

# Metabolic & Cardiovascular Services

**ChemPartner**  
—Dedicated to LifeScience—

## Overview of Capabilities

- Extensive experience in drug discovery research for disease of diabetes, renal failure and cardiovascular disorders.
- >2000 compounds have been screened with the *in vitro* assays.
- >100 *in vivo* projects have been performed for a dozen of global pharmaceutical and biotechnology companies.
- Experience of pharmacodynamic evaluation provided for IND Filing packages.
- Capabilities continues to expand.

## Frequently Used Readouts

- IC50 or ED50 compound potency and selectivity.
- *In vitro* or *ex vivo* enzyme activity.
- Blood or urine biochemistry, clotting time (APTT, PT, FIB)
- Leptin, Insulin, HbA1c, Albuminuria, Cytokines
- Lipid profile (TC, TG, HDL, LDL), Liver Function (ALT AST ALP).
- Fasting Blood Glucose (FBG) and Body Weight (BW).
- Blood Pressure (BP), Electrocardiograph (ECG).
- 24 hours food intake, urine or feces collecting.
- OGTT or ITT, Euglycemic Clamp (GIR).
- Tissues collecting and pathological measurement.
- HE or PAS staining and score estimation.

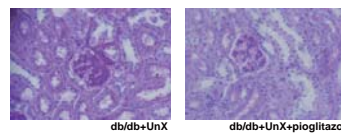
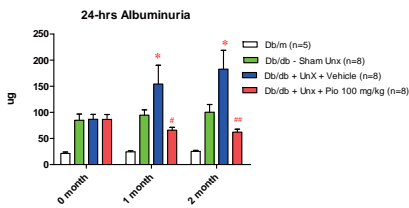
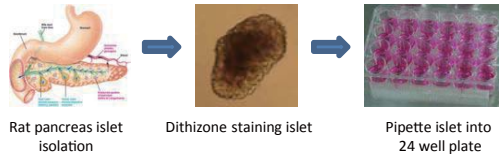
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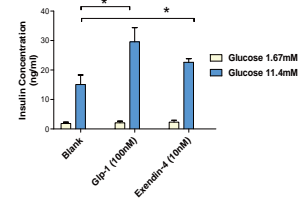
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# Ex vivo MOA studies

- Rodent, dog, monkey, human derived enzyme assay
- (DPPIV, Factor Xa)
- Rat hepatocyte isolate and insulin response assay
- Rat renal mesangial cell, podocyte, glomeruli isolation
- Insulin secretion test in primary pancreas islet (GISI)
- Glucose dependent insulin secretion in  $\beta$ -cells (GDIS)



Pioglitazone treatment alleviated the uninephrectomy accelerated glomerular sclerosis and Albuminuria increase



Compared to blank, GLP-1 and GLP-1 agonist Exendin-4 can significantly increase the insulin secretion in rat islet after glucose stimulation.

# Animal models

## Diabetes Mellitus

- HFD+STZ induced diabetes model
- NOD/ShiLtJ or BB rat type 1 diabetic model
- Db/db mice (BKS.Cg-Dock7m +/+ Leprdb/J)
- Ob/ob mice (B6.Cg-Lepob/J)
- Zucker Diabetic Fatty (ZDF) Rat



## Renal Disease

- kidney fibrosis (UUO) model
- Uninephrectomy (Unx) Diabetic
- Nephropathy (DN) Model
- Puromycin Aminonucleoside (PAN) induce nephrosis model
- Natriuresis/diuresis rat model
- Angiotensin II osmotic pump and Uninephrectomy induce acute renal injury

## Hypertension

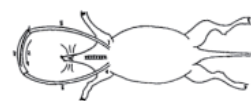
- Spontaneously Hypertensive Rat (SHR)
- Wistar-Kyoto (WKY) Rat
- Hypertensive Rat (SHR) With Telemetry
- High Salt Diet or ANG II Induced
- Hypertension

Pump 33 Dual Syringe Pump



Continuous infusion

AV-shunt



Extracorporeal circulation from carotid to jugular vein to form the thrombus.



STAGO Coagulometer

## Hyperlipidemia

- ApoE (-/-) Mice
- LDL (-/-) Mice

## Obesity

- High fat diet induce obese (DIO) rat
- High fat diet induce obese (DIO) mice

## Thrombosis

- Rat Arteriovenous (AV)-shunt model
- Rabbit Arteriovenous (AV)-shunt model
- FeCl<sub>2</sub> induce venous thrombus model
- Renal cortex bleeding time test

# In vitro screen for metabolic targets

- Multi-platforms assay for compound screening
- metabolic biomarker assay development and validation
- (Leptin, Adiponectin, Resistin)
- GLP1 total & active, Glucagon, Ghrelin, PYY
- C-peptide, GIP)
- Calcium flux assay (FLIPR, fluo4)
- cAMP assay (HTRF, LANCE, Luciferase)
- PPAR- $\alpha/\gamma$  and nuclear receptor assays
- Radioactive glucose transporter uptake assay
- 11-bHSD, DPPIV, and Factor Xa enzyme assays

