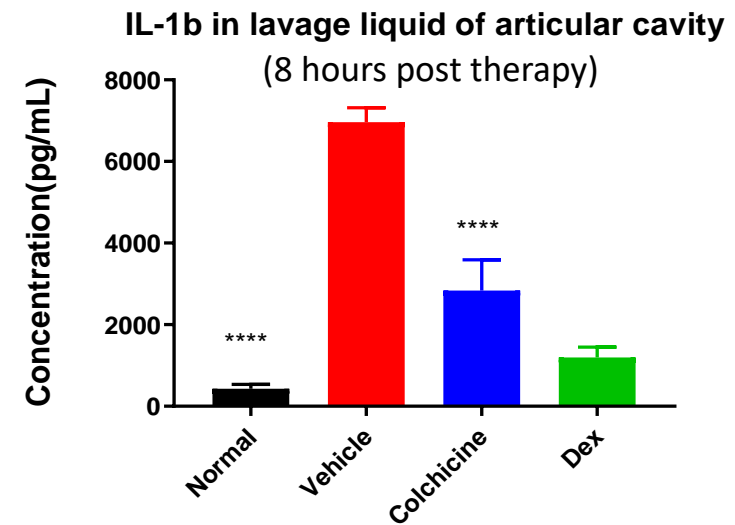
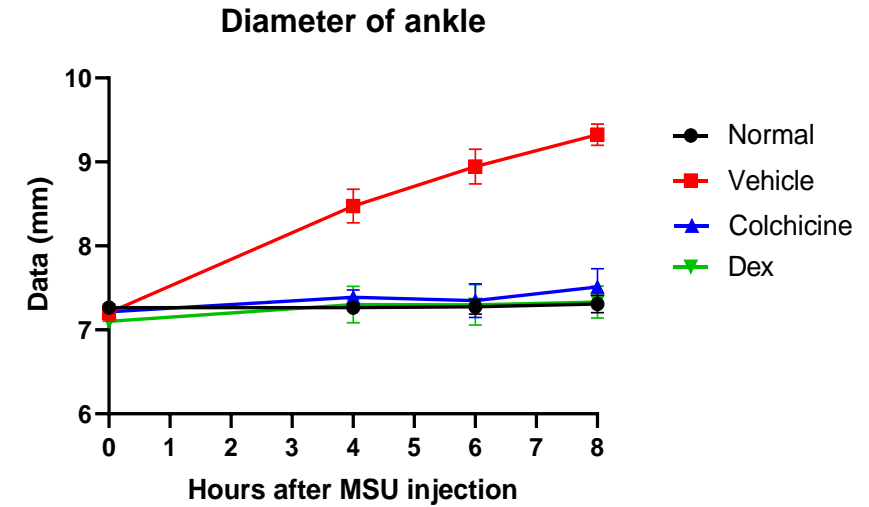
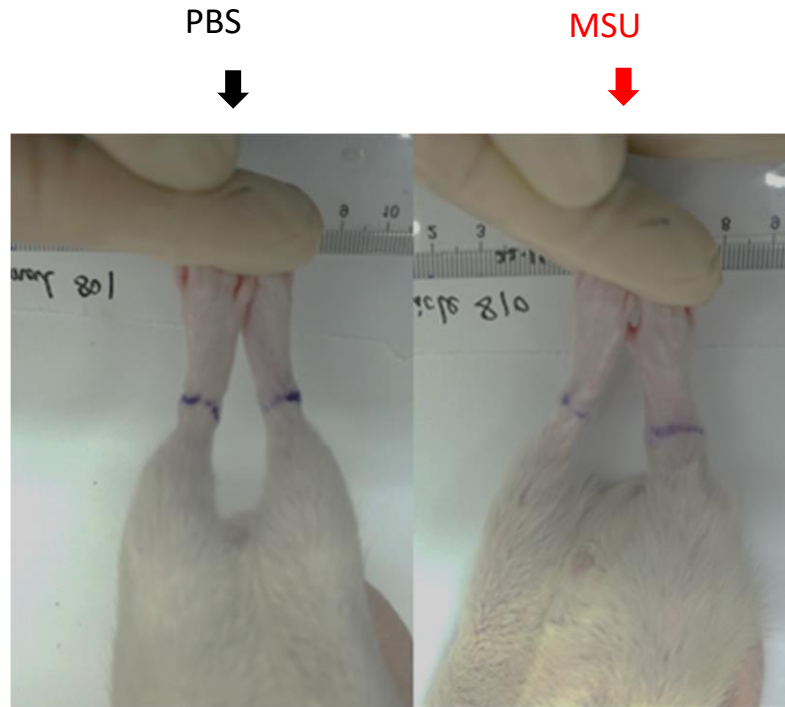
MSU 40X

Pathology scoring parameter		PBS	MSU
Infiltration cells	0-4	0	3
Pannus Severity	0-4	0	1
Cartilage Lesion Severity	0-4	1	2
Bone Resorption Severity	0-4	0	0

MSU articular injection in rat ankle

Model development and validation

Animals: Male SD rat

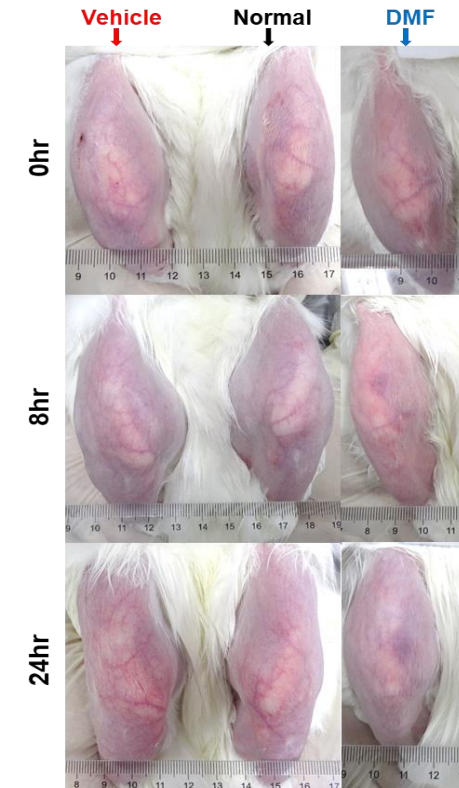
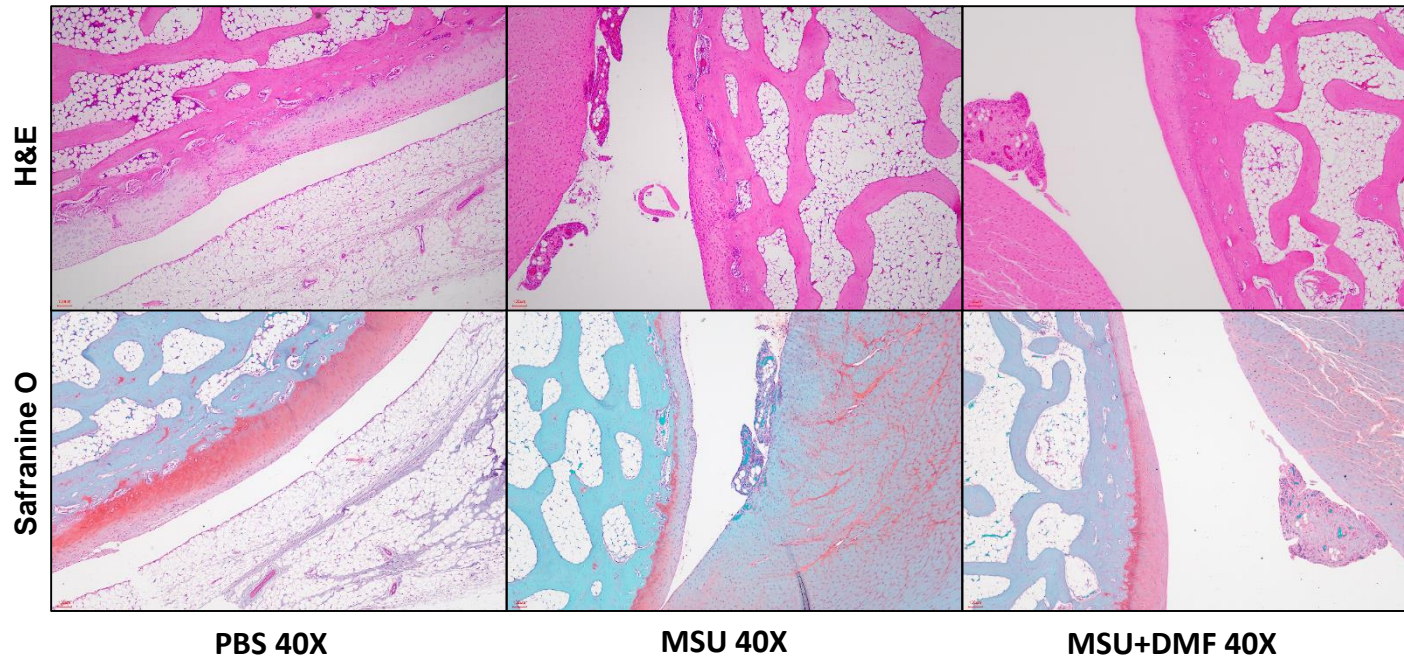
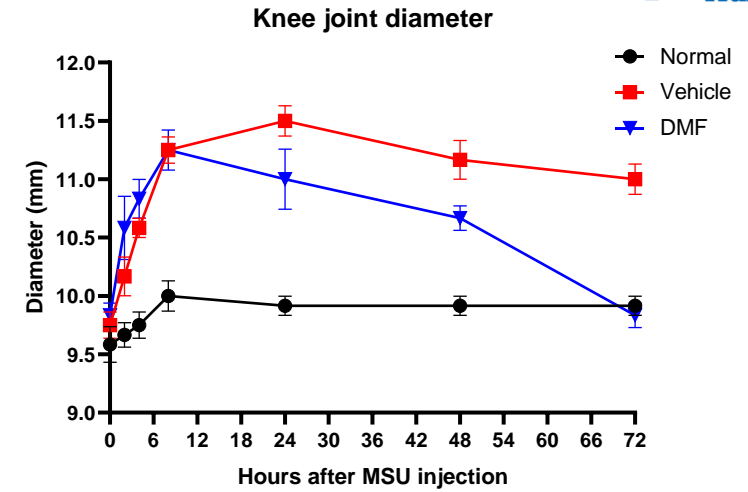


MSU articular injection in rabbit knee

Model development and validation

Animals: Female NZW rabbit

Pathology scoring parameter		PBS	MSU	MSU+DMF
Infiltration cells	0-4	0	1	1
Pannus Severity	0-4	0	2	0
Cartilage Lesion Severity	0-4	1	2	1
Bone Resorption Severity	0-4	0	0	0



WuXi AppTec autoimmune & inflammatory disease platform

List of inflammation and auto-immune disease models available at WuXi AppTec

Rheumatoid Arthritis

- Collagen induced arthritis (CIA) in DBA/1 mice or Lewis rats
- Collagen induced arthritis (CIA) in rabbits
- Collagen induced arthritis (CIA) in NHP
- Adjuvant induced arthritis (AIA) in Lewis rats
- hTNF α transgenic mice – a spontaneous model
- Anti-collagen antibody induced arthritis in mice

Experimental Autoimmune Encephalomyelitis

- MOG₃₅₋₅₅-induced EAE in mice
- MBP₆₈₋₈₆-Induced EAE in rats
- PLP₁₃₉₋₁₅₁-induced relapsing-remitting EAE in mice

Psoriasis

- Imiquimod-induced psoriasis in mice, rats and NHP
- IL-23 induced psoriasis in Mice

Systemic Lupus Erythematosus(SLE)

- SLE in MRL/MpJ-Fas/J mice
- SLE in NZB/W mice
- Pristane-induced lupus in mice

Gout

- MSU-induced air pouch inflammation in mice and rats
- MSU-induced acute gout in mice, rats and rabbits

Inflammation & CRC model

- DSS/AOM-induced colorectal cancer in mice

GvHD model

- Allogeneic bone marrow transplant induced-GvHD

Atopic Dermatitis

- DNCB-induced AD model
- MC903-induced AD model

Delayed Type Hypersensitivity (DTH) --Allergy

- mBSA-induced DTH in mice
- DNFB-induced DTH in mice
- Oxazolone-induced DTH in mice

Acute Inflammation models

- PMA-induced ear edema model
- LPS - induced cytokine production in mice and rats
- LPS - induced airway inflammation in mice and rats
- LPS/ATP-induced peritonitis model in mice
- Anti-CD3 antibody induced inflammation in mice
- CLP induced sepsis model in mice
- TNF- α shock model
- ConA- induced cytokine production in mice
- KLH-induced T cell dependent antibody response in mice
- Carrageenan-induced paw edema model
- Passive Cutaneous Anaphylaxis

Renal fibrosis model

- Unilateral ureteral obstruction in mice
- Aristolochic acid-induced renal fibrosis

WuXi AppTec autoimmune & inflammatory disease platform

List of inflammation and auto-immune disease models available at WuXi AppTec

Inflammatory Bowel diseases model

- DSS induced acute colitis in mice
- DSS induced chronic colitis in mice
- Oxazolone induced colitis in mice
- Oxazolone induced colitis in rats
- TNBS induced colitis in mice
- TNBS induced colitis in rats
- CD40 antibodies induced colitis in mice
- T cell transfer induced chronic colitis in mice
- Spontaneous colitis in IL10^{-/-} mice with Balb/c

Acute pancreatitis model

- Caerulein induced acute pancreatitis in mice
- L-Arg induced acute pancreatitis in mice
- L-Arg induced acute pancreatitis in rats

Experimental Sjogren's Syndrome (ESS) model

- Salivary glands protein induced ESS in Mice
- Radiation induced ESS in mice

Systemic sclerosis model

- Bleomycin induced systemic sclerosis in mice
- HOCL induced systemic sclerosis in mice

Liver fibrosis model

- CCL₄ induced liver fibrosis in mice
- Bile duct ligation in mice

Asthma model

- OVA induced asthma model in mice and rats
- HDM/ house dust mites induced asthma model in mice

Acute Inflammation models

- Zymosan-induced peritonitis model
- Thioglycollate-induced peritonitis model

interstitial cystitis models and Bladder Pain estimation

- CYP induced acute interstitial cystitis in mice and rats
- CYP induced chronic interstitial cystitis in mice and rats

Pulmonary fibrosis model

- Bleomycin induced lung fibrosis in mice
- Silica-induced silicosis in mice

Alopecia areata model

- Skin grafted induced AA in mice
- CD8+ T cell transfer induced AA in mice
- Testosterone-induced hair growth inhibition in mice

Cancer therapy induced gut syndrome model

- Radiation induced gut syndrome/colitis model in mice
- Chemotherapy induced gut syndrome/colitis model in mice



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