药明康德
WuXi AppTec

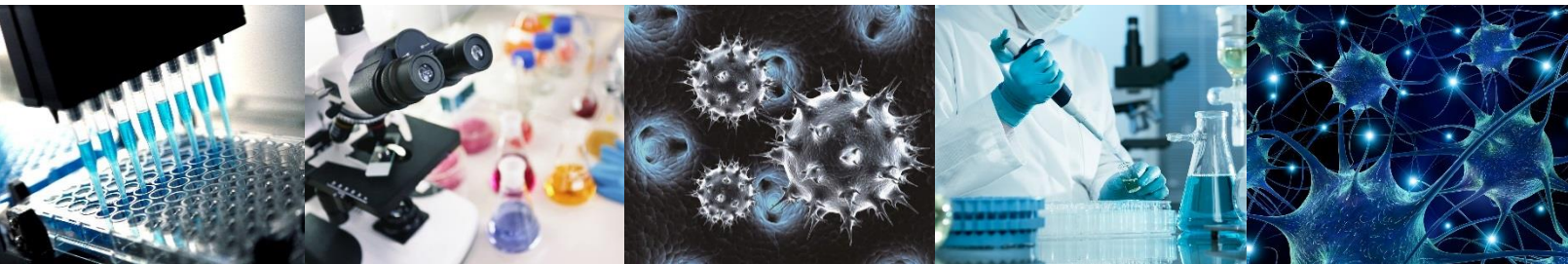
Research Service Division (RSD)
Enabling Unbounded Possibilities

WuXi Biology

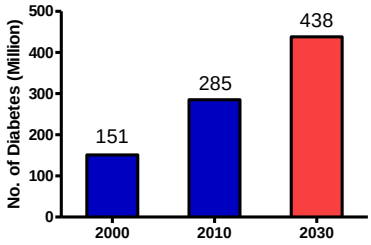
Diabetes Service Platforms

Full scale of diabetes assays and models
To accelerate your drug discovery process

www.wuxiapptec.com



Prevalence

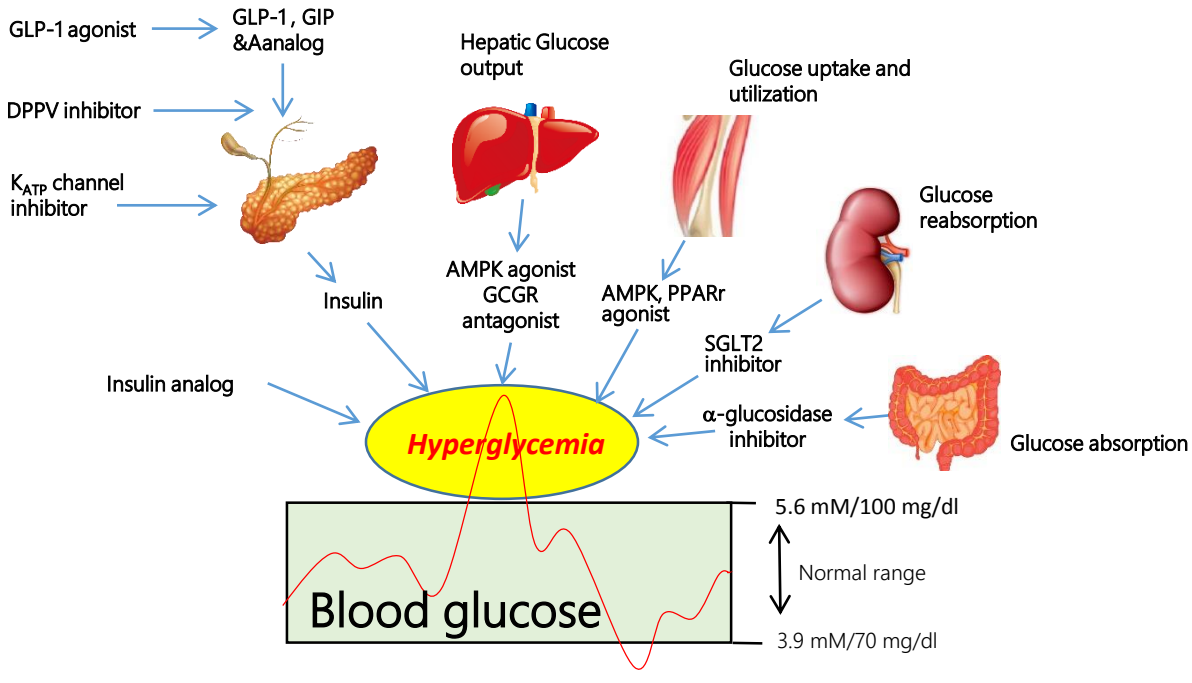


- 6.4% of adult population in 2010
- 54% increase 2010 to 2030
- 36% in India and China alone

Reference: DRCP, 2010 , 87:4

China: 2007-2008 (NEJM 362;12, 2010)	China: 2010 (JAMA. 2013, 310:948)
9.7% Diabetes 15.5% Prediabetes	11.6% Diabetes 50.1% Prediabetes

Mode of Action in Treatment of Diabetes



In Vitro Assay Services

Category	Name/Target (human if not specified)	Cell line	Ligand binding /Enzyme assay	Function assay
INS & Analog	Insulin-R A (short)	CHO	I-125	phosphorylation
	Insulin-R B (long, exon 11)	CHO	I-125	phosphorylation
	IGF-1R	H19-7	I-125	phosphorylation
	IR/GLUT4	3T3-L1 adipocytes	[3H]Deoxy-D-glucose	glucose uptake
	IR		[14C]-glucose	lypogenesis
	IR		[14C]-glucose	Glycogen formation
GLP1R	GLP-1R	HEK293	FRET/I-125	cAMP
GCGR	Glucagon R	HEK293	I-125	cAMP, Ca
SGLT	SGLT1	CHO		[14C]Methyl a-D-glucopyranoside (AMG)
	SGLT2	CHO		
	SGLT2 (rat)	CHO		
DPP	DPP4，8， 9		Luminescent	
NHR	PPAR-gamma		Fluorescent	

Applications

- New drug R&D
- In vitro pharmacological profiling of compounds, insulin and/or biosimilars
- Biosimilar equivalence assessment, quality testing
- IND filling

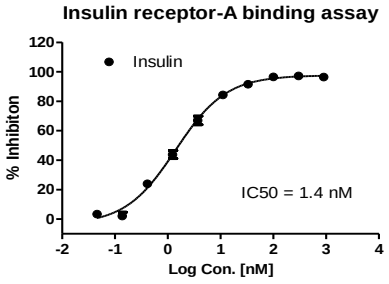
- Complete recording and achieving of samples, assay procedures, raw data and results
- Data authenticity
- Assay traceability
- CFDA on site inspection

Insulin Assay

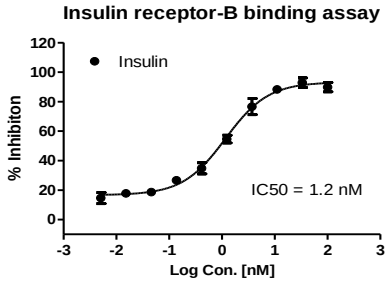
Affinity: Binding Assay

Method: Radioligand filtration binding assay
Format: 96-well

Stable cell line: CHO-INSRA, WuXi



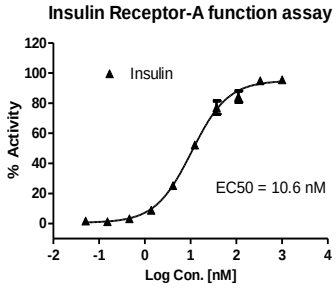
Stable cell line: CHO-INSRB, WuXi



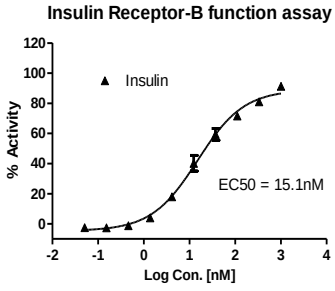
Function: Phosphorylation Assay

Method: Alpha screen assay (phosphorylation)
Format: 384-well

Stable cell line: CHO-INSRA, WuXi

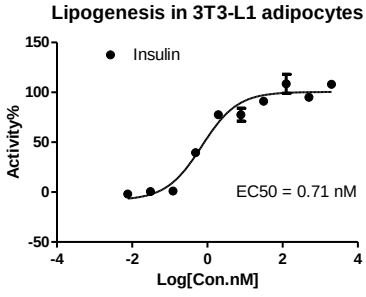


Stable cell line: CHO-INSRB, WuXi



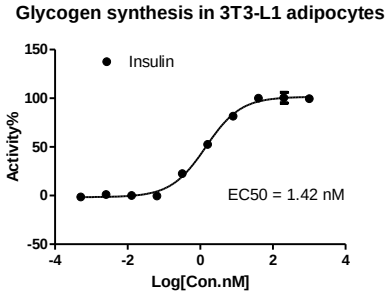
Lipogenesis Assay

Cell line: 3t3-L1, ATCC
Method: Radioactive assay
Format: 96-well



Glycogen Synthesis Assay

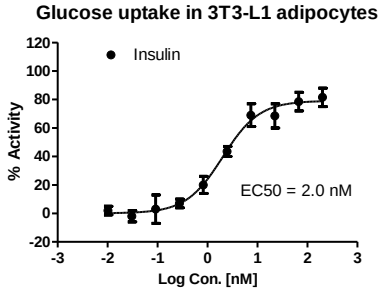
Cell line: 3t3-L1, ATCC
Method: Radioactive assay
Format: 96-well

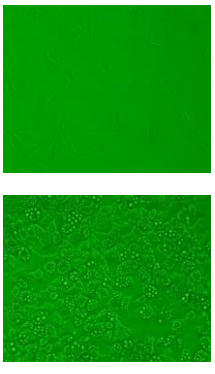


Glucose Uptake Assay

Glucose Uptake Assay

Cell line: 3T3-L1, ATCC
Method: Radioactive assay
Format: 96-well





3T3-L1 (ATCC, CL-173™)

Induction

Adipocytes

SGLT2/1 Assay

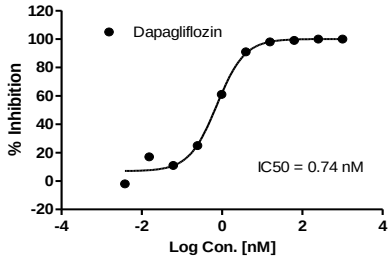
Transporter assay

Method: Radioactive assay

Format: 96-well

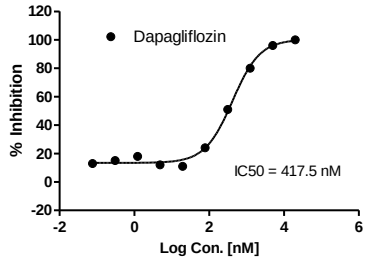
Stable cell line: CHO-hSGLT2, WuXi

hSGLT2 transporter assay



Stable cell line: CHO-hSGLT1, WuXi

hSGLT1 transporter assay



GLP-1R Assay

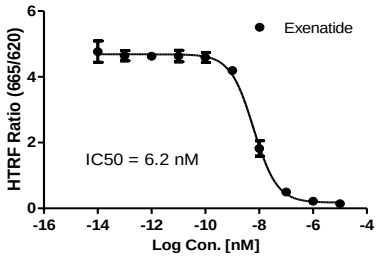
Affinity: Binding Assay

Method: Tag-lite assay

Format: 384-well

Stable cell line: HEK-GLP-1R, WuXi

GLP-1 receptor binding assay (Tag-lite)



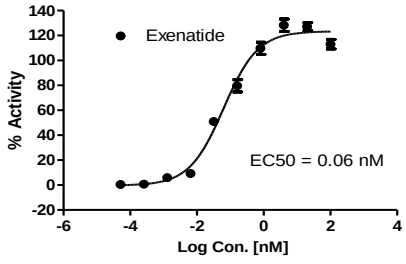
Function: cAMP Assay

Method: TR-FRET cAMP assay

Format: 384-well

Stable cell line: HEK-GLP-1R, WuXi

GLP-1 receptor cAMP assay



Glucagon Receptor Assay

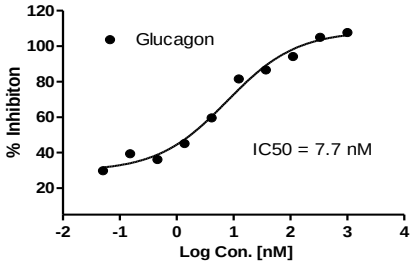
Affinity: Binding Assay

Method: Radioligand filtration binding assay

Format: 96-well

Stable cell line: HEK-GCGR, WuXi

GCGR receptor binding assay



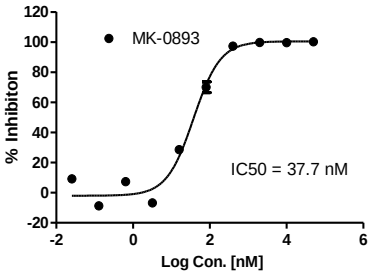
Function: cAMP Assay

Method: TR-FRET cAMP assay

Format: 384-well

Stable cell line: HEK-GCGR, WuXi

GCGR receptor cAMP assay-antagonist mode



DPP Assay

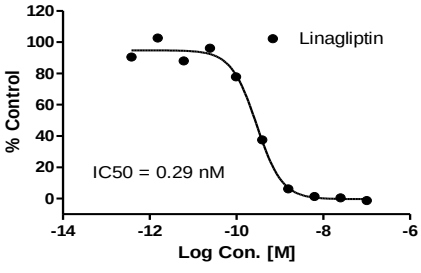
Primary Screening

Enzyme: DPP4

Method: Luminescent assay

Format: 384-well

DPP4 inhibition assay



PPAR-γ Assay

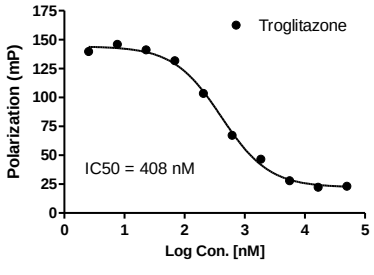
Primary Screening

Enzyme: PPARγ-LBD

Method: Fluorescence polarization

Format: 384-well

PPAR-gamma Binding Assay



NHP Diabetes Resource

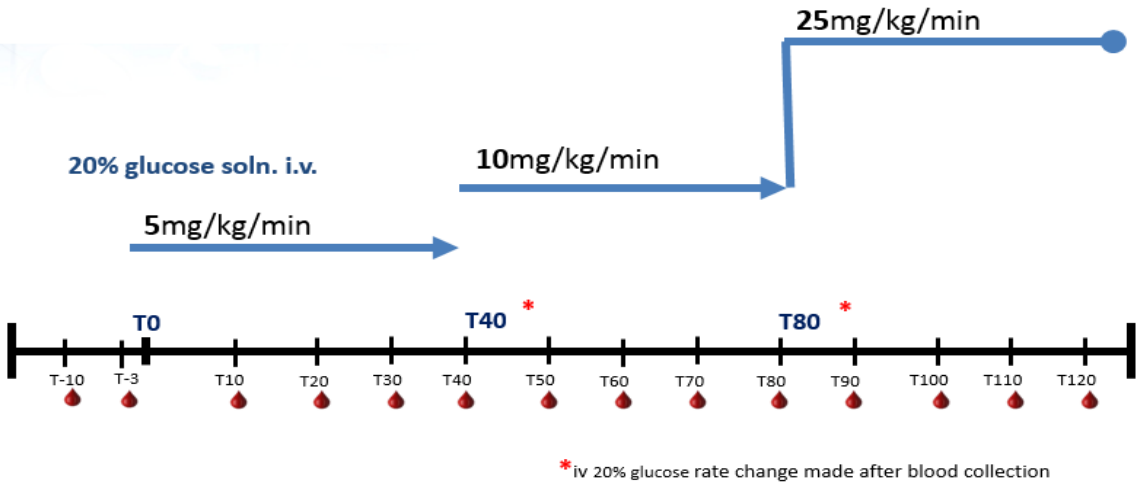
Fat NHP:
High fat diet induced, spontaneous

Diabetes study:
- Oral Glucose Tolerance Test (OGTT)
- Mixed Meal Tolerance Test (MMTT)
- Intravenous Glucose Test (IVGTT)
- Insulin Tolerance Test (ITT)
- Graded Glucose Infusion (GGI)
- Glucose Clamping

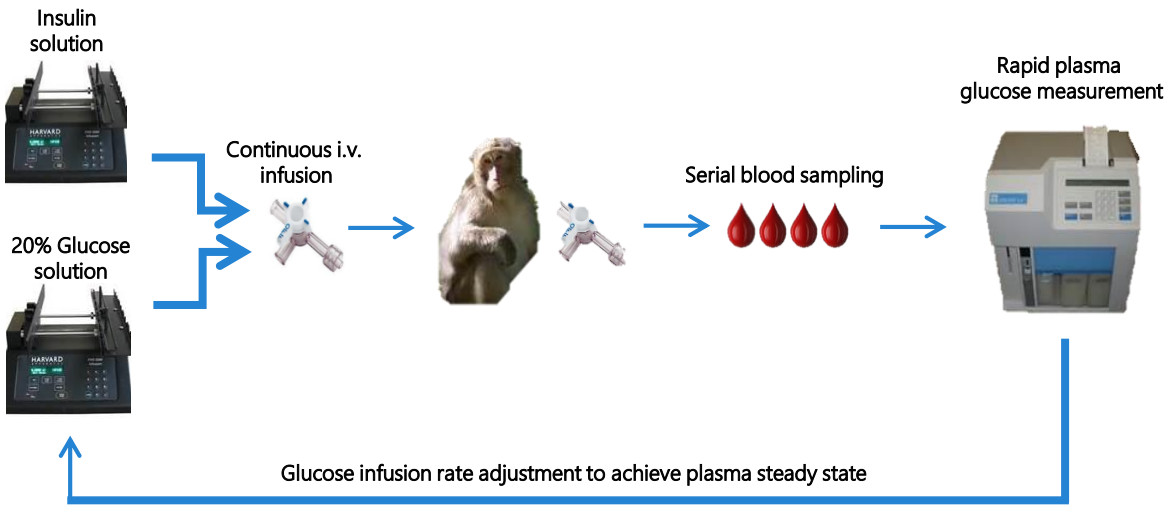
Imaging:
- MRI liver fat content quantitation
- MRI liver fibrosis detection
- MRI blood vessel imaging
- Body composition measurement by DEXA

Tissue biopsy:
- Liver
- Kidney
- Muscle
- Fat
- Brain

Graded Glucose Infusion

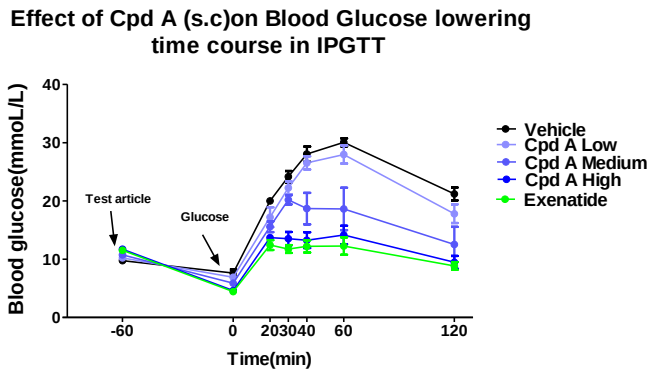


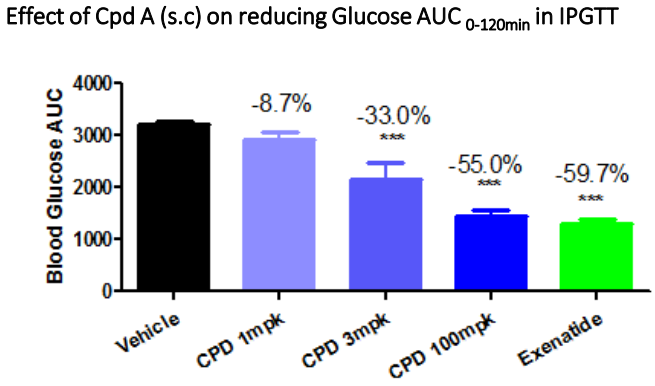
Glucose Clamping



Glucose Tolerance Test (Acute)

Introduction:
An assay to assess glucose tolerance including oral glucose (OGTT), intraperitoneal glucose(IPGTT) or intravenous glucose (IVGTT) to fasted animals
Species: Mouse, rat and NHP
Endpoint: Blood glucose and Insulin
Throughput: 8 animals/group; 5~8 groups
Groups in a standard assay: Vehicle, Positive control, Testing compounds with 3 doses
Turnaround time : ~5 days/each study

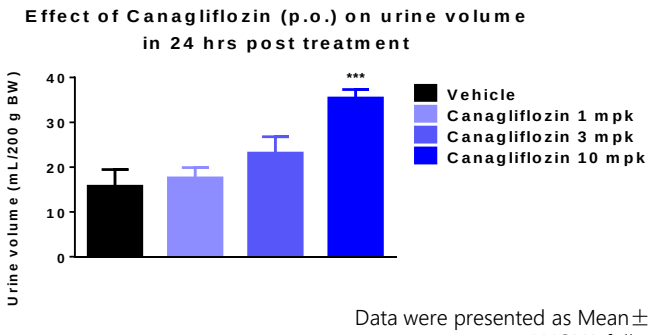


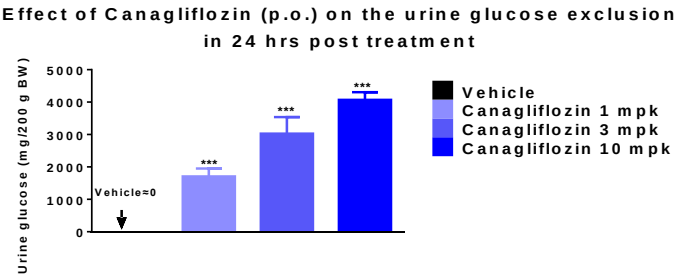


Data were presented as Mean ± SEM, n=5 per group, ***p<0.001 *vs.* vehicle, one way ANOVA followed by Dunnett's test

Urine Glucose Assay

Introduction:
An assay to measure urine glucose
Species: Rat and NHP
Endpoint: Urine volume; Urine glucose; Blood glucose
Groups in a standard assay: Naïve(Vehicle), Positive control, Testing compounds with 3 doses; n=4~6 animals/group
Turnaround time : 2 days/each study



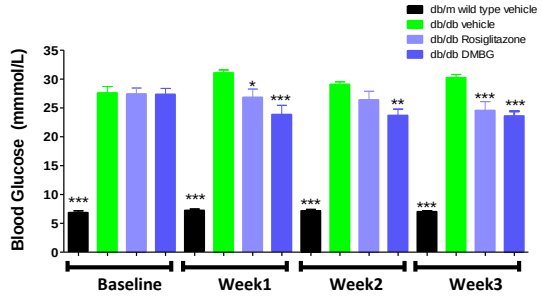


Data were presented as Mean±SEM, n=5 per group, *** p<0.001 vs vehicle group, one way ANOVA followed by Dunnett multiple comparison test.

db/db mouse model

Introduction:
A commonly used model to assess the anti-diabetic effect in db/db mice
Species: Mouse
Model: C 57 BL/KsJ.db male mice
Endpoint:
Body weight, food intake, water intake, blood glucose, GTT, insulin, GLP-1, GTT, HBA1C/fructosamine, pancreases histology stain
Throughput: 10~12 animals/group; 5~8 groups
Groups in a standard assay: Vehicle, Positive control, Testing compounds with 3 doses
Turnaround time : ~6 weeks/each study

Effect of Rosiglitazone and DMBG (p.o) on Blood Glucose (mmol/L) in db/db mice



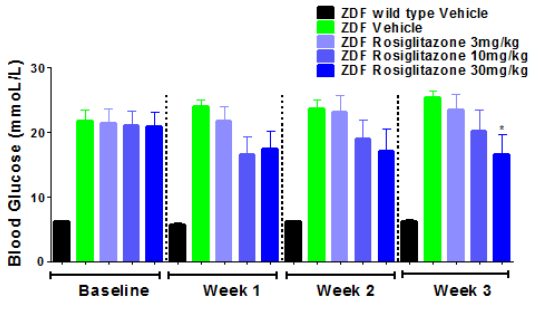
Data were presented as Mean ± SEM, n=12 per group, *p<0.05,**P<0.01, ***p<0.001 *vs.* vehicle, one way ANOVA followed by Dunnett's test

7-8 weeks old db/db mice were treated with Cpds for three weeks.

ZDF rat model

Introduction:
A commonly used model to assess the anti-diabetic effect in ZDF rat
Species: Rat
Model: Zuker fa/fa male rats
Endpoint:
Body weight, food intake, water intake, blood glucose, insulin, GLP-1, GTT, HBA1C/fructosamine, pancreases histology stain
Throughput: 8 animals/group; 5~8 groups
Groups in a standard assay: Vehicle, Positive control, Testing compounds with 3 doses
Turnaround time : ~6 weeks/each study

Effect of Rosiglitazone on Blood Glucose in ZDF rats



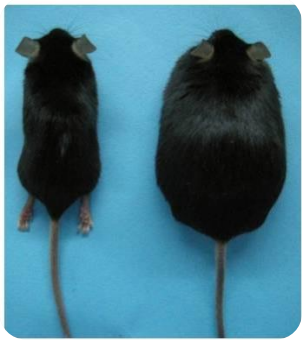
Data were presented as Mean ± SEM, n=8 per group, *p<0.05 *vs.* vehicle, one way ANOVA followed by Dunnett's test

7-10 weeks old ZDF rats were treated with Rosiglitazone for three weeks.

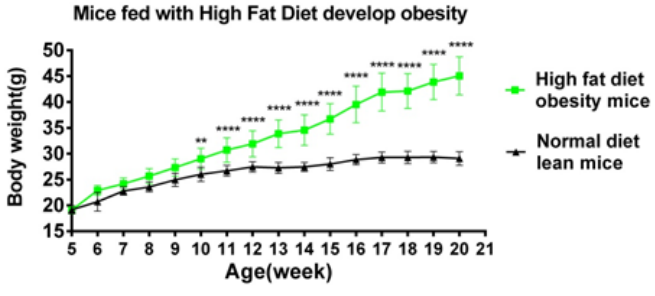
High Fat Diet Induced Obesity (DIO) model

Introduction:
- Mice fed with HFD (Research Diet D12492) for 12~14 weeks to assess anti-obesity agents
- 200 DIO mice /month ready to use

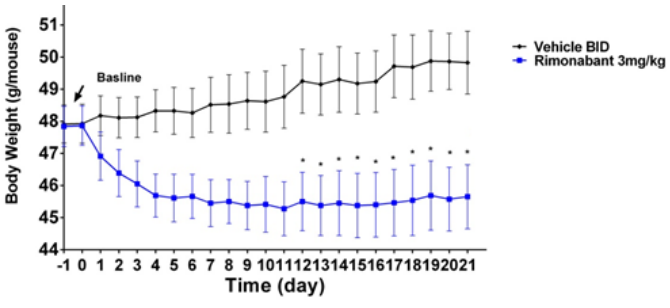
Species: Mouse and NHP
Endpoint:
Body weight, food intake, GTT, total Cholesterol (TC), Triglyceride (TG), ALT, AST, TG in, liver/muscle Insulin, GLP-1, HBA1C ,Leptin, HE/Oil red O stain, Fat pad, etc.
Throughput: 8 mice/group; 5~8 groups
Groups in a standard assay: Vehicle, Positive control, Testing compounds with 3 doses
Turnaround time : ~6 weeks/each study



Mice fed with High Fat Diet develop obesity



Anti-obesity effect of Rimonabant chronic treatment



Data were presented as Mean ± SEM, n=8 per group, *p<0.05, **p<0.01 *vs.* vehicle, one way ANOVA followed by Dunnett's test

High Fructose Diet model

Introduction:
A model induced by feeding with High Fructose Diet (HFD) to assess dyslipidemia

Species: Rat and NHP

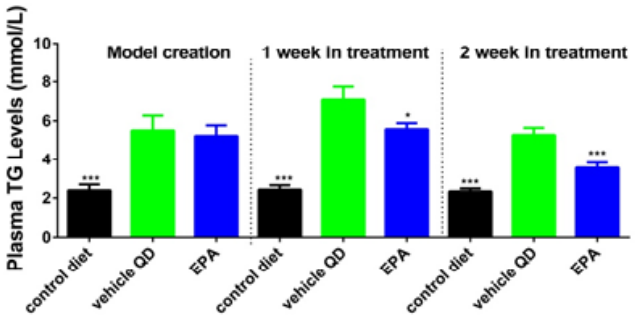
Endpoint: Body weight, food intake, Total cholesterol (TC), Triglyceride (TG), HDL-C, LDL-C, etc.

Throughput: 8 rats/group; 5~8 groups

Groups in a standard assay: Vehicle, Positive control, Testing compounds with 3 doses

Turnaround time : ~4 weeks/each study

Effect of EPA on Plasma TG levels



Data were presented as Mean ± SEM, n=8 per group, *p<0.05,**P<0.01, ***p<0.001 *vs.* vehicle, one way ANOVA followed by Dunnett's test

Contact

Henry Lu
Vice President, Biology
Henry_lu@wuxiapptec.com

Longji Xu
Director, Business Development
Xu_longji@wuxiapptec.com

Changqing Cao
Executive Director
Cao_changqing@wuxiapptec.com

Wei Liang
Director
Liang_wei_sb066@wuxiapptec.com