

# InnoStar Introduction to Pharmacology Platform



Shanghai InnoStar Bio-tech Co., Ltd. (InnoStar) was established in 2010. As a leading contract research organization, we strive for excellence through our services with high quality, win customers by recognized reputation, add values by technical innovation, and maintain efficiency by streamlined management. Our business scope covers screening and discovery services, nonclinical pharmacodynamics, nonclinical pharmacokinetics, nonclinical safety evaluation, clinical sample bioanalysis, biomarkers and translational research. InnoStar was listed on the STAR Market of Shanghai Stock Exchange on September 3, 2024 (Stock code: 688710).

#### Nantong InnoStar (320,000+ Sqft 500+Staff) Screening and Discovery Services Nonclinical Pharmacokinetics Nonclinical Safety Evaluation Nonclinical Pharmacodynamic • Radioisotope Platform InnoStar (HQ) Ophthalmology Integrated (190,000+ Sqft 570+Staff) **Evaluation Platform** Nonclinical Safety Evaluation Clinical Bioanalysis Biomarkers and Translational Medicine **Shenzhen InnoStar** InnoAllianceU.S. (110,000+ Sqft 80+Staff) Screening and Discovery Services Clinical Bioanalysis **Huangshan InnoStar** Nonclinical Pharmacokinetics (717,600+ Sqft) Nonclinical Safety Evaluation • Primate Laboratory, Animal Breeding, and Research Lab

OECD GLP

AUT

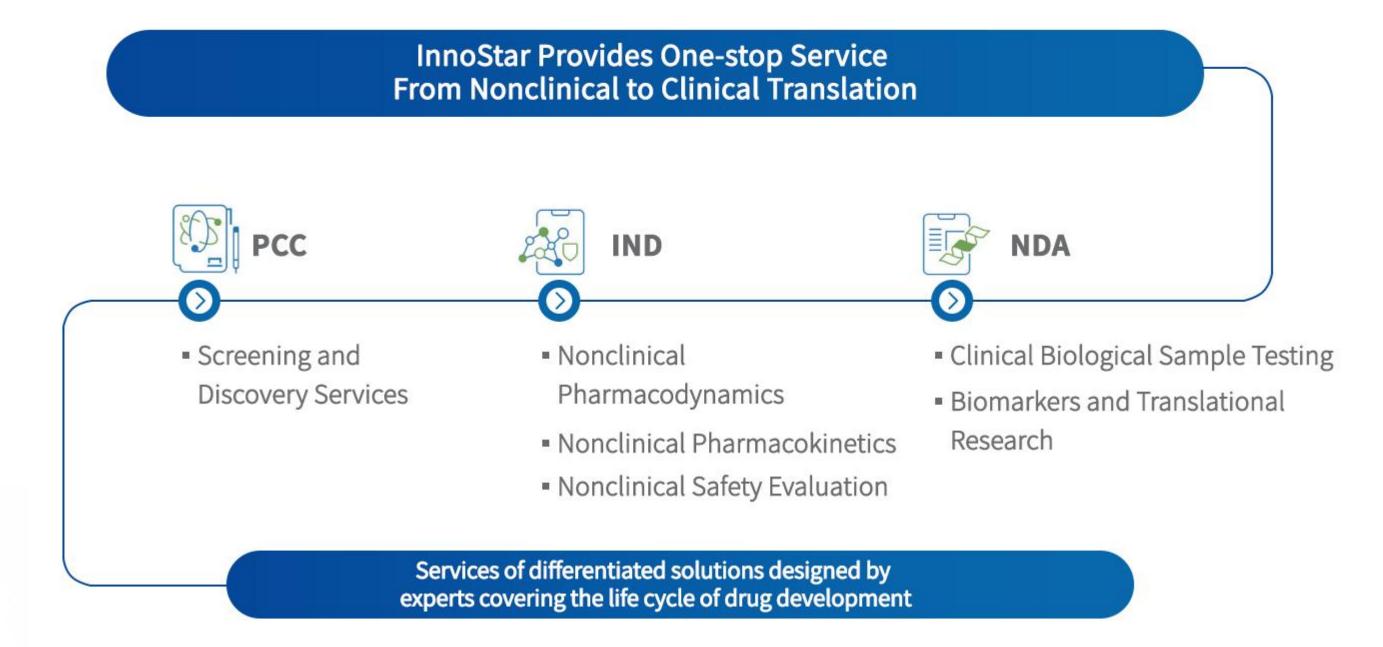
AAALAC

AUT

美国CAP

AUT

#### **SCOPE OF BUSINESS**



#### PROJECT EXPERIENCE

920+ Already served New drug development clients	100+ Annual average IND package completed amount	30+ Annual NDA/BLA package completed amount
200+ We have served on both international	140 Overseas IND	3
and domestic "first-of-its-kind" innovative drug research and development projects.	Application Successful	FDA NDA/BLAs

注: 数据统计区间: 2015-2024.12.31



**NMPA GLP** 

AUT

**U.S.FDA GLP** 

INSP



## 目录页



P1-2.Company Introduction 01	P10-11.In vitro efficacy 10-11
Company Introduction 01	In vitro efficacy verification project 10
The company's corporate culture and development strategy ————————————————————————————————————	Cell proliferation assay 10
Introduction to Company Basic Information — 01	Cell invasion test 10
Company Overview Introduction 01	Cell adhesion test
corporate culture 01	Cell migration assay — 11
Introduction to the company's main business 02	Protein phosphorylation assay
	Cell cycle tests 11
DE Denverente instrumente	Apoptosis test
P5. Represents instruments 05	Mixed lymphocyte reaction test
and equipment 全能型成像系统	In vitro activity assay of antibody drugs
数字pcr仪05	Protein immunoblotting — - — - — - — - — - — - 11
凝血分析仪 05	
尿液分析仪05	P12.Organoid platform 12
多功能酶标仪05	
小动物活体成像仪05	This platform has established a database of organoids — 12
血生化分析仪05	Colorectal cancer organoids — 12
血液细胞分析仪05	Lung cancer organoids 12
	Liver cancer organoids
Pharmacology Platform Platform Introduction	P13-14.In vivo tumor13-14 efficacy platform CDX xenograft mouse subcutaneous repeated
In vitro cell pharmacological studies 07	Subcutaneous tumor model - subcutaneous 13 transplantation of human tumor cells In situ tumor model
Study on drug efficacy in tumor 07	in situ tullion modet
Nonclinical Pharmacodynamics Platform 08	Humanized mouse model 14
Non-tumor efficacy studies 08	
P9.Screening and Discovery 09	P15-22.In vivo non tumor15-22 drug efficacy platform Internal respiratory disease model
Services Screening Strategies for Small Molecule Chemicals/Pre-drugs - 09	Chronic obstructive pulmonary disease (COPD) 15
Screening Strategies for Nucleic Acid Drugs 09	In vivo metabolic disease model 16
Screening Strategies for ADC 09	Obese mouse model (C57, db/db)16
Screening Strategies for Antibody Drugs 09	In vivo autoimmune disease model
Screening Strategies for CGT & Delivery Systems — 09	rheumatoid arthritis
Early Pharmacodynamics Evaluation 09	Internal nervous system disease model 18
Early Pharmacokinetics Screening — - — - — - — - 09	Parkinson's disease 18
Early Toxicity Prediction And Screening 09	pain
Isotope Labeling and Imaging 09	Learning and memory 20
	Locomotion 20

Other disease	models in the body —-——- 20
Osteoarthri	tis (Rabbit) 21
Non human pr	imate disease model21
Diabetes	21
NASH	22
Obesity	22
P23-24.F	Project experience 23-24
CGT Pharmaco	ology Project (ongoing+completed) 23
CGT Pharmaco	ology Application Project 23
IND	23
Excellent expe	rience in CGT pharmacological research — 23
Overview of In	noStar Project Experience 24

## Representative instruments and equipment





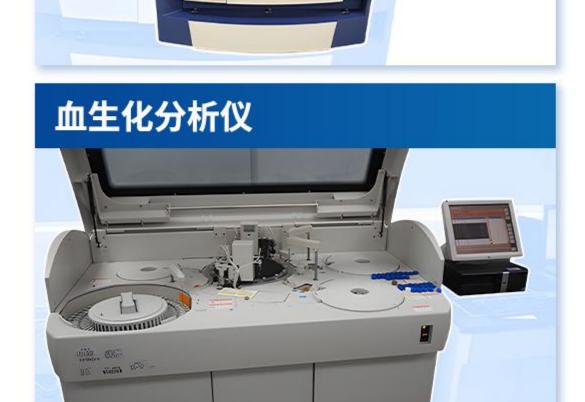


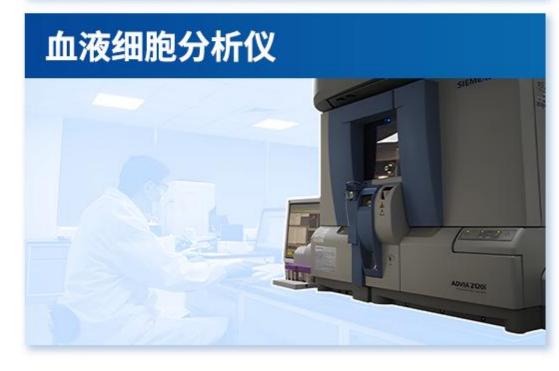




多功能酶标仪









## Platform Introduction

#### **Platform Introduction**

The Non-clinical pharmacodynamic platform is underpinned by a highly skilled professional technical team, advanced equipment, and a comprehensive selection of cell banks and in vivo disease pharmacodynamic models. Leveraging a wealth of in vitro and in vivo pharmacological efficacy models, InnoStar offers a broad array of pharmacodynamic evaluations for new drug development across multiple levels—overall, cellular, molecular, and genetic. This ensures the acceleration of customer research projects by providing essential insights at the earliest stages of drug development.

#### **Service content**

Early screening drug platform



In vitro drug efficacy platform



Organoid platform



In vivo tumor model



In vivo non tumor model



Non human primate disease model



#### Non-clinical pharmacology platform-tumor mode



### In vitro cell pharmacological studies

#### In vitro cell efficacy verification

- More than 180 cell lines, more than 80 cell lines with Luc
- It involves 16 organizations (including brain, lung, liver, breast, prostate, lymph and so on)
- Cell proliferation assay
- Protein phosphorylation assay
- Cell migration assay
- Apoptosis test Cell cycle tests
- Cell invasion experiment Cell adhesion experiments
- Mixed lymphocyte reaction test
- Cytotoxicity assays (ADCC, CDC, ADCP)
- In vitro activity testing of antibody drugs
- Protein immunoblotting
- Target protein expression
- Cell factor expression
- Flow cytometry identification

#### Organoid models

- Organoid culture
- Pathological identification
- Molecular biology identification



### Study on drug efficacy in tumor

#### Subcutaneous tumor model

- Subcutaneous transplantation of human tumor cells
- Subcutaneous transplantation of murine tumor cells
- Ovarian cancer, stomach cancer, myeloma, colon cancer, lung cancer, breast cancer, prostate cancer, cervical cancer, cavity squamous cell carcinoma, kidney cancer.....

#### **Humanized mouse model**

- PBMC humanized mouse model
- HSC humanized mouse model

#### **Tumor metastasis**

Bone metastasis from cancer

#### In situ tumor model

- In situ transplantation of glioma
- In situ transplantation of lung cancer
- Colorectal cancer in situ transplantation
- In situ transplantation of gastric cancer
- Pancreatic cancer in situ transplantation
- In situ transplantation of liver cancer
- Prostate cancer in situ transplantation
- In situ transplantation of renal cancer
- In situ transplantation of bladder cancer



- intestinal cancer
- cancer of the liver
- carcinoma of the lungs

#### **Nonclinical Pharmacodynamics Platform**



## Non-tumor efficacy studies

#### **Autoimmune and** inflammatory diseases

- Arthritis deformans
- Systemic lupus erythematosus (SLE)
- Colitis (DSS, TNBS)
- psoriasis
- disseminated sclerosis

#### Respiratory illness

- PAH
- pulmonary fibrosis
- asthma (OVA)
- acute lung injury
- Chronic obstructive pulmonary disease (COPD)

#### Non-human primate models

- diabetes mellitus
- NASH
- fat
- Hypertension (under construction)
- Kidney disease (under construction)

#### Other

- Osteoarthritis (Rabbit)
- chloasma
- Male hair loss
- acne

#### Metabolic system diseases

- Obesity mouse model (C57, db/db) Diabetes and complications
- NASH (STZ/HFD)
- insulin resistance
- Hepatic cirrhosis model (CCL4)
- Positive glucose clamp test
- Hyperuricemia
- Kidney fibrosis
- hypertension

#### **CNS** disease

- Stroke (tMCAO, pMCAO)
- agitans paralysis
- depressed
- cephalagra
- pain

- senile dementia
  - kinetism
  - Learning and Memory



www.innostar.cn www.innostar.cn

## **Screening and Discovery Services**

Multidisciplinary cooperation to provide early screening services for drug characteristics. Accelerating the R&D process with valid and reliable data support.

Genotoxicity Prediction

**Toxicity Studies** 

Genetic Toxicity Screening

■ In Vitro Cardiac Toxicity Screening

In Vitro Carcinogenicity Prediction

Reproductive And Developmental

In Vivo General Toxicity Screening

■ In Vitro Photogenotoxicity Screening

#### **Screening Strategies for Small** Molecule Chemicals/Pre-drugs

- Plasma Stability
- Metabolic Stability In Hepatic Microsomes And Hepatocytes
- Metabolite Identification (Liver Microsomes, Hepatocytes, etc.)
- In Vivo Metabolite Identification (Blood, Urine, Feces, etc.)
- Plasma Protein Binding Capacity
- CYP Inhibition (Single Site)
- PK Analysis (Rat, Mouse, Dog\*, Monkey\*)
- Early Pharmacodynamics Evaluation (in Vitro/ in Vivo)

#### **Screening Strategies for Nucleic Acid Drugs**

- PK-PD Analysis through Monkey Liver Puncture
- Plasma Stability
- Metabolic Stability in Liver S9 Fraction and Hepatocytes
- Metabolite Identification
- PK Analysis and Biodistribution (Target Organ(s))
- Early Pharmacodynamics Evaluation (in Vitro/In Vivo)
- Toxicity Prediction
- In Vitro/in Vivo Toxicity Screening

#### **Screening Strategies** for Antibody Drugs

- Early Antibody Target Screening
- Early Pharmacodynamics Evaluation (in Vitro/in Vivo)

**Screening Strategies for ADC** 

- Plasma Stability
- Breakdown in Tumor Cells
- Metabolism in Lysosomes, Acidified Liver S9 Fraction
- PK Analysis
- Early Pharmacodynamics Evaluation (in Vitro/in Vivo)
- In Vitro/in Vivo Toxicity Screening

#### **Screening Strategies** for CGT & Delivery Systems

- In Vivo General Toxicity Screening
- Biodistribution Studies
- In Vitro Tumor Formation Studies
- In Vitro/in Vivo Pharmacokinetics and Toxicity Screening for New Accessories of Delivery System

#### Early Pharmacodynamics Evaluation

In Vivo Platform (Tumor / Non-tumor Models) | In Vitro Platform

#### **Early Pharmacokinetics Screening**

Fast Pk Tests (Rat, Mouse, Dog\*, Monkey\*) Blood-brain Barrier Studies | Metabolism Studies | Biodistribution Studies

#### **Early Toxicity Prediction And Screening**

Genetic Toxicity | Cardiac Toxicity | Carcinogenicity | In Vitro Photogenotoxicity Reproductive And Developmental Toxicity | In Vivo General Toxicity

#### Isotope Labeling and Imaging

89Zr, 68Ga, 124I labeling | Biodistribution Studies Micro-SPECT/CT、Micro-PET/MR in Vivo Imaging Studies

Note: \*Marked means availability of research services in non Naïve laboratory animals.

## In vitro efficacy

More than 180 cell lines, more than 80 Luc cell lines It involves 16 organizations, including brain, lung, liver, breast, prostate, lymph, etc

### In vitro efficacy verification project

Cell proliferation assay

Cell migration assay

Cell invasion test

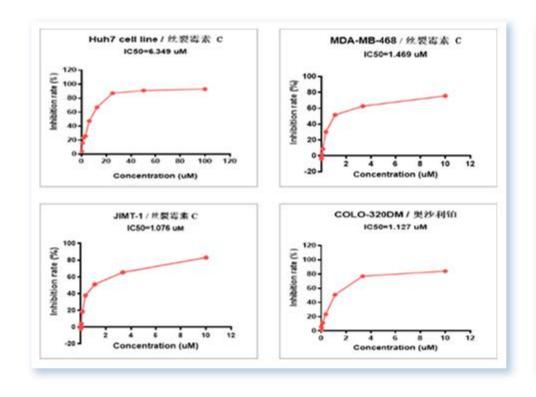
Cell adhesion test

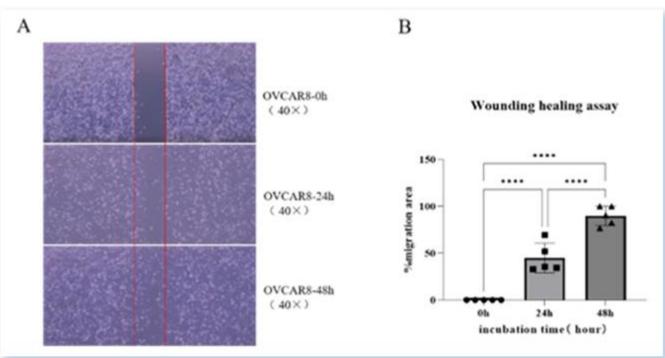
- Protein phosphorylation
   Cell cycle tests assay
- In vitro activity assay of antibody drugs

- Apoptosis test
- Mixed lymphocyte reaction test
- Protein immunoblotting

#### Cell proliferation assay

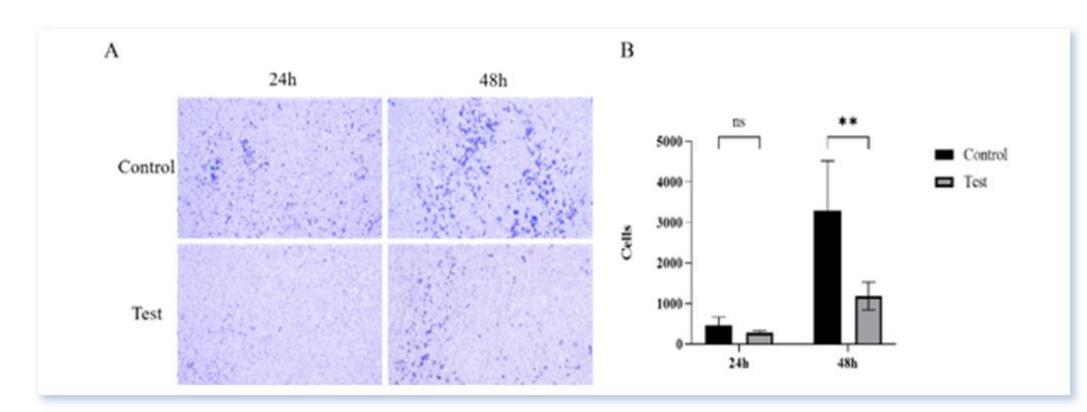
Cell proliferation inhibition assays are commonly used methods in ex vivo biological activity testing, primarily for screening and evaluating the effects of drugs on tumor cells. Tumor cell proliferation inhibition tests can provide preliminary data support for in vivo experiments. These tests help optimize the conditions and parameters of in vivo experiments. Cell proliferation inhibition assays also serve as a basis for safety assessments in in vivo experiments. By cross-verifying and complementing tumor cell proliferation inhibition tests with in vivo experiments, a more comprehensive evaluation of the anti-tumor efficacy and safety of drugs can be achieved.





#### Cell invasion test, using

Using Transwell hole membrane to isolate the upper and lower culture chambers, the upper chamber is cultured with cell solution/drug, and the lower chamber is added with inducer/drug. The cells migrate to the lower chamber through the Transwell hole membr-ane, and the migration ability can be observed and measured by staining or microscope

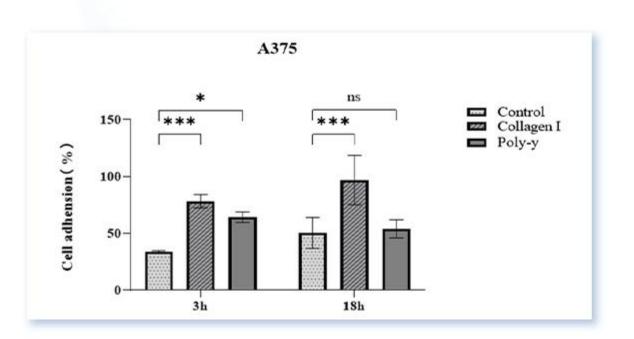


## In vitro efficacy

In vitro efficacy verification project

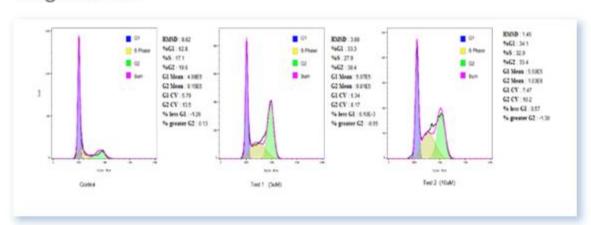
#### Cell adhesion assay

96-well plate was coated with different substrates, cells were inoculated and PBS was washed to remove unattached cells. Then CTG was incubated and fluorescence intensity was detected by microplate reader to reflect the number of adhered cells



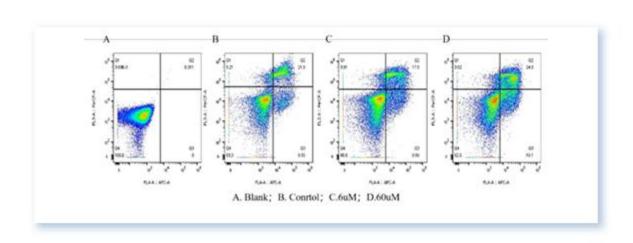
#### Cell cycle test

After the drug acts on the cells, the DNA content is detected by flow cytometer PI staining method to reflect the cell cycle c-hange after drug treatment



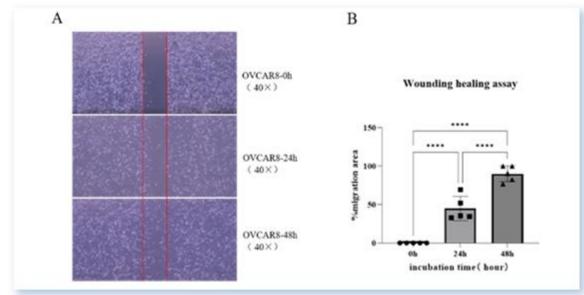
#### Cell apoptosis assay

Apoptosis assay involves staining cells with Annexin V/PI and then performing flow cytometry. Annexin V binds to PS on the surface of early apoptotic cells, while PI penetrates the cell membranes of midto-late apoptotic and necrotic cells, staining the nuclei red. The combination of these two stains allows for the detection of early and late apoptotic cells within a cell population



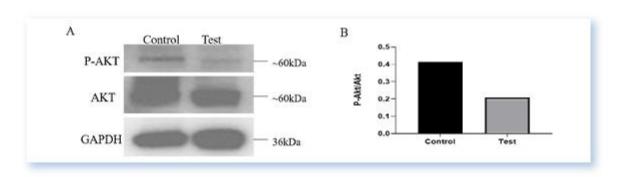
#### Cell migration assay

A linear scratch was made in the culture dish, and then the migration of cells at different time points was observed



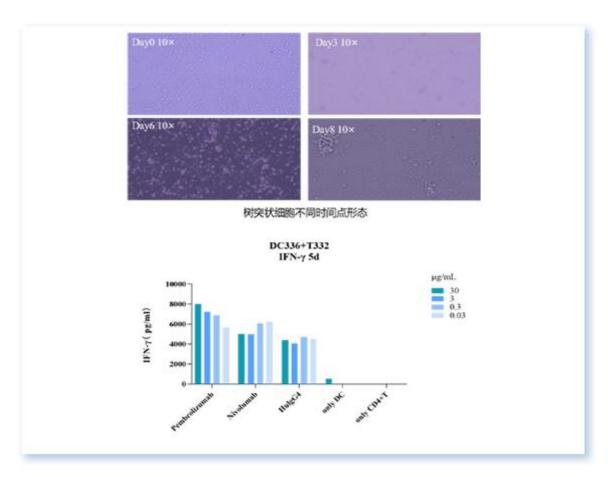
#### **Protein phosphorylation assay**

protein blotting was used to detect phosphorylated proteins after treatment of cells with different drugs/phosphatase inhibitors



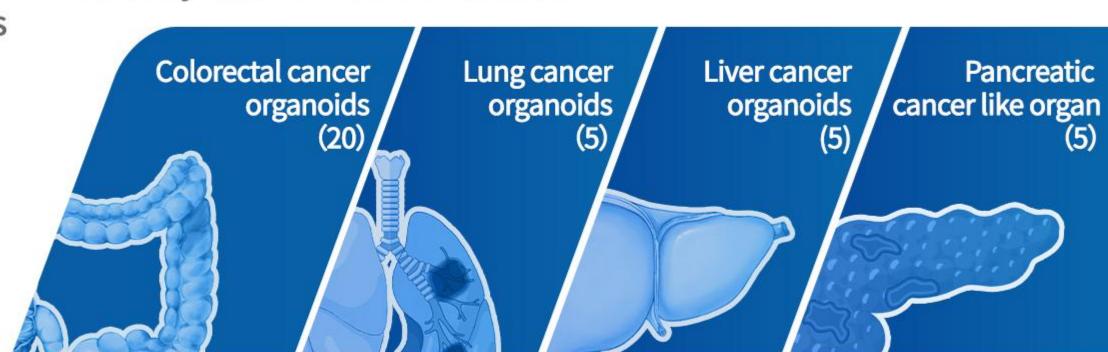
#### In the mixed lymphocyte reaction test

GM-CSF and IL-4 were used to induce peripheral blood mononuclear cells to become iDCs, and TNF-α and LPS were added to induce their differentiation into mDCs; then they were mixed with CD4+ T cells for culture, and the content of cytokines in the supernatant was detected

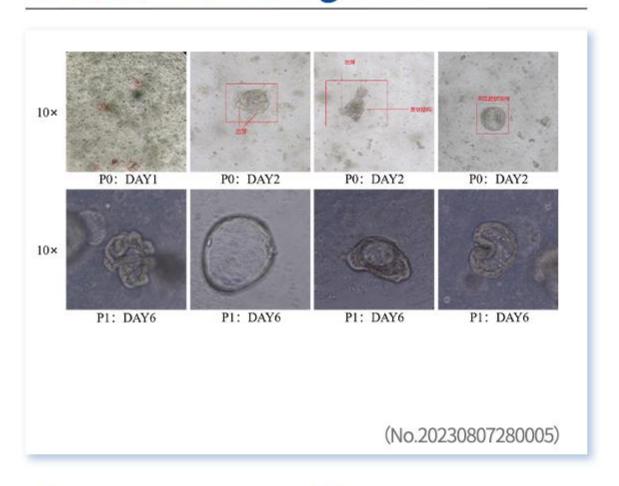


## Organoid platform

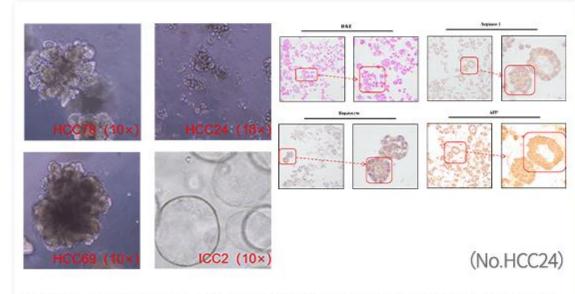
This platform has already established a database for organoids



#### **Colorectal cancer organoids**

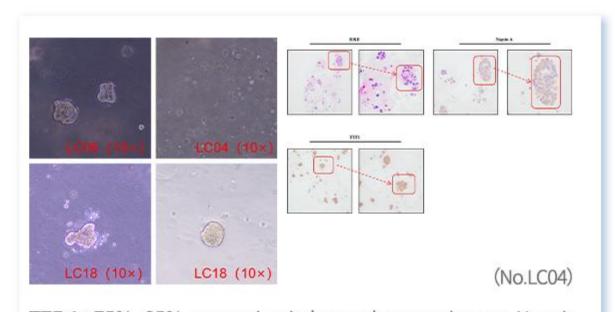


#### Liver cancer organoids



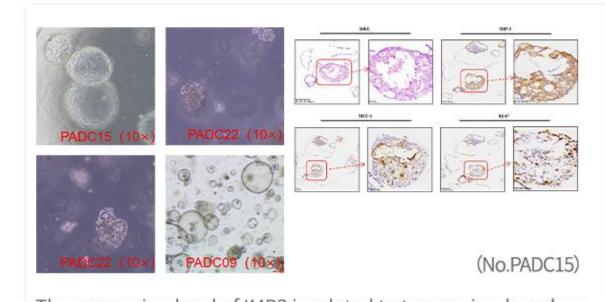
Arginase: Arginase, divided into Arg1 and Arg2.Arg1 is highly expressed in HCC, with a positive rate of 96.2%; Hepatocellular carcinoma (HCC) often shows positive expression; AFP: Alpha fetoprotein, with a positive rate of 36.7%, has a positive rate of 6.7% in liver cirrhosis.

#### **Lung cancer organoids**



TTF-1: 75% -85% expression in lung adenocarcinoma, Napsin A: 70% -90% of lung adenocarcinoma is expressed. TTF-1 and Napsin A are currently one of the best antibody combinations for diagnosing lung adenocarcinoma.

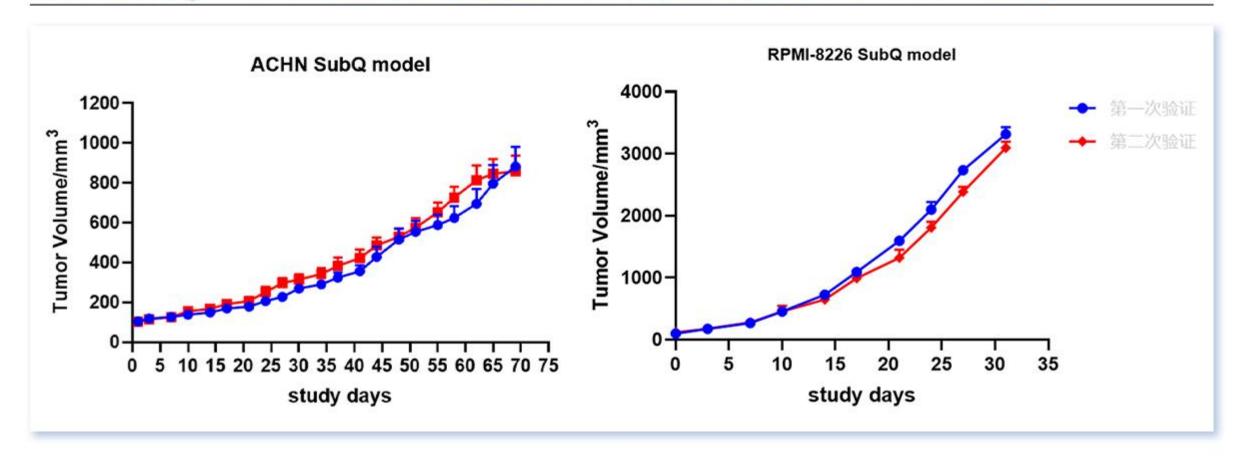
#### Pancreatic cancer like organ



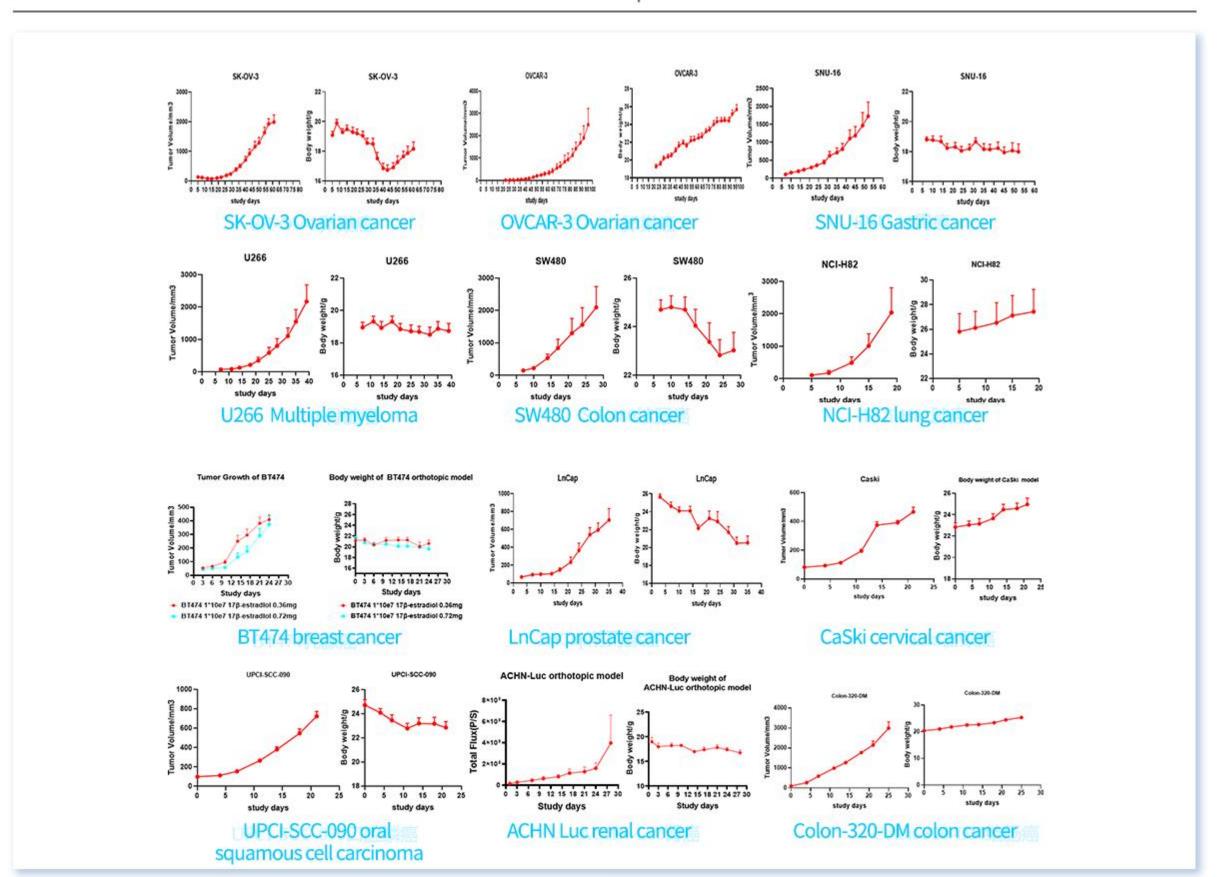
The expression level of IMP3 is related to tumor size, lymph node metastasis, depth of tumor invasion, and TNM staging in patients with pancreatic cancer. The positive expression rate of MUC1 in pancreatic cancer tissues was 67.4%, which is associated with lymph node metastasis and TNM staging in pancreatic cancer. The positive expression rate of Ki-67 protein in pancreatic cancer tissues was 94.4%, which is correlated with the degree of tissue differentiation in pancreatic cancer.

## In vivo tumor drug efficacy platform

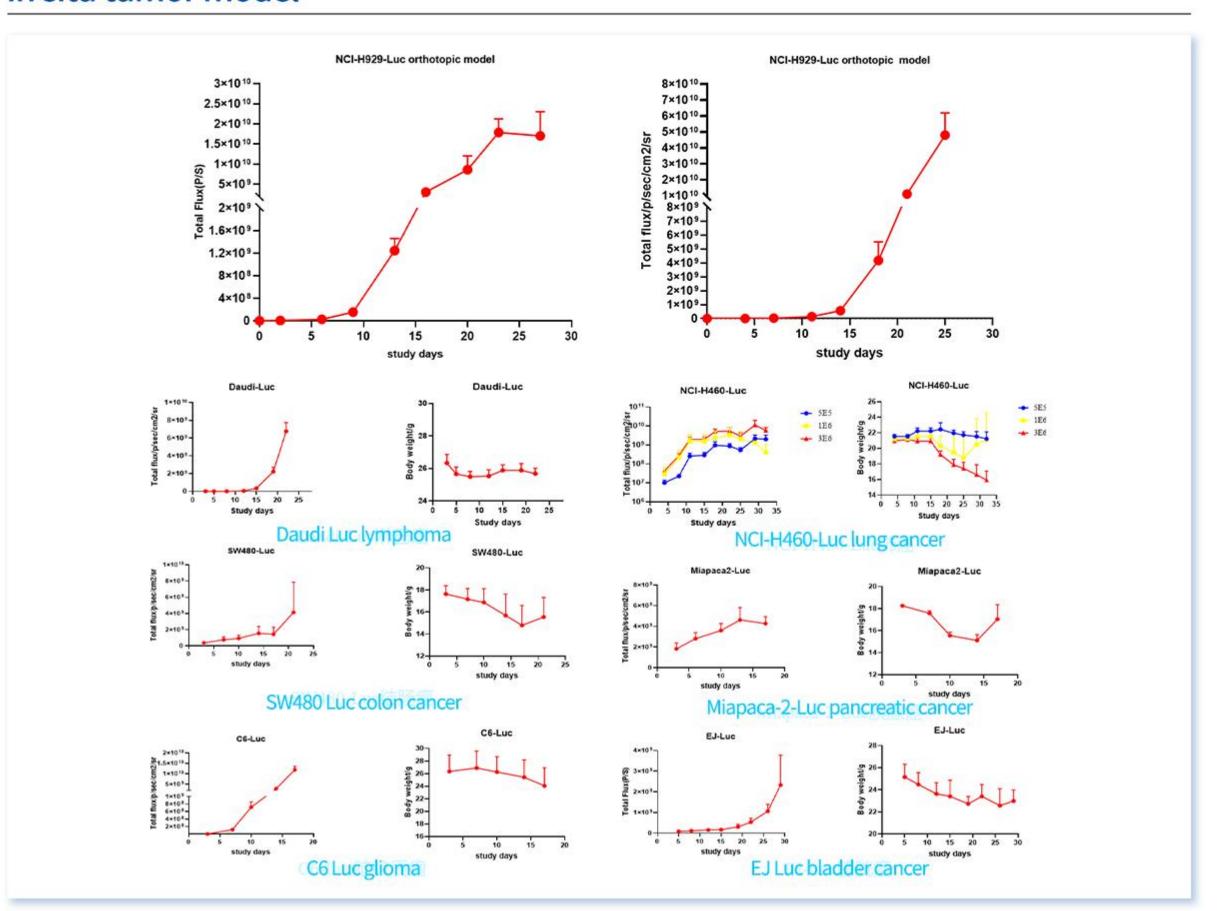
#### CDX xenograft mouse subcutaneous repeated validation model



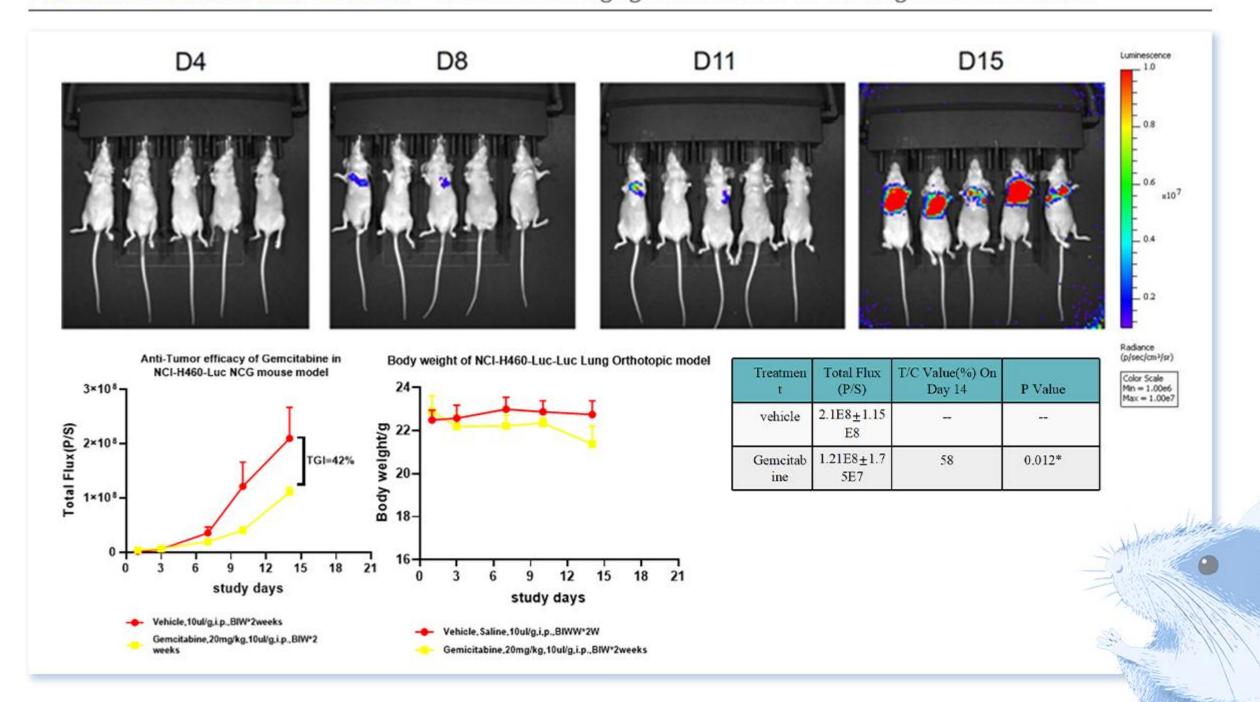
#### Subcutaneous tumor model subcutaneous transplantation of human tumor cells



#### In situ tumor model



#### Humanized mouse model Trend chart of imaging results of NCI-H460-Luc lung cancer in situ model



 $\mathbf{1}$ 

www.innostar.cn www.innostar.cn

## In vivo non tumor pharmacological research

(48) In vivo non tumor pharmacological research

#### Internal respiratory disease model

■ Chronic obstructive pulmonary disease (COPD) asthma pulmonary fibrosis

- pulmonary hypertension
- Acute Lung Injury

#### **COPD Animal Models**

Internal respiratory disease model

Tobacco smoking is the most important risk factor for COPD and the most common COPD-inducer employed in in vivo studies. In addition, to mainstream cigarette smoke, environmental cigarette smoke may also contribute to respiratory symptoms and COPD.

Mice and rats are the most commonly used to induce COPD model

Guinea pigs

Dogs	Table 3. Pre-clinical research methods in vivo used in new drug discovery and development.							
Monkeys –	Study	Treatment	Model Species	Experimental Intervention	Results			
Parameter measurements:  -Pathologies:  • Airway remodeling  • Lung inflammation  • Goblet cell hyperplasia  • Alveolar enlargement  • Increased airway wall thickness and airspace size  -Blood samples:  • Total cell and Macrophages, lymphocytes  • neutrophils  • Macrophages and neutrophils (Cells)  • Mediators and cytokines: IL-8, TNF-α, IFN-γ, KC, TNF-α, MIP-2, MIP-1α, MCP-1, TNF-α, IL-12, IL-4,—CXCL-10, CCL-22  -In vivo tracheal and airway responsiveness;	Horio et al., 2017	Galectina (Gal) -9 administered subcutaneously once daily from 1 day before PPE instillation to day 5	Female C57BL/6 mice (8–10 weeks old)	Lungs were intratracheally instilled with two units of PPE diluted in 50 µL of saline via 24-gauge catheter on day 0	Infiltration of neutrophils was inhibited and MMP levels decreased			
	Melo et al, 2018	Atorvastatin, 1, 5, and 20 mg, treated from day 33 until day 64 via inhalation for 10 min once a day	Male C57BL/6 mice (8 weeks old/18–22 g)	Administered intranasally 4 × 0.6 U of porcine pancreatic elastase (PPE) every other day (days 1, 3, 5 and 7).	Induced lung tissue repair in mice with emphysema			
	Pinho-Ribeiro et al., 2017	Atorvastatin and simvastatin administered via inhalation for 15 min (1 mg/mL, once/day)	Male C57BL/6 mice (8–10 weeks old)	Mice exposed to 12 cigarettes a day for 60 days, then treated for another 60 days	Improved lung repair after cigarette smoke-induced emphysema, accompanied by a reduction in oxidative stress markers.			
	Sun et al., 2017	Simvastatin administered intra-gastrically at a dose of 5 mg/kg/day followed by CS	Male Sprague Dawley (SD) rats (6 weeks old/110–20 g)	Animals were passively exposed (whole body) to smoke from 20 cigarettes in a box for 1 h, twice a day, 5 days a week, for 16 weeks	Partial blockage of airway inflammation, and MMP production			
	Susuki et al., 2009	Curcumin (100 mg/kg) administrated daily by oral gavage throughout a 21-day period	Male C57BL/6J mice (9 weeks old)	Administered intratracheal porcine pancreatic elastase (PPE), or exposed to CS (60 min/day for 10 consecutive days, or 5 days/week for 12 weeks)	Inhibited PPE-induced increase in neutrophils, inhibited increase in neutrophils and macrophages in BAL, and attenuated increase in air space induced by CS			
	Kennedy-Feitosa et al., 2018	Inhalation of 1 mg/mL or 10 mg/mL eucalyptol for 15 min per day	Male C57BL/6 mice (8 weeks old/18–25 g)	Mice exposed to 12 cigarettes a day for 60 days, then treated for another 60 days without exposure to smoke	Lung repair, reduced inflammatory cytokines and NE levels, and increased elastin and TIMP-1 levels.			
, <del>, -</del>	Boo et al., 2020	LJ-2698 (50 µg/kg) administrated by oral	FVB mice	One week after drug treatment, 0.25 units of PPE was intratracheally	Induction of anti-inflammatory cytokine production			

gavage six times per

week for 5 weeks.

(8 weeks old)

intratracheally

instilled into the

lungs of the mice

and recruitment of

M2 macrophages

Animal information: SD/C57, male, 6-8 weeks old. Induction: Cigarette smoke induced by intratracheal injection of LPS. Expected positive control: Roflumilast, 10 mg/kg. CS: QD, 持续12周; LPS: 1d, 14d Roflumilast , P.O., QD Parameter measurement: Weight: BIW Pulmonary function • Inflammation: IL-6, IL -  $\beta$ , TNF -  $\alpha$ • Pathology: HE and PAS The COPD model animals showed the decreased respiratory function.

#### In vivo metabolic disease model

- Obese mouse model (C57, db/db)
- Hyperuricemia
- Diabetes and its complications

NASH(STZ/HFD)

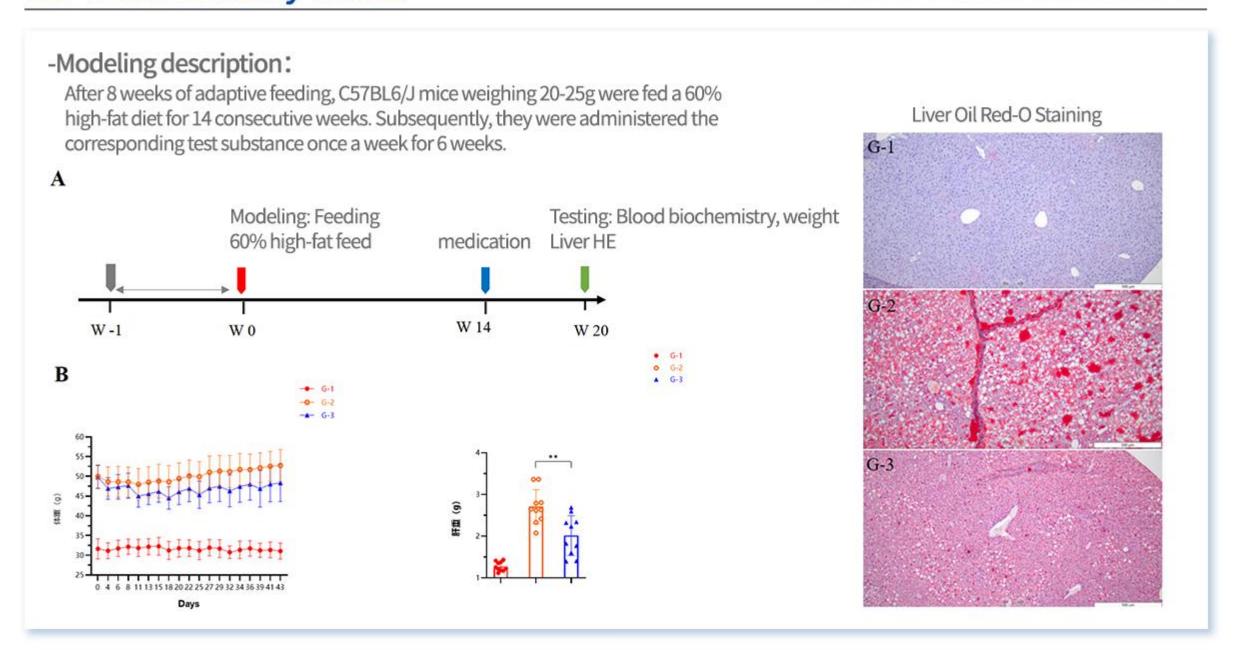
- Renal fibrosis
- Insulin resistance

Cirrhosis model (CCL4)

- Hypertension
- Glucose clamp test

#### C57 mouse obesity model

In vivo metabolic disease model



## In vivo non tumor pharmacological research

#### In vivo autoimmune disease model

■ Arthritis deformans

Colitis (DSS, TNBS)

△ Foot Swelling Rate、

**Arthritis Scoring** 

- Systemic lupus erythematosus (SLE)
- psoriasis

disseminated sclerosis

Treatment

Rat Hind Paw Swelling

#### Collagen-Induced Arthritis Model

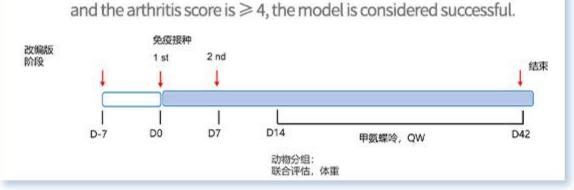
In vivo autoimmune disease model

Treatmen

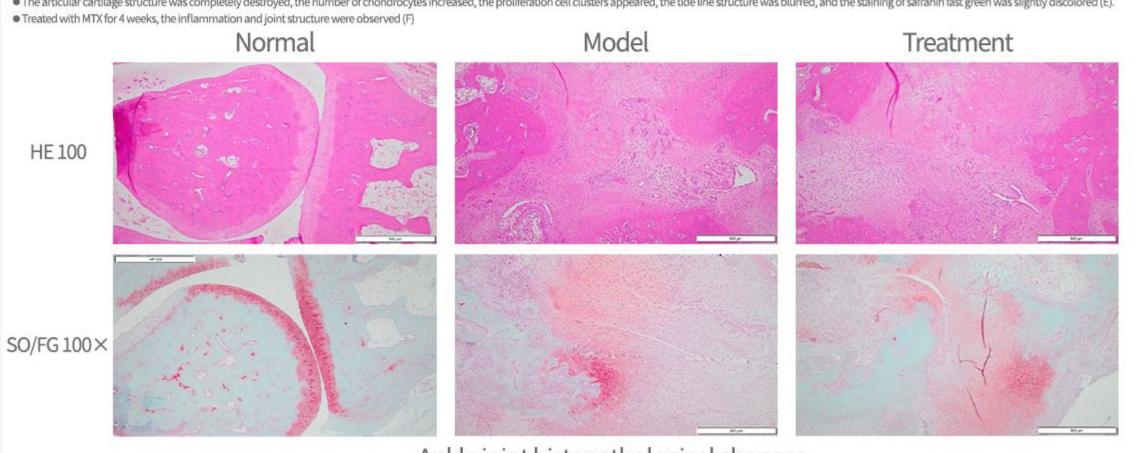
# -Animals: Lewis rats, female; 130-150g; -Group: Each group consists of N=5, including the initial treatment group, model group, and control group (methotrexate, MTX, 0.9 mg/kg, QW, PO, for 4 weeks), with three doses of test compounds. -Method:

D0: CII/IFA emulsion (2 mg/ml) was administered via intradermal injection, with the injection site located at the base of the tail (0.1 ml) and two positions on the back (0.2 ml each).

D7: Re-immunize with the same dosage and method.
D14: When at least one foot and ankle joint of a rat is swollen,



- The normal group of rats showed normal structure of articular cartilage and absence of damage in the synovium (A),
- The CIA model rats showed apparent infiltration of inflammatory cells, severe proliferation of articular chondrocytes (B);
- The articular cartilage structure was intact, the number of chondrocytes was normal, the tide line was intact, and the staining of safranin fast green was good(D).
   The articular cartilage structure was completely destroyed, the number of chondrocytes increased, the proliferation cell clusters appeared, the tide line structure was blurred, and the staining of safranin fast green was slightly discolored (E).

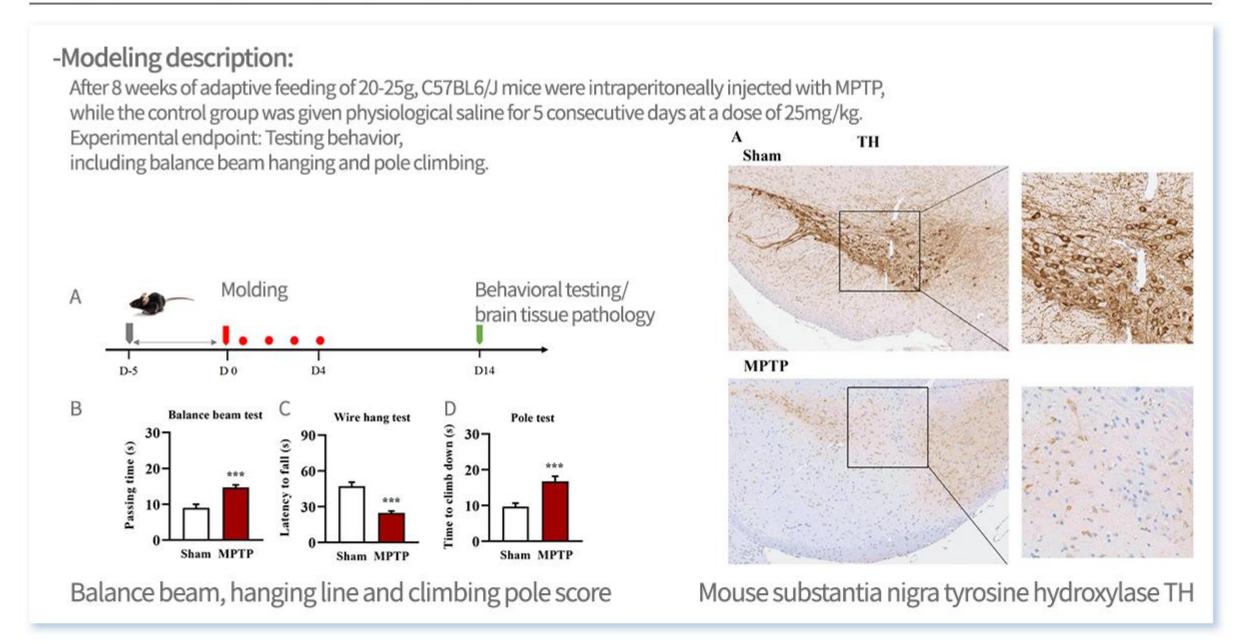


Ankle joint histopathological changes

# Internal nervous system disease model ■ Stroke (tMCAO, pMCAO) ■ Migraine ■ Learning and memory ■ Parkinson's disease ■ pain ■ Locomotion ■ Depression ■ Senile dementia

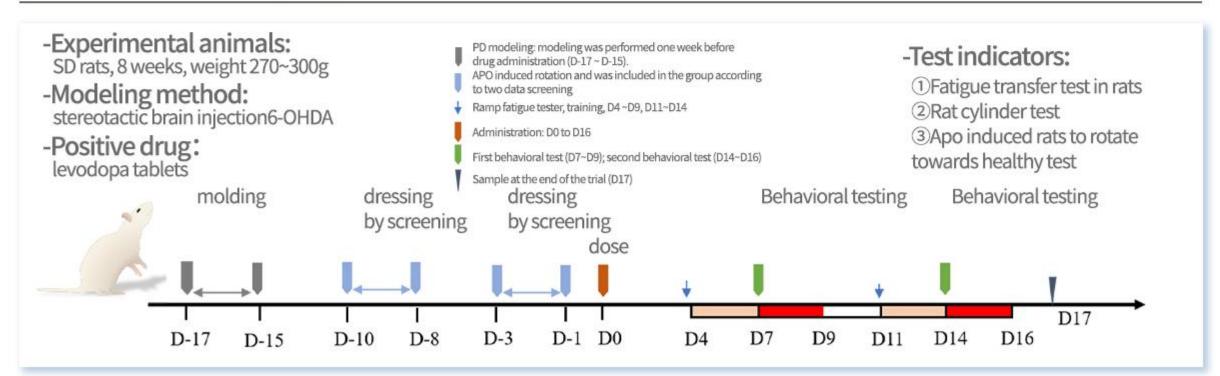
#### Mouse Parkinson's (PD) model

Internal nervous system disease model



#### Rat Parkinsonian (PD) model

Internal nervous system disease model

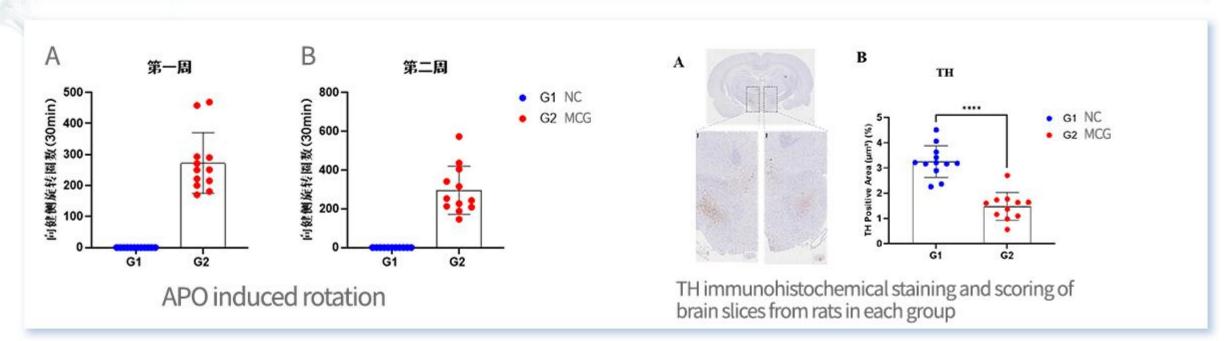


www.innostar.cn www.innostar.cn

## In vivo mon tumor pharmacological research

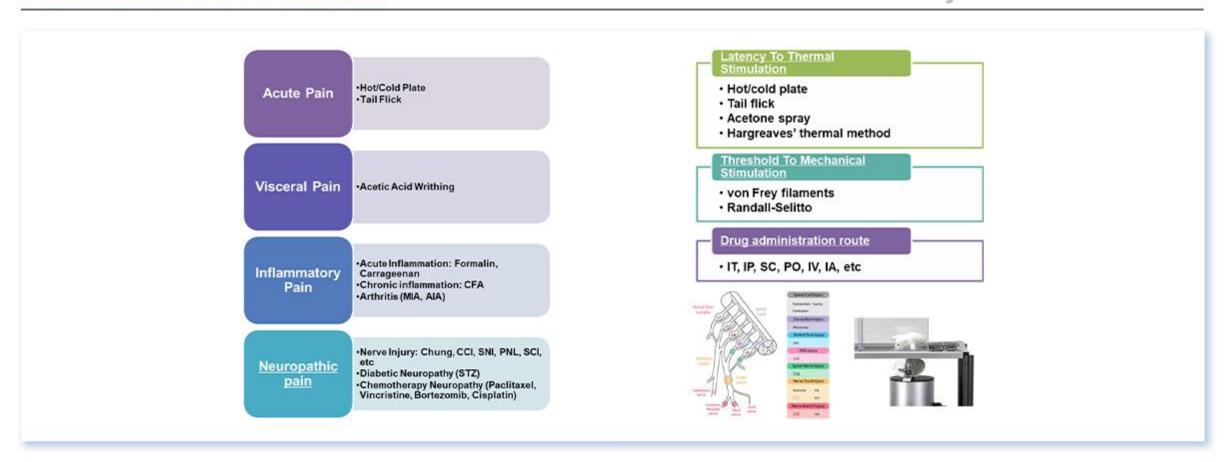
#### Rat Parkinson's (PD) model

Internal nervous system disease model



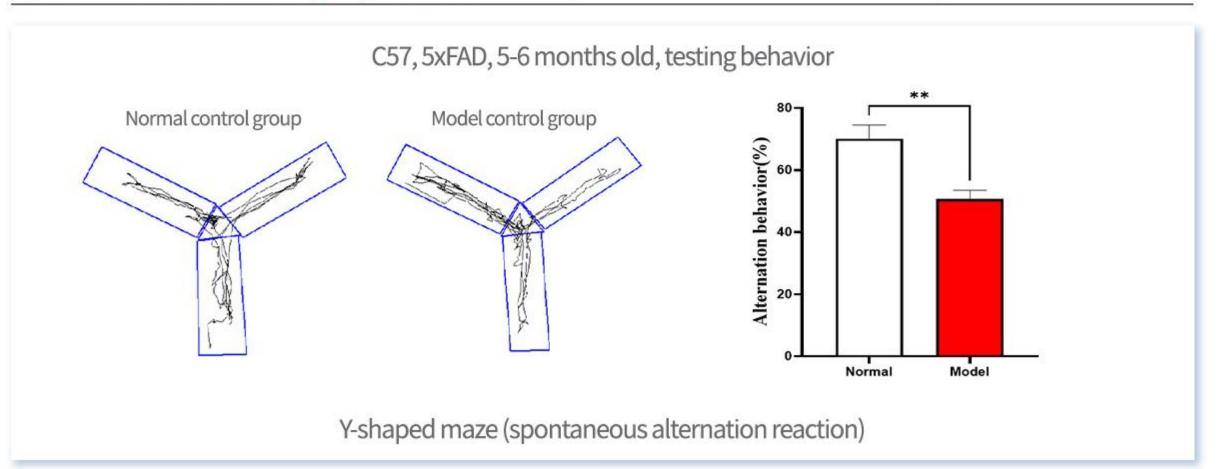
#### Pain Model and Detection

Internal nervous system disease model



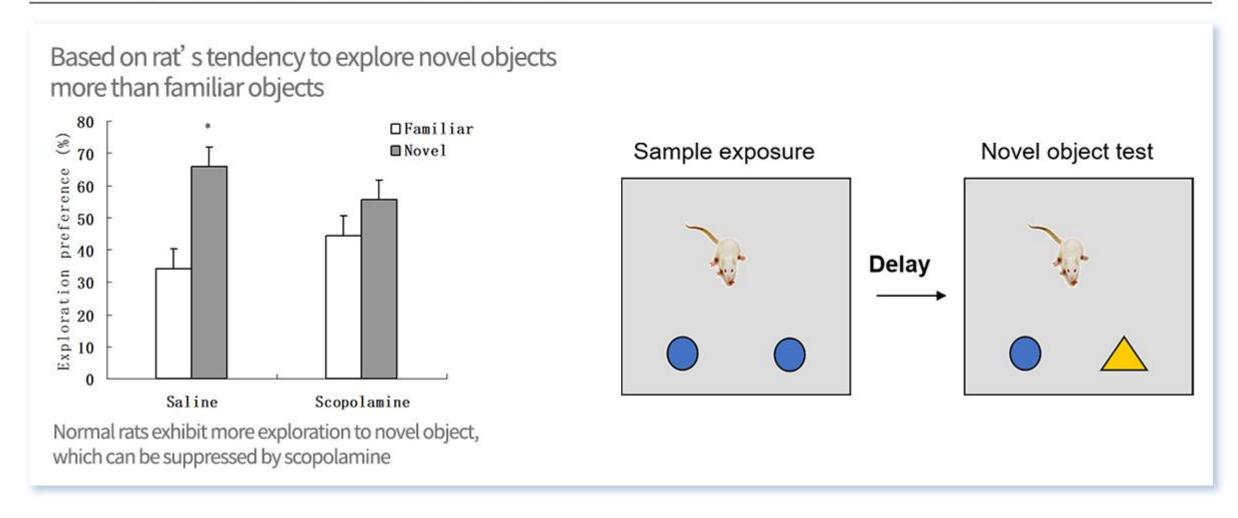
#### Alzheimer's Disease (AD) mouse model

Internal nervous system disease model



#### New object recognition and detection

Internal nervous system disease model



#### Sports behavior testing

Internal nervous system disease model



#### Open Field Test (locomotion)

Measures spontaneous activity of rodents, providing great value to neuropsychological drug research



#### **Rotarod Test**

Measure motor coordination and balance, used to screening drugs which have side effects on motor coordination



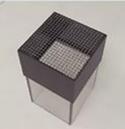
**Grip Strength Meter** 

Used to assess neuromuscular abnormalities



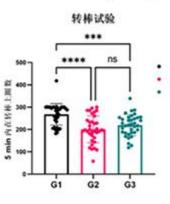
#### Pole Test

A simple behavior test used to assess motor dysfunction after stroke, or striatal dopamine depletion



#### **Grid Test**

measures long-term behavioral deficits and allows observation of subtle behavioral dysfunctions in Parkinson disease. Tillerson and Miller (2003)



### Other disease models in the body

■ Osteoarthritis (Rabbit)

Melasma

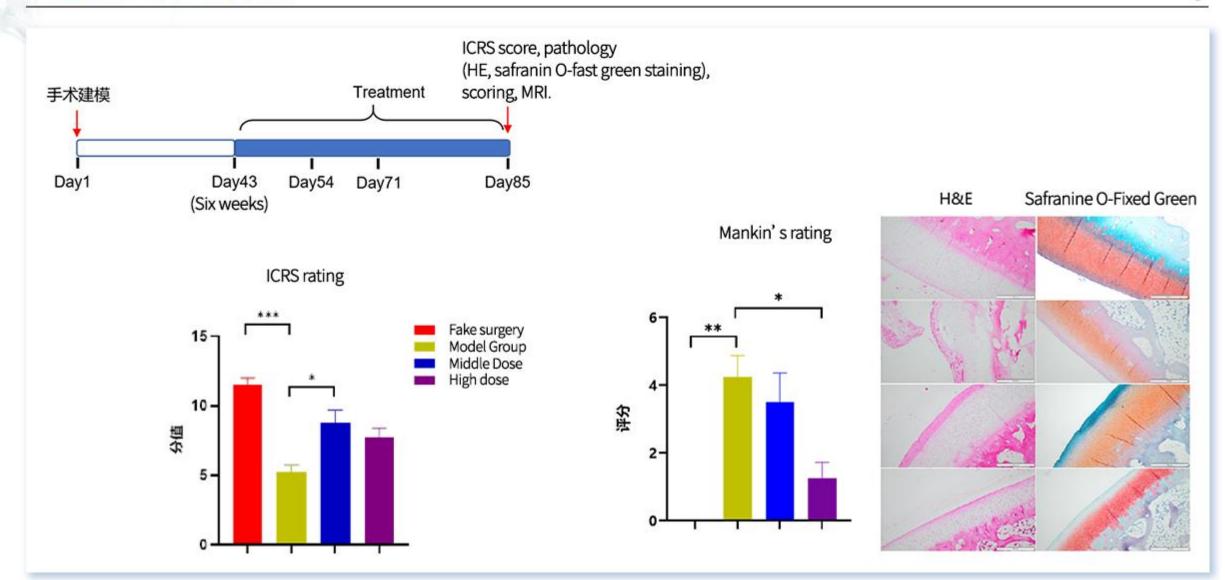
- Male hair loss

Acne vulgaris

## In vivo non tumor pharmacological research

#### Rabbit KOA model

Other disease models in the body



#### Non human primate disease model

Diabetes

**■NASH** 

Obesity

#### Efficacy in non-human primates

Non human primate disease model

#### -Study on the efficacy of crab monkey medicine (siRNA screening)

- Liver function, blood routine, four kinds of blood lipid, four kinds of coagulation, electrocardiogram, blood pressure, etc
- More than 100 liver punctures with no errors or infections

#### -Non-human primate, monkey model development

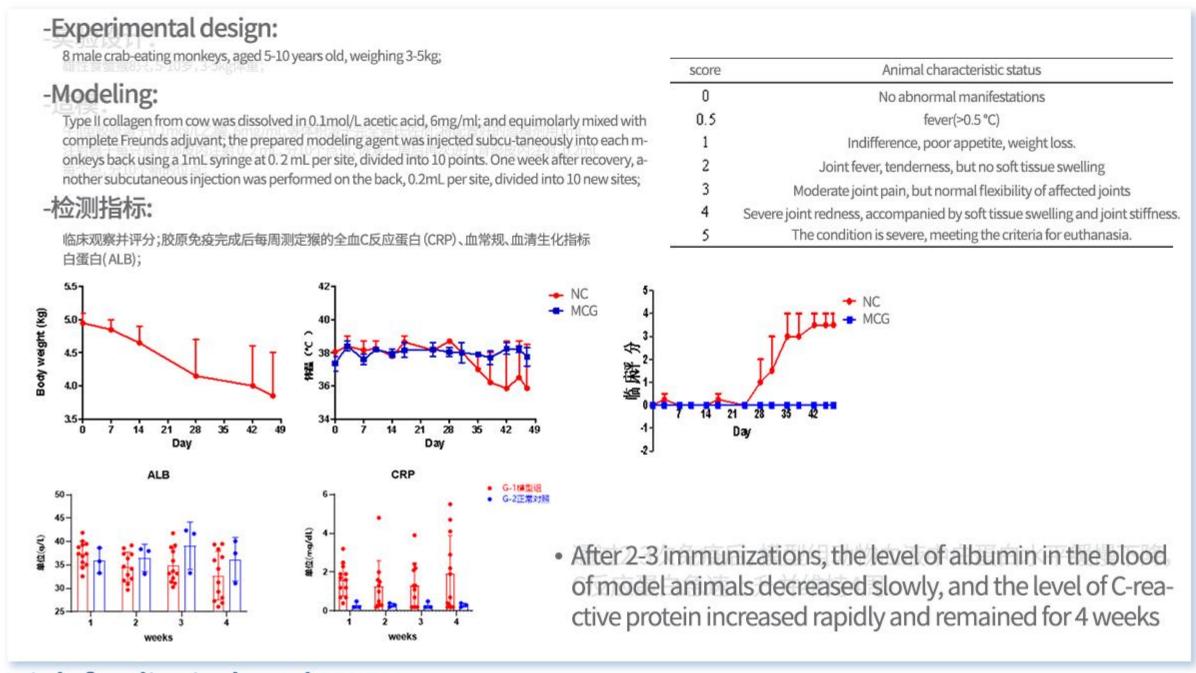
- Spontaneous disease model
- Induced disease mode



Category	Indication	Validation			
	Diabetes				
	Hypertension	Biomarkers (blood)			
Spontaneous	Hyperlipidemia				
disease model	NASH & NAFLD				
	Alzheimer's disease	Biomarkers (blood & CSF); Behavior			
	Parkinson's disease				
Spontaneous	MPTP Parkinson's disease	Biomarkers (blood & CSF); Behavior; IHC			
isease model	MCAO				

#### Rhesus monkey arthritis model

Non human primate disease model



## High fat diet induced NASH model in rhesus monkeys

Non human primate disease model

#### -experimental design:

group	animal	Administer	Administration	Dosage
	quantity	medication	method	measurement
Group-1	8	NA	NA	NA
High fat feed group				
Group-2 High fat feed group	8	STZ	I.V	35mg/kg

Liver function and blood lipid abnormalities
were observed in model animals

AST

LDL-C

HDL-C

G-1

G-2

G-3

G-1 STZ+60%

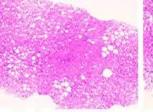
G-2 60%

G-2 60%

G-2 60%

After screening, 18 rhesus monkeys were selected to enter the experiment, and then all the feed was replaced with high-fat feed to induce NASH model. After 4 weeks of feeding, 10 animals were randomly selected to be given 35mg/kg dose of STZ to induce type 2 diabetes model. After the model was established, high-fat feed was continued to be fed.

STZ+60% high fat feed



In histopathology, HE staining showed moderate vacuolization in the liver, with vacuoles of varying sizes accumulated in hepatocytes and fused into a large vacuole, which squeezed the nucleus of hepatocytes to one side, indicating that the accumulation of fat in the liver was more serious and formed fatty hepatitis.

Blood biochemical analysis shows that after STZ-induced type 2 diabetes in rhesus monkeys, continued high-fat feeding for 2 months resulted in elevated liver function (AST/ALT) and lipid-related indicators (TG/TC/LDL-C) in serum compared to normal controls and animals fed only regul-ar diet. These changes accelerated the formation of NASH. In contrast, there was no significant difference between animals fed only regular diet and normal controls, although TC and LDL-C showed a slight upward trend, indicating that the induction period needs to be extended.

## Project experience

(ongoing+completed)

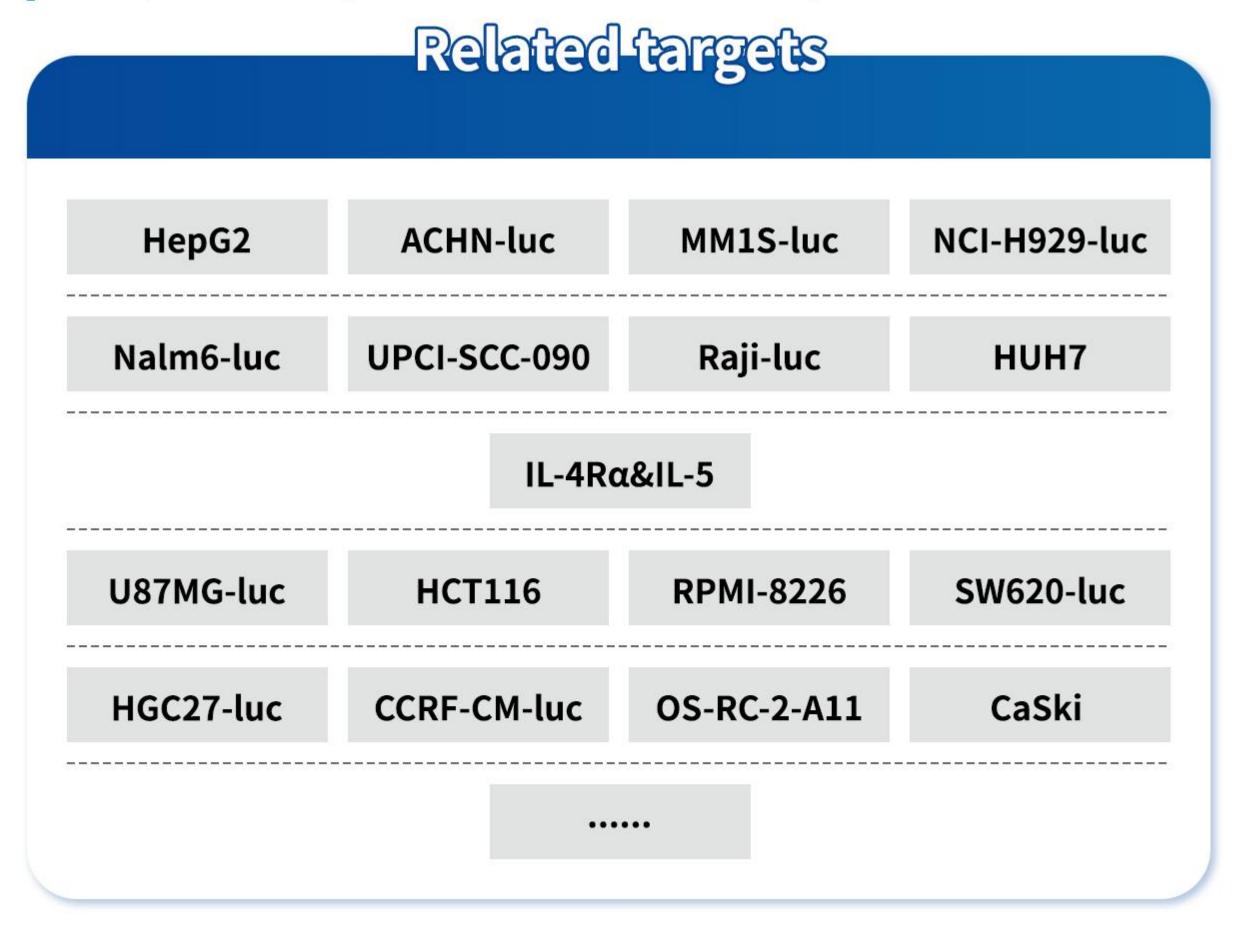
~60 20+ 5

CGT Pharmacology Project CGT Pharmacology

Application Project IND

**Application Project** 

Exceptional experience in CGT efficacy research.



#### Overview of InnoStar Project Experience

pharmaceu- tical chemicals	•••••	Molecular glue drugs	PROTAC medicinal			eptide drugs			Small molecul chemica drugs All kinds of innovation tar	al 🗭
biologicals	Carrier delivery of drugs	recombination protein	fusion protein		pr	oecologi- cal oducts robiotics	Monoclor dies, bispeci esPolyanti le antibody, antibody),	oody IgS ral antibo- fic antibodi- body (trip- quadruple TCENano- odies	ADC (single tary double antibo double payloa PDC, RDC, AC	get, dy, d),
Cell/ gene therapy medicinal	*****	Oncolytic drugs Oncolytic bacteria, oncolytic viruses	Gene therapy products Viral vectors, non-viral vectors gene editing.		th	Immune erapy pro R-T, TIL, TCR-T, Treg, CAR-	ducts		n cell therap products SC, MSC, HSC, etc	у
Vaccines and drugs	*****	Therapeutic vaccines Therapeutic cancer vaccines (PCV-TAA, TSA)	prophylactic vaccine Inactivated/virus attenuated, recombinant protein vaccine, mRNA vaccine, etc						•	
Nucleic acid drugs	•••••	miRNA	Aptamer		AS	60	circRN	IA :	siRNA	•
radiophar- maceuticals	*****	For diagnostic only radioph maceutica	ar- radiopha		apeuti narmad icals	c use ceu-				•
traditional Chinese medicine	•••••	Ancient class prescriptio Chinese medic compound preparation	on compou cine preparat					Chinese medicine innovation drugs		•

 $\mathbf{a}$ 

## IN RESEARCH



Shanghai InnoStar Biotechnology Co., Ltd

#### SHANGHAI HEADQUARTERS

No. 199 Guoshoujing Road, China (Shanghai) Pilot Free Trade Zone

#### **BUSINESS CONSULTING**

Tel:+86-21-60211999

Email: services@innostar.cn marketing@innostar.cn



Scan the code to follow