



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

GASTROINTESTINAL INDICATIONS MODELS:

Gastrointestinal Transit Model: Colonic Propulsion Test

- » Validated with identified compounds used for the treatment of irritable bowel syndrome.
- » Glass bead inserted into the distal colon
- » Glass bead expulsion used as a measure of colonic spasticity and reflexivity.
- » May be used with morphine or other opioids to identify treatments for constipation.

Gastrointestinal Transit Models: Fecal Output and Charcoal Transit

- » Validated with opioid compounds that cause constipation
- » Fecal output: fecal number and weight observed over time
- » Charcoal Transit: amount of charcoal content in stomach and passage into intestine after oral gavage
- » Drugs that attenuate morphine-induced constipation have potential therapeutic utility for treatment of opioid-induced constipation

UROLOGY INDICATIONS MODELS:

Diuretic Induced Stress Test (Micturition)

- » Validated with antimuscarinics prescribed to mitigate urgency, frequency and urge incontinence
- » Furesomide injected prior to compound or vehicle dosing
- » Measurement of latency to first urinary event, frequency of urination events and volume of urine/event

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