



Melior Discovery has pioneered an efficient and systematic approach to find new uses for existing drugs and drug candidates. By applying the unique multiplexed *theraTRACE*[®] indications discovery platform, Melior can quickly evaluate a compound in multiple, high quality *in vivo* models in order to test the molecule's potential use in a variety of therapeutic areas. In response to growing demands, we are now able to offer this same expertise applied to the design and execution of *in vivo* studies utilizing individual efficacy models.

theraTRACE[®] Platform

Uniquely powerful approach
to Indications Discovery

- not "hypothesis driven"
- highly predictive functional animal models
- "systematic serendipity"
- multiplexing know-how makes this possible

GLUCOSE TOLERANCE TEST

- » Validated with approved type II diabetic drugs
- » Animals dosed with compound, challenged with glucose and blood glucose levels monitored over time
- » Optional insulin, leptin and adiponectin levels can be monitored throughout study

INSULIN TOLERANCE TEST

- » Validated with approved type I and II diabetic therapies
- » Animals dosed with insulin, target peptides and/or compound followed by monitoring of blood glucose
- » Animals can be challenged with glucose solution
- » Serum insulin levels and other diabetic markers can be tracked

ZUCKER RAT AND DB/DB OR OB/OB MOUSE MODEL

- » Genetic model of type II diabetes and obesity (leptin receptor or protein mutation)
- » Blood glucose levels increase over weeks
- » Chronic dosing with approved type II diabetic agents produces sustained lowering of blood glucose
- » Mouse DEXA may be used to measure lean and fat mass
- » Telemetry system utilized to measure metabolic state
- » Analysis of type II diabetic markers can be performed throughout studies
- » Terminal total pancreatic insulin and IHC analysis of pancreas β -cells

STZ MOUSE AND RAT MODEL

- » Chemically induced model of type I diabetes provoking pancreatic β -islet cell depletion
- » Blood glucose levels increase
- » Dosing with approved type I and some type II diabetic agents lowers blood glucose
- » Analysis of type I diabetic markers

DIET-INDUCED OBESITY

- » Obesity monitored in animals fed a high fat diet
- » Multiple blood parameters assessed under acute and chronic dosing paradigms
- » Weight gain and food intake monitored chronically
- » DEXA may be used to measure lean and fat mass
- » Can be coupled with single or multiple OGTT's or ITT's as animals become increasingly glucose intolerant
- » Telemetry system may be utilized to measure metabolic state

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