

Siripharma Labs provides a full range of preclinical contract research services for

- PK, PD and customized disease models (oncology, metabolic and inflammatory diseases)
- Consulting, study design, protocol preparation, data reporting and report generation

# Services

# **Formulations**

- Small molecules admixed in the animal chow
- Small molecules in suspensions for PO administration
- Small molecules as solutions for IP, SC and IV administrations
- Biologics as solutions for IP, SC and IV administrations

# **PK models**

- PO, IP, SC and IV administrations
- All PK parameters using an established and validated method will be provided

## Target establishment

- Mechanism based PK/PD models
- PK/PD models in customized disease models

# **Tolerability and early toxicity studies**

- MTD, NOAEL
- Single and repeated dose rat/mouse studies with 14 day observation period
- In life observations (body weight, water and food consumption and clinical observations)
- Necropsy with pathologist's reports

## **Pharmacology models**

- Oncology/tumor models
- Inflammatory disease models
- Metabolic disease models

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# **Tumor models**

#### Syngeneic tumor (ectopic/orthotopic) models

- 4T1 breast cancer model
- 4T1 surgical resection model
- B16 melanoma model
- Panc02 pancreatic cancer model
- SMA560 glioblastoma model
- LL2 lung cancer model
- A20B lymphoma model

### Xenograft tumor (ectopic/orthotopic) models

- RPMI and ARH77 multiple myeloma models
- SKOV3 and A2780 ovarian cancer models
- MCF7 and MD-MB-453 breast cancer models
- LNCaP, DU145 and PC3M prostate cancer models
- HT29 and LoVo6 colon cancer models
- A549 lung cancer model
- Panc01 and MiaPaca2 pancreatic cancer models
- U373 and U97 glioblastoma models
- Molt4 and ALL leukemia models

#### **Experimental metastatic tumor models**

- PC3M prostate cancer bone/lung metastasis models
- 4T1 breast cancer bone/lung metastasis models

## Spontaneous tumor models

- HER2 spontaneous mammary cancer model
- TRAMP spontaneous prostate cancer model
- APC min mouse intestinal polyposis model

### **Angiogenesis models**

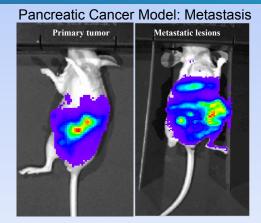
- Matrigel plug assay
- Rip-Tag2 model

#### **Other cancer models**

- Cancer cachexia
- PC3M and 4T1 cancer pain models

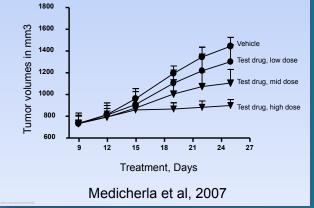
## **Tumor cell line screens**

• Customized cell panels for cyto-toxicity studies

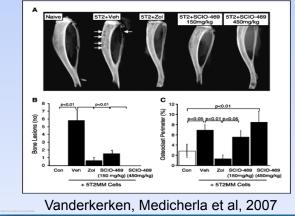


Medicherla et al, 2007

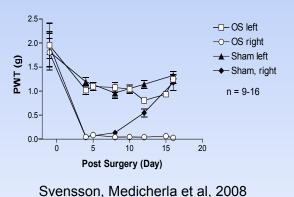
#### Multiple Myeloma Model: Tumor Burden



#### Multiple Myeloma Model: Bone Lesions



#### Osteosarcoma Pain Model: Allodynia



# **Inflammatory disease models**

## Inflammatory bowel disease models

- DSS induced mouse model of IBD
- TNBS induced mouse/rat models of IBD
- Oxazolone induced mouse model of IBD
- DSS induced tumorigenesis in APC Min mouse
- APC Min mouse intestinal polyposis model
- Irritable bowel syndrome pain model

## **Rheumatoid Arthritis models**

- Collagen induced mouse/rat models of arthritis
- Adjuvant induced mouse model of arthritis
- Carrageenan induced paw edema model

## Lung inflammation and fibrosis models

- Mouse BHR model
- · Cigarette smoke induced mouse model of COPD
- Bleomycin induced mouse/rat models of lung fibrosis
- IL-13 k/o mouse model for asthma/lung fibrosis

#### Skin inflammation models

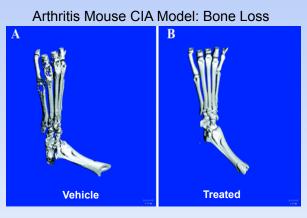
- Mouse dermatitis model
- Mouse diabetic impaired wound healing model

## **Bone inflammation models**

- Rat model of fracture healing
- Rat model of osteoporosis
- Rat periodontal model of bone loss
- Osteoclastogenesis/osteoblastogenesis cell models

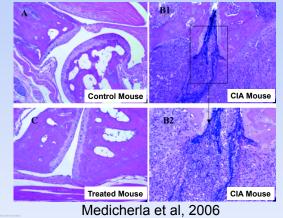
## **Pain models**

- Mouse osteosarcoma pain model
- Mouse cancer pain models
- Mouse/rat abdominal pain models
- Rat diabetic pain model
- Mouse/rat arthritic pain models
- Carrageenan, hot plate and post-surgical pain models
- Rat fracture pain model

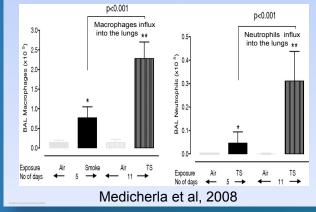


Medicherla et al, 2006

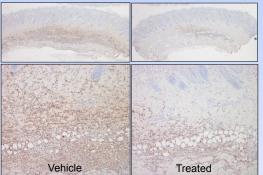
#### Arthritis Mouse CIA Model: Joint Inflammation



### Smoke Induced COPD Model: Cell Traffic



#### LPS Skin Inflammation Model: Histology



Medicherla et al, 2010

# Metabolic disease models

### **Type 2 diabetes models**

- Diet induced mouse/rat models of insulin resistance
- Spontaneous mouse/rat models of type 2 diabetes
- Euglycemic clamps: OGTT, IVGTT and IPGTT tests

#### Animal models of diabetic complications

- Streptozotocin induced diabetic neuropathy model
- Db/db diabetic nephropathy model
- Db/db diabetic impaired wound healing model

### Metabolic syndrome models

- Diet induced mouse/rat metabolic syndrome models
- SHR.Ob model of metabolic syndrome

#### **Obesity models**

- High fat diet induced mouse/rat models of obesity
- Ob/ob mouse and fa/fa fatty rat models of obesity

#### Hyperlipidemia models

- Diet induced mouse models of hyperlipidemia
- Spontaneous models of hyperlipidemia: LDL/Apo-E k/o
- Models involved in lipoprotein metabolism

#### **Atherosclerosis models**

• Diet induced and LDL/Apo-E k/o atherosclerosis models

#### Hypertension and heart disease models

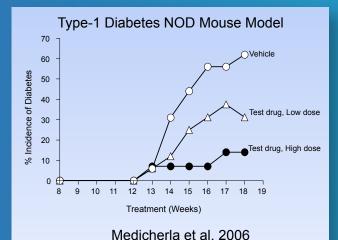
- Salt/chemical induced rat/mouse models of hypertension
- Spontaneous models of hypertension (SHR and ZDF)
- Coronary artery ligation and aortic constriction models

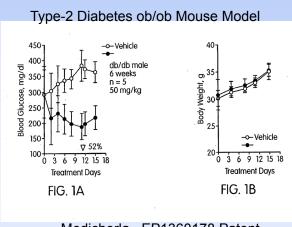
#### **Type-1 diabetes models**

- STZ and alloxan induced models of type-1 diabetes
- Spontaneous models: NOD mouse and BB rat

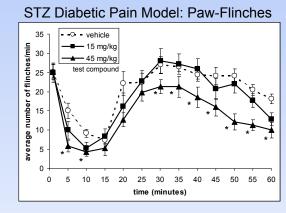
#### **Other models**

- In-vitro assays (glucose uptake, lipolysis, etc) as required
- Ex-vivo studies as warranted









#### Sweitzer, Medicherla et al, 2004

Db/db Diabetic Wound Healing Model: Wound Scores

