

# METABOLIC &

# CARDIOVASCULAR

## OVERVIEW OF CAPABILITIES

- Extensive experience in drug discovery focusing on Diabetes/Obesity, Renal, Liver and Cardiovascular diseases. Serving global pharmaceutical and biotechnology companies
- Special *in vitro* assays to support drug screen
- Complex disease animal models for studies in areas of diabetes/obesity, liver disease, kidney injury and heart disease.
- Experience with IND Filing
- Strong capability of assay and animal model development

## FREQUENTLY USE READOUTS

- Compound potency and selectivity, IC50, EC50
- Blood, or urine biochemistry, blood hematology
- Metabolic factors:
  - » Leptin, Insulin, HbA1c, Albuminuria, Cytokines
  - » Lipid profile (TC, TG, HDL, LDL), Liver Function (ALT AST ALP)
  - » Food intake, Blood Glucose, OGTT, IPGTT, ITT
- Blood Pressure (BP)
- Histopathological assessment (pancreas: islet, insulin; liver: tissue damage, inflammation, steatosis, fibrosis; aorta: *en face*; kidney: tissue damage, fibrosis; etc.)

# IN VITRO ASSAYS FOR METABOLIC TARGETS

- Metabolic biomarker assay development and validation
- GLP1, DPPIV, DPPVIII, PCSK9 (protein, LDL uptake)
- URTA1 inhibition
- SGLT1 & SGLT2 inhibition
- Mitochondria function assay: ROS, membrane potential



MicroBeta<sup>2</sup> Plate Counter



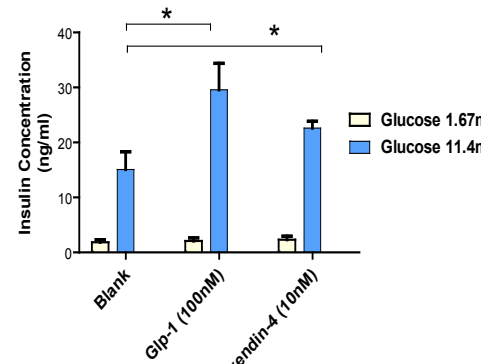
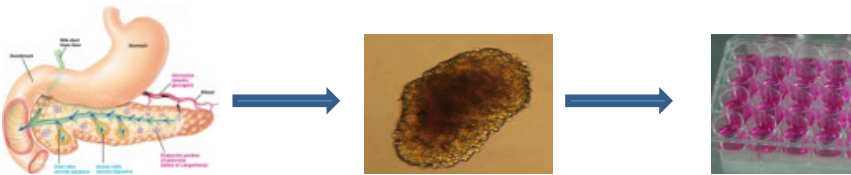
EnVision<sup>®</sup> Multilabel Plate Reader



MD Flexstation

## IN VITRO/EX VIVO MOA STUDIES

- Cell models of liver injury, e.g. APAP, ETOH
- Rat pancreas islet isolation and Glucose Stimulated Insulin Secretion assay (GSIS assay)
- Rat renal mesangial cell, glomeruli isolation and analysis



GLP-1 AND GLP-1 AGONIST EXENDIN-4 SIGNIFICANTLY INCREASE INSULIN SECRETION IN RAT ISLETS

## ANIMAL MODELS OF METABOLIC DISEASES

### Diabetes Mellitus/Obesity

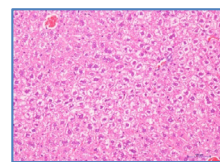
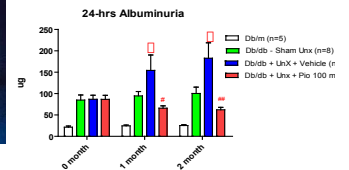
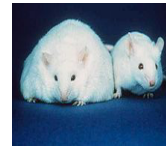
- HFD+STZ induced diabetes model
- Db/db, Ob/ob mice
- Zucker Diabetic Fatty (ZDF) Rat
- High fat diet induce obese (DIO) rat or mice

### Liver Disease

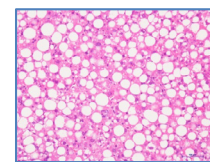
- Bile Duct Ligation (BDL) model
- Carbon tetrachloride (CCL4) induced liver fibrosis model
- NASH model (MCD, HF-LMCD, HF-LMCD-CCL4, High fat-high cholesterol-fructose model)
- Drug induced liver injury (APAP)
- Alcoholic Liver Disease (ALD)

### Renal Disease

- Unilateral ureteral obstruction Kidney (UUO) model
- Uninephrectomy (Unx)Diabetic Nephropathy (DN) Model
- Acute Kidney Injury-Ischemic Reperfusion Mouse Model (AKI: acute, sub-chronic)



NORMAL LIVER



FATTY LIVER

### Cardiovascular Disease

- Golden hamster hyperlipidemia model
- Spontaneously Hypertensive Rat (SHR)
- ApoE (-/-) Mice, LDL (-/-) Mice model