

# Shaping drug discovery.



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At NoAb BioDiscoveries, we are unique in our ability to offer the highest quality drug discovery research services, as well as new and innovative technologies to facilitate our clients' drug discovery efforts. Our focus on ADME & PK solutions has allowed us to be an invaluable resource for clients who are screening and developing drug candidates. Our commitment is to ensure the best outsourcing experience for our sponsors, by providing the tools and the trust to help their drug discovery programs take shape.



[noabbiodiscoveries.com](http://noabbiodiscoveries.com)



## Expertise

### Reaching new peaks of excellence.

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Since 2001, our sponsors have relied on our team of skilled and experienced scientists to help solve their drug discovery challenges. The combination of extensive research and development expertise, along with our dedication to building long-term partnerships with our clients, allows us to consistently exceed our sponsors' expectations. Our continued success as a drug discovery partner is based on our ability to provide significant insights, in addition to high quality results.

## Confidence

### Building lasting relationships.

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At NoAb BioDiscoveries, we pride ourselves in our reputation for providing exceptional communication and quality of service. Our sponsors trust the quality of our science, and rely on our continued support to help propel their drug discovery programs. Our animal care and use program is certified by the CCAC in accordance with the standards of Good Animal Practice® in Science. All surgical procedures are performed in-house under strict guidelines by our highly skilled and experienced scientists, ensuring quality, flexibility, and timeliness. We invite you to consider NoAb BioDiscoveries for your next round of ADME/PK studies, and let us take your drug development programs to the next level of success.

## *In vivo* PK studies

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At NoAb BioDiscoveries, we skillfully design and perform standard and specialized PK studies according to clients' specifications. The studies typically involve the use of fully conscious animals that have been appropriately catheterized for drug administration and sample collection. NoAb BioDiscoveries' animal care and use program is certified by the CCAC in accordance with the standards of Good Animal Practice® in Science.

### Our *in vivo* studies include:

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- **Standard pharmacokinetic determinations in conscious rats, mice, and guinea pigs**  
Catheters are implanted in the carotid artery (for blood sampling) and jugular vein (for i.v. dosing and blood replacement).
- **Serial CSF and plasma collection in freely moving rats**  
This unique model allows a comparison of CSF and plasma concentrations and AUCs of the drug and enables the determination of drug penetration of the blood CSF and/or blood brain barriers.
- **Hepatoportal and jugular vein catheterized rats**  
To determine the relative contribution of the intestines and liver to elimination.
- **Carotid artery, jugular vein and bile duct catheterized rats**  
To measure biliary elimination of drugs and metabolites.
- **Carotid artery and jugular vein catheterized rats with intra-duodenal dosing**  
If drug instability in the stomach is suspected, drugs can be delivered via a catheter directly to the duodenum to by-pass the stomach.

## *In vitro* ADME assays

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NoAb BioDiscoveries offers high-quality, high efficiency ADME profiling with appropriate assays to help select and prioritize leads. The results of these assays coupled with preliminary toxicity evaluations assist in developing the hits from high-throughput screening (HTS) into leads and then optimizing those leads into promising drug candidates.

### Our *in vitro* ADME assays include:

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- **Cell permeability**  
Using the industry standard, Caco-2 cell model.
- **Plasma protein binding**  
Using a 96-well equilibrium dialysis method and higher throughput HSA and AGP assays.
- **Metabolic stability**  
Using plasma, hepatocytes or subcellular fractions for Phase I and II enzymes.
- **Enzyme inhibition**  
Using specific probe substrates (5 CYP subtypes) or fluorogenic substrates (9 CYP subtypes).
- **Enzyme induction**  
Gene expression based (DTEx™) and enzyme activity based (CYP 3A4, CYP 1A2, CYP 2B6).
- **P-gp substrate/inhibitor determination**  
Using the MDCK-MDR1 cell line.
- **Cytotoxicity**  
Using MTS, LDH and DNA endpoints.

## Bioanalytical services

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NoAb BioDiscoveries provides a thorough range of internal bioanalytical support services for *in vitro* ADME and *in vivo* PK studies. Our bioanalytical group has developed and validated many proprietary methods in support of preclinical research programs. Our research scientists have the experience and knowledge to resolve various challenges, delivering clients high quality analytical data in a timely manner.

### Our bioanalytical services include:

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- **Rapid method development, qualification and sample analysis**  
For single compound and cassette/multiple analyte dosing studies.
- **Metabolite profiling studies**  
Including reactive metabolites.
- **Customer specific screening assays**  
Radiochemical, Fluorescent, ELISA, etc.
- **Instrumentation:**
  - LC-MS/MS: Sciex API 4000 Series & API 4000 QTrap Series
  - HPLC: Waters Alliance 2695 series, including UV, PDA and ECD platforms
  - LSC & Luminescence: PE MicroBeta TriLux
  - Fluorescence – PE Fusion-alpha

## DTE<sup>x</sup>™ gene expression analysis

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DTE<sup>x</sup>™ is NoAb BioDiscoveries' proprietary microarray-based technology that allows our team to simultaneously survey the gene expression levels of 145 ADME associated genes. Since all genes on the DTE<sup>x</sup>™ microarray are involved in drug metabolism, conjugation or transport, NoAb's expert scientists can interrogate the DTE<sup>x</sup>™ microarray for both reported and unreported drug effects on gene expression. All DTE<sup>x</sup>™ genes have been selected as members of individual, drug-associated gene expression pathways. This serves as both an internal control for induction of DTE<sup>x</sup>™ gene expression and as a measure of drug selectivity in the modulation of DTE<sup>x</sup>™ gene expression.

### DTE<sup>x</sup>™ services:

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- **DTE<sup>x</sup>™ – ABC\***  
Gene expression profiling of 48 human efflux drug transporters.
  - **DTE<sup>x</sup>™ – ADME\***  
Gene expression profiling of efflux and uptake transporters, Phase I and II metabolic enzymes and nuclear X receptor-transcription factors.
  - **DTE<sup>x</sup>™ – Custom\***  
Gene expression profiling of client-selected genes from NoAb's DTE<sup>x</sup>™ gene inventory.
- \* Validation of DTE<sup>x</sup>™ Microarray results by Real-Time PCR available upon request.

