

Metabolic and Cardiovascular Disease Research

Solution

Shanghai Model Organisms
Center, Inc. (SMOC)

Our mission is editing genes and
decoding life.

Our vision is to become the leader
in the field of genetically modified
animal models, helping people
understand the life science and
improving quality of life around
the world.

Our values are Innovation, Dedic-
ation, Friendship and Responsibility.

INTRODUCTION

Metabolic and cardiovascular diseases are accountable for nearly 18 million deaths worldwide each year and impose an enormous burden on individuals and society.

It is critical to select appropriate animal models to accelerate the pace of drug development from laboratory research to clinical application.

1. Type II diabetes / High Fat Diet Induced Diabetic Mice



Fat high feed



Fat mice

Principle: Long-term feeding of high-fat diets can cause obesity and increased fasting blood glucose in mice along with fat accumulation and insulin resistance in the body to mimic human type II diabetes.

Sample requirements: C57BL/6JSmoc mice of 6–8 weeks old

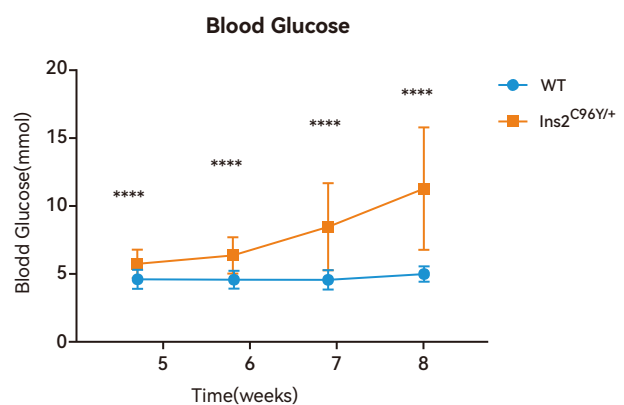
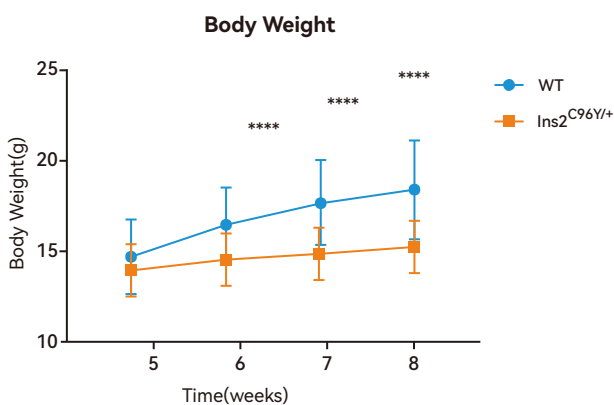
Testing instruments and consumables: 60% fat high feed, Roche blood glucose meter, glucose, insulin

Service cycle: 10–12 weeks

Technical indicators: Provide testing services including the testing of fasting blood glucose, body weight, GTT, and ITT as well as continuous multi-point blood collection services.

2. Type I diabetes / Ins2-C96Y(Akita-like mice)

The C96Y mutation in the Ins2 gene results in abnormal insulin processing, which leads to islet cell malfunction and death. The C57BL/6JSmoc-Ins2^{C96Y/+} mice develop severe hyperglycemia.



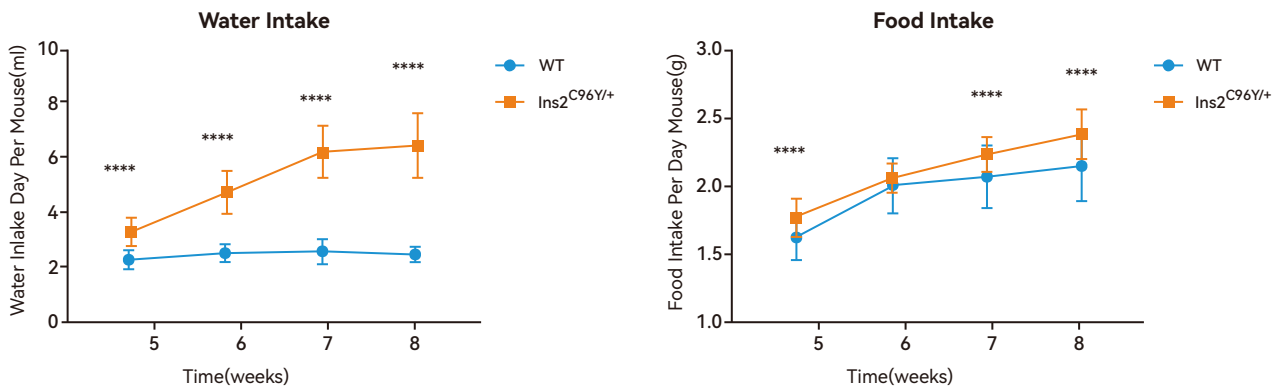


Fig1. The basic symptoms of ins2-C96Y mice compared with their littermate ins2^{wt/wt} controls.

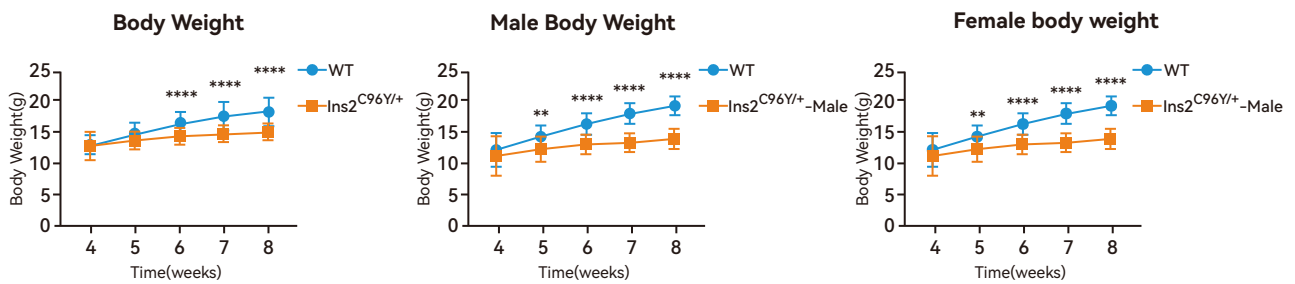


Fig2. Body weight of ins2-C96Y mice compared with their littermate Ins2^{WT/WT} control. The body weight of ins2-C96Y mice was significantly lower than that of littermates.

3. Humanized GLP-1R model

Glucagon-like peptide-1 receptor (GLP-1R) is one of the most effective targets for the treatment of type 2 diabetes mellitus. We have independently developed a humanized GLP-1R mouse model, which provides a powerful tool for drug screening and drug efficacy experiments.

Protein expression profile

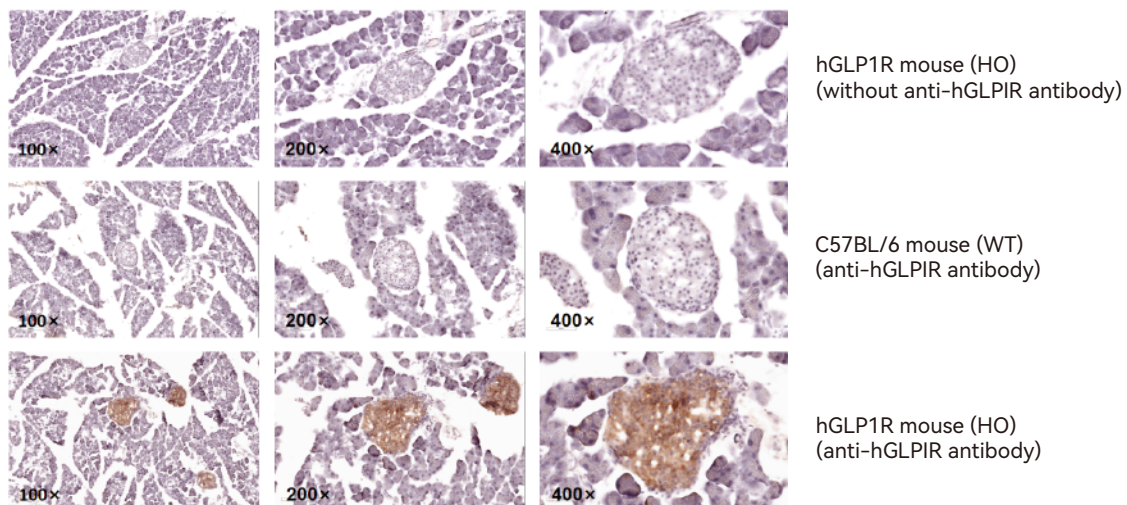


Fig1. Analysis of hGLP1R expression by IHC.

Drug efficacy evaluation

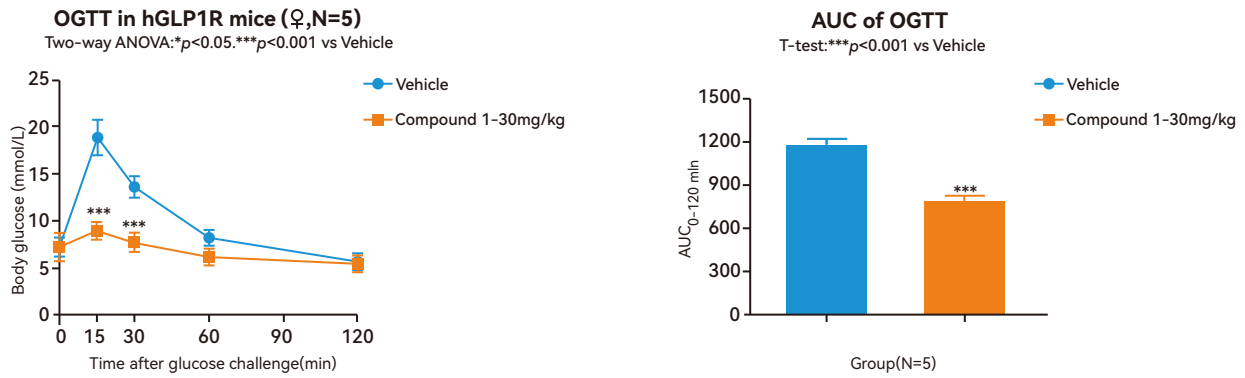


Fig2. Hypoglycemic efficacy of the test compound in humanized GLP-1R mice.

4. Humanized PCSK9 mouse model

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a protease that regulates low density lipoprotein receptor (LDLR) protein levels. We created humanized PCSK9 mice that carry the human PCSK9 gene and its 3'UTR region, making them appropriate for screening antibody drugs and nucleic acid drugs.

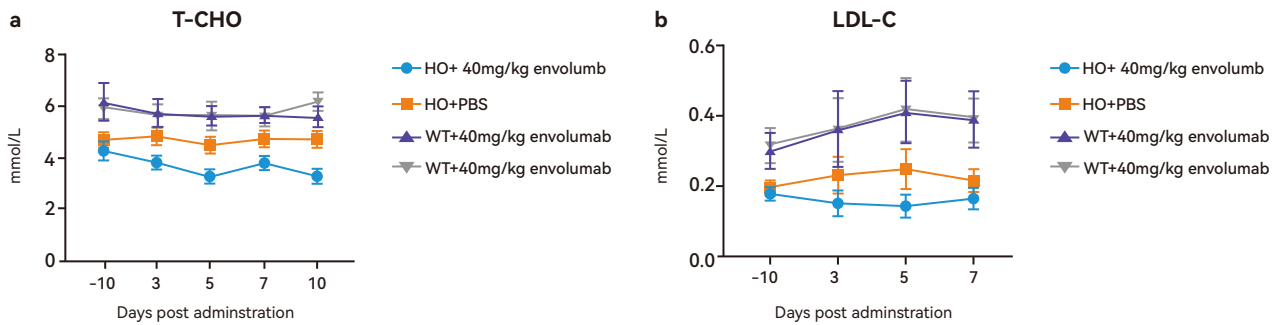


Fig1. Impact of evolocumab treatment on CHOL and LDL-C levels in humanized PCSK9 homozygous mice.

More Models

Gene	Cat.NO.	Model	Types	Disease Connection	Notes
Abcc8	NM-KO-2103220	Abcc8-KO	Knockout	MODY	
Akt2	NM-KO-190742	Akt2-KO	Knockout	T2DM	
Ar	NM-CKO-00110	Ar-Flox	Conditional Knockout	T2DM	The expected phenotype may be observed in the above-mentioned mice that bred with Fabp4-cre mice.
Ctf1	NM-KO-190546		Knockout	T2DM	
Fem1b	NM-KO-191164	Fem1b-KO	Knockout	T2DM	
Foxm1	NM-CKO-2100393	Foxm1-Flox	Conditional Knockout	T2DM	The expected phenotype may be observed in the above-mentioned mice that bred with Pdx1-cre mice.
Foxo1	NM-CKO-200177	Foxo1-Flox	Conditional Knockout	MODY	The expected phenotype may be observed in the above-mentioned mice that bred with ins2-cre mice.
Hnf4a	NM-CKO-190062	Hnf4a-Flox	Conditional Knockout	MODY	The expected phenotype may be observed in the above-mentioned mice that bred with ins2-cre mice.
Ins2	NM-KI-190096	Ins2-C96Y	Point Mutation	T1DM	
Irs1	NM-KO-190827	Irs1-KO	Knockout	T2DM	
Lep	NM-KO-00034	Lep-KO	Knockout	T2DM	
Lepr	NM-KO-190663	Lepr-KO	Knockout	T2DM	
Met	NM-CKO-200328	Met-Flox	Conditional Knockout	GDM	The expected phenotype may be observed in the above-mentioned mice that bred with Pdx1-cre mice.
Phox2a	NM-KO-201323	Phox2a-KO	Knockout	T2DM	
Prlr	NM-CKO-210028	Prlr-Flox	Conditional Knockout	GDM	The expected phenotype may be observed in the above-mentioned mice that bred with Pdx1-cre mice.
Senp1	NM-CKO-200277	Senp1-Flox	Conditional Knockout	T1DM	The expected phenotype may be observed in the above-mentioned mice that bred with Fabp4-cre mice.
Tgm2	NM-KO-191051	Tgm2-KO	Knockout	MODY	
Apoe	NM-KO-190565/ NR-KO-190003	Apoe-KO(2)/ Apoe-KO(SD)	Knockout	Atherosclerosis	
Nos	NM-KO-18022	Nos-KO	Knockout	Hypertensive Disease	
GCGR	NM-HU-215004/ NR-HU-225066	hGCGR/hGCGR(5D)	Humanization	/	Drug Discovery of Diabetes
GLP1R	NM-HU-200220	hGLP1R	Humanization	/	Drug Discovery of Diabetes
PCSK9	NM-HU-00075	hPCSK9	Humanization	/	Drug Discovery of Cardiovascular Disease
Pdx1	NM-KI-18042	Pdx1-2A-CreERT2	Knockout	/	Cre Mice Specific for β Cells
Ins2	NM-KI-225022	Ins2-CreERT2	Knockout	/	Cre Mice Specific for β Cells
Ace2	NM-KI-200187	Ace2-2A-CreERT2	Knockout	/	Cre Mice Specific for Ace2 Positive Cells
Cdh5	NM-KI-200173	Cdh5-2A-CreERT2	Knockout	/	Cre Mice Specific for Vascular Endothelial Cells
Tagln	NM-KI-200144/ NR-KI-210134	Tagln-Cre/ Tagln-Cre(SD)	Knockout	/	Cre Mice Specific for Myocardial Cells
Tek	NM-KI-210133	Tek-Cre(SD)	Knockout	/	Cre Mice Specific for Vascular Smooth Muscle Cells
Fabp4	NM-KI-200060	Fabp4-2A-DreERT2	Knockout	/	Cre Mice Specific for Adipocytes
Ucp1	NM-KI-190105	Ucp1-Cre	Knockout	/	Cre Mice Specific for Brown Fat Cells

*Disease Connection: It is possible that the phenotypes of above-mentioned mice are not the same as those reported models.

Metabolism and Spontaneous Activity Assay

Comprehensive Lab Animal Monitoring System

Introduction

Comprehensive Lab Animal Monitoring System (CLAMS) is a system of metabolic cages which allows for simultaneous measurement of numerous metabolic parameters. It is widely used in metabolic diseases, circadian rhythm, sleep and other studies that require continuous detection of basic metabolic indicators and daily activity.

Parameter sampling

Scales:

Simultaneous multiparameter assessment of 1 to 12 test animals. Sampling point can be accurate to 1 data point /12min.

Output parameters:

Oxygen consumption: The volume of O₂ consumed in one hour per kilogram of body weight (ml/kg/hr).

Carbon dioxide production : The volume of CO₂ produced in one hour per kilogram of body weight (ml/kg/hr).

Respiratory exchange ratio (RER) : CO₂ Production / O₂ Consumption

Heat : The amount of heat produced per hour in one kilogram of body weight (kcal/kg/hr) .

Movement in horizontal direction [XY], counts : The movement of the animal in the horizontal direction (X and Y coordinates) per hour.

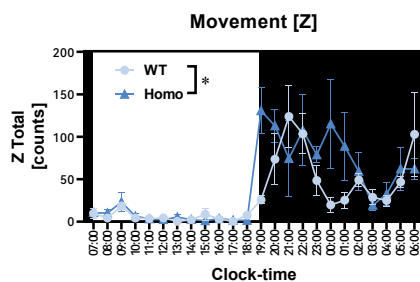
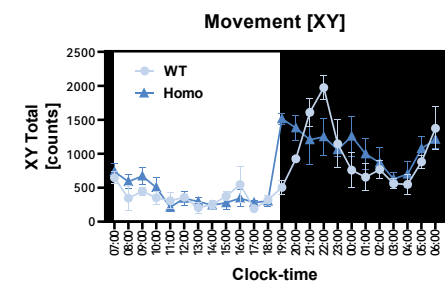
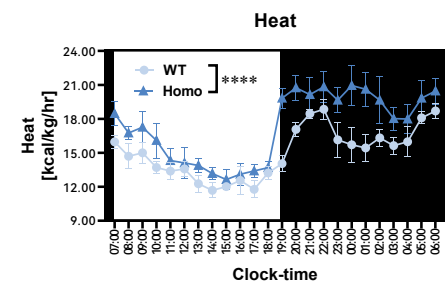
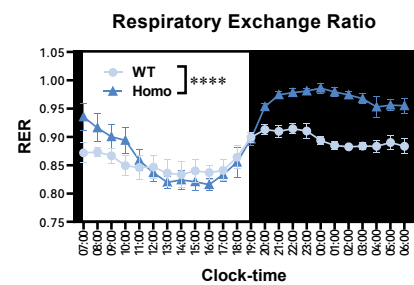
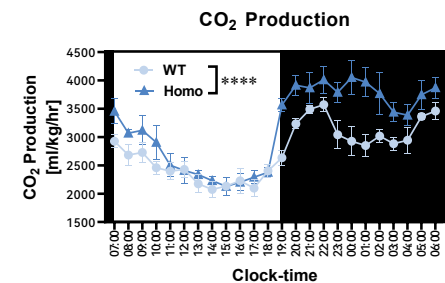
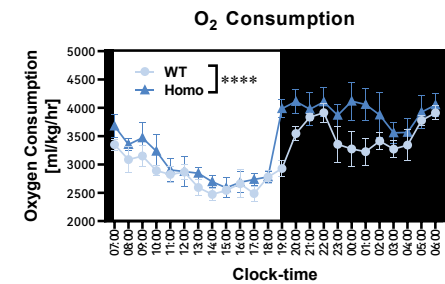
Movement in vertical direction [Z], counts : The movement of the animal in the vertical direction (Z coordinate) per hour.

Food intake(g) : The amount of food consumed.

Water intake(g) : The amount of water consumed.

(A) O₂ consumption, (B) CO₂ production, (C) Respiratory Exchange Ratio (RER) , (D) Heat, (E) Movement in horizontal direction [XY] and (F) Movement in vertical direction [Z] of X gene mutated mice (n=4) and their WT littermates (n=4) in Automated Metabolic and Behavioral Monitoring.

Data Presentation



[1] Jereme G. Spiersa et al. Noninvasive assessment of altered activity following restraint in mice using an automated physiological monitoring system. *Stress* 2017, 20:76-84.

[2] Karthikeyani Chellappa et al. The leptin sensitizer celastrol reduces age-associated obesity and modulates behavioral rhythms. *Aging Cell* 2019, 18: e12874.

[3] Jeannette G. Lumaban et al. The Fragile X proteins Fmrp and Fxr2p cooperate to regulate glucose metabolism in mice. *Human Molecular Genetics* 2015, 24:2175-2184.