INDIGO BIOSCIENCES

Nuclear Receptor & *In Vitro* Toxicology Solutions

LUBIO SCIENCE

Your distributor in Switzerland

LubioScience GmbH
Baumackerstrasse 24
8050 Zürich
+41 (0)41 417 02 80
info@lubio.ch
www.lubio.ch

Accelerating Scientific Decisions™

Discover how we accelerate scientific decision-making throughout the discovery process using innovative products and services and expert support.

INDIGO BIOSCIENCES

About INDIGO

INDIGO Biosciences, Inc. is a leading provider of nuclear receptor and *in vitro* toxicology solutions that accelerate scientific decision-making. We supplement the world's largest portfolio of nuclear receptor kits and services and *in vitro* toxicology solutions with greater results readability, reproducibility, and faster turnaround times. Our solutions, plus supportive team and reliable science and platforms aim to reduce the time, cost, and risk associated with the discovery process.

Our Mission

To accelerate scientific decision-making throughout the discovery process using innovative products and services and expert support.

Why Organizations Trust Us

- Largest Portfolio of Nuclear Receptor Assays
- Clear Reproducible NR & IVT Results
- Team Committed to Your Study's Success
- Fast Lab Results for Accelerated Decision-Making
- Reliable Science, Platforms, & People

Assay Kit Platform

Our nuclear receptor assay products are cell-based reporter assay systems. They feature engineered nuclear receptor-specific reporter cells prepared using our unique CryoMite™ process. Once thawed, reporter cells are ready for immediate use. Test compounds can be screened for agonist or antagonist activities against human nuclear receptors expressed within the cytoplasm and nuclear environments of healthy, dividing mammalian cells.

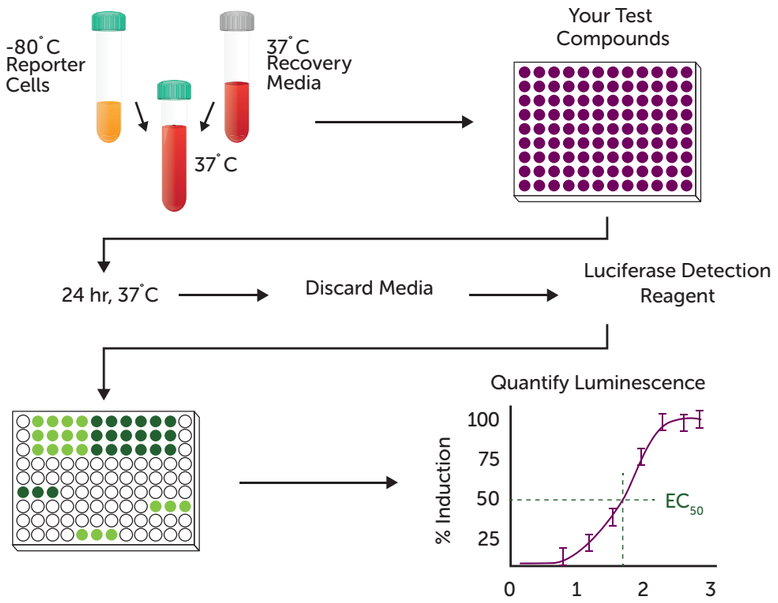
Our reporter systems utilize fire fly luciferase reporter gene technology to provide optimal assay sensitivity and dynamic range when quantifying nuclear receptor activity. Following ligand activation, the nuclear receptor complex acts to induce expression of the luciferase reporter. Upon addition of detection reagent, the intensity of light emission from the luciferase reaction directly correlates to the activation status of the nuclear receptor. All of our nuclear receptor reporter assay systems incorporate a detection reagent specially formulated to provide stable light emission over at least 1 hour, thus allowing users to dispense detection reagent into all assay wells prior to commencing activity measurements. This eliminates the need for a luminometer equipped with injectors, allows plates to be processed in batch, and dramatically reduces the start-to-finish read-time of assay plates.

Product Format

INDIGO Biosciences' nuclear receptor reporter assays are optimally configured for processing in 96- and 384-well format assay plates. Single plate kits (3x 32-, 1x 96-, and 1x 384-well) are offered as all inclusive assay systems. Each kit includes nuclear receptor reporter cells, an assay plate, all required reagents (optimized culture media, positive-control agonist, and detection reagent), as well as a detailed Technical Manual.

Bulk Reagent Packs are offered to accommodate the needs of HTS users. These products are custom scaled for 96- and 384-well plate assays, and provide nuclear receptor reporter cells, optimal culture media, positive-control ligand, luciferase detection reagent, and a detailed Technical Manual. Bulk Reagent Packs do NOT include assay plates because HTS facilities typically stock large quantities of such plates.

Note: *INDIGO's toxicology assays are available only in a 2x48-well format. With the exception of the kit for the Expression Profiling of Clinically Relevant CYPs, all products are provided as all-inclusive kits. Please visit the INDIGO site for more details.*



Kits & Services

Assays

Human Assays

Androgen Receptor AR (NR3C4)		
Constitutive Androstane Receptor 1 CAR-1 (NR1I3i1)	Constitutive Androstane Receptor 2 CAR-2 (NR1I3i2)	Constitutive Androstane Receptor 3 CAR-3 (NR1I3i3)
Estrogen Receptor Alpha ERα (NR3A1)	Estrogen Receptor Beta ERβ (NR3A2)	
Estrogen-Related Receptor Alpha ERRα (NR3B1)	Estrogen-Related Receptor Gamma ERRɣ (NR3B3)	
Farnesoid X Receptor FXR (NR1H4)		
Glucocorticoid Receptor GR (NR3C1)		
Liver Receptor Homolog-1 LRH-1 (NR5A2)		
Liver X Receptor Alpha LXRα (NR1H3)	Liver X Receptor Beta LXRβ (NR1H2)	
Mineralocorticoid Receptor MR (NR3C2)		
Peroxisome Proliferator- Activated Receptor Alpha PPARα (NR1C1)	Peroxisome Proliferator- Activated Receptor Beta/ Delta PPARβ/δ (NR1C2)	Peroxisome Proliferator-Activated Receptor Gamma PPARγ (NR1C3)
Pregnane X Receptor PXR (NR1I2)		
Progesterone Receptor PGR (NR3C3)		
Retinoic Acid Receptor Alpha RARα (NR1B1)	Retinoic Acid Receptor Beta RARβ (NR1B2)	Retinoic Acid Receptor Gamma RARγ (NR1B3)
RAR-related Orphan Receptor Alpha (RORα; NR1F1)	RAR-related Orphan Receptor Gamma (RORγ; NR1F3)	
Retinoid X Receptor Alpha (RXRα; NR2B1)	Retinoid X Receptor Beta (RXRβ; NR2B2)	Retinoid X Receptor Gamma (RXRγ; NR2B3)
Thyroid Hormone Receptor Alpha TRα (NR1A1)	Thyroid Hormone Receptor Beta TRβ (NR1A2)	
Vitamin D Receptor VDR (NR1I1)		

Ortholog Assays

Rat Androgen Receptor (rAR; nr3c4)	Zebrafish Androgen Receptor (zAR; nr3c4)		
Rat Aryl Hydrocarbon Receptor (rAhR)			
Mouse Constitutive Androstane Receptor (mCAR; nr1i1)	Rat Constitutive Androstane Receptor (rCAR; nr1i1)		
Zebrafish Estrogen Receptor Alpha (zERα; nr3a1)			
Mouse Farnesoid X Receptor (mFXR; nr1h4)	Rat Farnesoid X Receptor (rFXR; nr1h4)	Cyn Monkey Farnesoid X Receptor (cFXR; nr1h4)	Dog Farnesoid X Receptor (dFXR; nr1h4)
Mouse Glucocorticoid Receptor (mGR; nr3c1)	Rat Glucocorticoid Receptor (rGR; nr3c1)		
Mouse Liver X Receptor Alpha (mLXRα; nr1h3)			
Mouse Liver X Receptor Beta (mLXRβ; nr1h2	Rat Liver X Receptor Beta (rLXRβ; nr1h2)		
Mouse Peroxisome Proliferator-Activated Receptor Alpha (mPPARα; nr1c1)	Rat Peroxisome Proliferator-Activated Receptor Alpha (rPPARα; nr1c1)	Cyn Monkey Peroxisome Proliferator-Activated Receptor Alpha (cPPARα; nr1c1)	Dog Peroxisome Proliferator-Activated Receptor Alpha (dPPARα; nr1c1)
Mouse Peroxisome Proliferator-Activated Receptor Delta (mPPARδ; nr1c2)	Rat Peroxisome Proliferator-Activated Receptor Delta (rPPARδ; nr1c2)	Cyn Monkey Peroxisome Proliferator-Activated Receptor Delta (cPPARδ; nr1c2)	Dog Peroxisome Proliferator-Activated Receptor Delta (dPPARδ; nr1c2)
Rodent (Mouse/Rat) Peroxisome Proliferator-Activated Receptor Gamma (mrPPARγ; nr1c3)	Rat Peroxisome Proliferator-Activated Receptor Gamma (rPPARγ; nr1c3)	Cyn Monkey Peroxisome Proliferator-Activated Receptor Gamma (cPPARγ; nr1c3)	Zebrafish Peroxisome Proliferator-Activated Receptor Gamma (zPPARγ; nr1c3)
Mouse Pregnane X Receptor (mPXR; nr1i2)	Rat Pregnane X Receptor (rPXR; nr1i2)	Cyn Monkey Pregnane X Receptor (cPXR; nr1i2)	Dog Pregnane X Receptor (dPXR; nr1i2)
Mouse RAR-related Orphan Receptor Gamma (mRORγ; nr1f3)			
Zebrafish Thyroid Hormone Receptor Beta (zTRβ; nr1a2)			

Nuclear Receptor Panel Assay Kits

Estrogen Receptor PANEL (ERα; ERβ)
Liver X Receptor PANEL (LXRα; LXRβ)
Peroxisome Proliferator-Activated Receptor PANEL (PPARα; PPARβ/δ; PPARγ)
Retinoic Acid Receptor PANEL (RARα; RARβ; RARγ)
Retinoid X Receptor PANEL (RXRα; RXRβ; RXRγ)
Thyroid Hormone Receptor PANEL (TRα; TRβ)

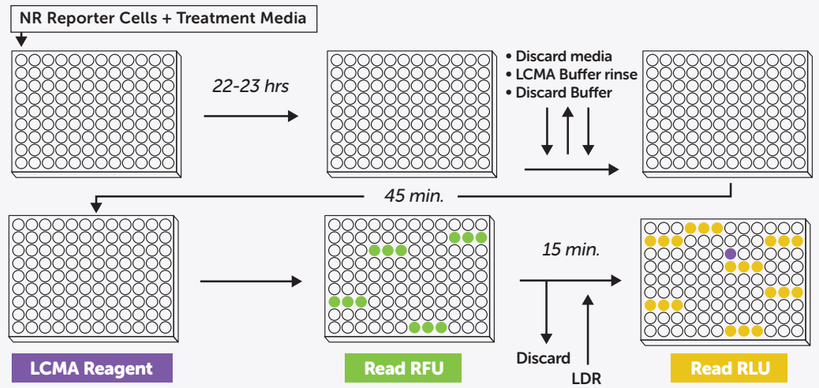
Other Signaling Pathway Assay Products

Aryl Hydrocarbon Receptor (AhR) & Rat Aryl Hydrocarbon Receptor (rAhR)
Nuclear Factor κB (NFκB)
Nuclear Factor (erythroid-derived 2)-like 2 (Nrf2)
Transforming Growth Factor Beta (types I/II) (TGFβ)

Live Cell Multiplex

The Live Cell Multiplex (LCM) Assay provides an efficient fluorecence-based method of quantifying the relative number of live cells resident in treated wells of an assay plate. While the LCM Assay may be performed as a stand-alone assay, it has been specifically optimized to be run in multiplex with any of our 96-well, 2x48-well, or 3x32-well Nuclear Receptor Reporter Assay System products.

The LCM Assay allows users to validate their primary Nuclear Receptor Assay data by determining if their test compound treatments exert mitogenic, cytostatic or cytotoxic activities on the reporter cells. The occurrence of such adverse non-specific effects will always undermine the accurate assessment of a test compound's potency and/or efficacy as a modulator of nuclear receptor function.



In Vitro Platform

Xenobiotic-induced liver injury is a major cause of human morbidity and mortality. A key reason for this problem is our inability to predict hepatotoxicity at the preclinical stage using currently available model systems. Such models include in vivo animal models and *in vitro* models based on human-derived liver cells or transformed cell systems. Species differences in xenobiotic disposition and mechanisms of cytotoxicity can make whole animal studies unreliable for extrapolation to human. In addition, whole animal models are costly and of low throughput. Therefore, it is essential to develop *in vitro* models that are more predictive of hepatotoxicity, particularly those that are based on human or "humanized" component cells.

There are two major limitations to the use of human liver cells or their derivatives. First, there are currently limited sources of fresh human hepatocytes worldwide and, when available, they often suffer from low viability and high batch-to-batch variability. Second, the freezing process used to preserve primary hepatocytes and the transformation process needed to make stable and proliferating cell lines results in changes in cell differentiation, proliferation, and metabolic processes.

Toxicology Assays

Assay Kit for *In Vitro* Screening for Drug-Induced Hepatotoxicity

The emergence of liver toxicity is a major reason for the termination of clinical drug trials, as well as post-market withdrawal of approved drugs. The assay kit for *in vitro* screening for drug-induced hepatotoxicity allows researchers to rapidly identify those compounds that induce liver toxicity. The kit utilizes upcyte® hepatocytes, prepared using our proprietary CryoMite™ process, which yields high viability post-thaw and provides the convenience of immediately dispensing cells into assay plates. This all-inclusive assay kit allows users to bring processes previously only offered as contract screening services into their own laboratories.

see Figure 1

Assay Kit for Expression Profiling of Clinically Relevant CYPs

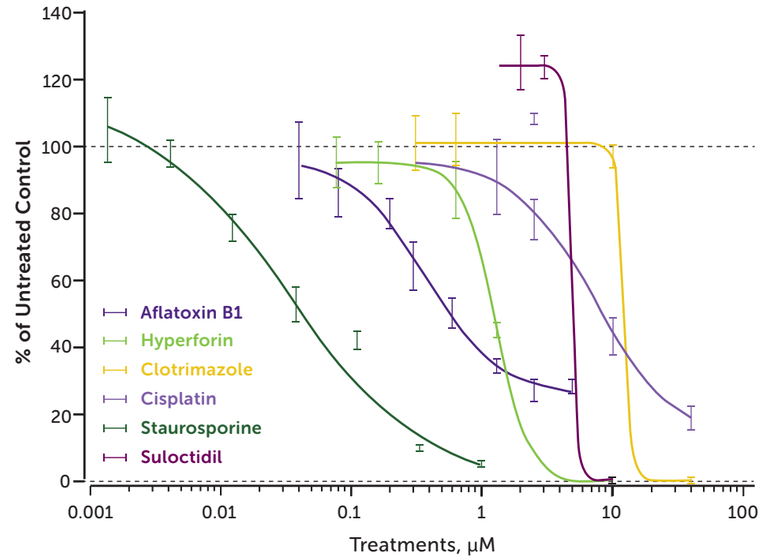
Assessing drug-induced changes in the expression of Cytochrome P450 (CYP) genes provides a reliable predictive indicator of altered metabolic activity in vivo. It is estimated that CYPs are involved in the metabolism of 70 to 80% of drugs currently on the market, making understanding their metabolic actions crucial to the drug development process. Our gene expression assay kit provides optimized reagents for the culturing and treatment of upcyte® hepatocytes to assess drug-induced changes in the expression of seven clinically relevant CYPs: CYP3A4, CYP1A1, CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP2E1.

Human P-Glycoprotein/MDR1 Drug Interaction Assay

Determining if a drug candidate will have incidental interactions with P-Glycoprotein (P-gp, aka MDR-1, or ABCB1) is an important component of the safety assessment process. A drug that is also either a substrate or an inhibitor of MDR-1 transporter activity can significantly alter the rate of absorption, distribution, metabolic conversion, and eventual excretion of co-administered drugs, thereby shifting their therapeutic effects and toxicologic profiles. Because of this, assessing a new drug's potency as an interactor with P-gp, and thus its potential liability for inducing downstream drug-drug interactions, is mandated by the FDA. Our all-inclusive assay kit for the assessment of MDR-1 drug interaction allows users to rapidly assess drug candidates as either inhibitors, substrates, or non-substrates of P-gp, and make critical decisions about potential drug candidates with confidence.

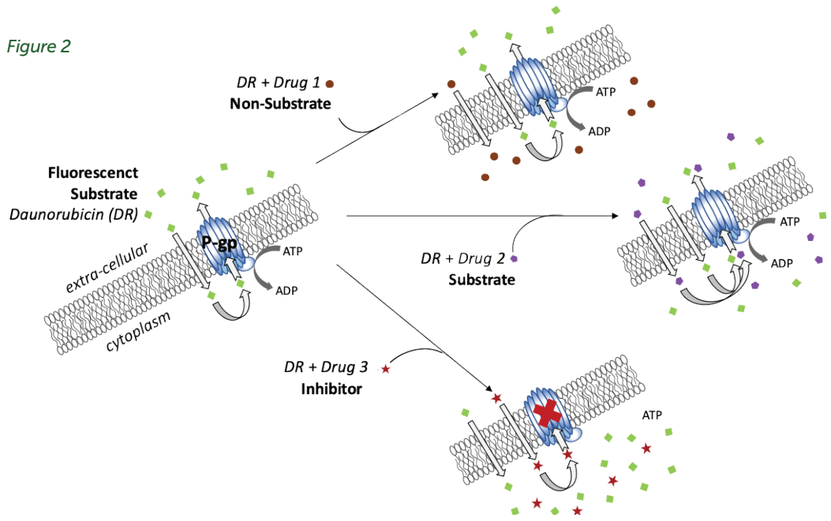
see Figure 2

Figure 1



	Aflatoxin B1	Hyperforin	Clotrimazole	Cisplatin	Staurosporine	Suloctidil
IC50, µM	0.3726	1.263	12.45	7.156	0.03337	4.84

Figure 2



Kits & Services

Research Screening Services

To empower confident decision-making throughout the discovery process, our technology generates clear single receptor or full-panel screening results, making for better interpretation and more accurate data. Employing a luminescence-based method and our proprietary CryoMite™ preservation process, we provide reproducible results lot to lot about the efficacy, potency, and selectivity of your compounds, plus comprehensive lab reports that include helpful graphics, summaries, and insights.

Nuclear Receptor Reporter Assays

We have the largest portfolio of cell-based nuclear receptor assays in the world, helping you identify compounds with the highest selectivity and the lowest potential for unwanted effects and off-target responses. Our broad portfolio of nuclear receptors makes us the preferred source for single receptor or full-panel screenings. Whether for nuclear receptor or in vitro toxicology solutions, our intellectual property, ease of use, and quick turnarounds will get you to the next phase of discovery, faster.

Nuclear Receptor Reporter Panels

Defining the system that each NR participates in can be approached in several ways, such as sequence similarity, potential disease implication, or transcriptional networks. The latter is particularly helpful since it encompasses NRs to which there are no known endogenous ligands (orphan receptors) or have few selective pharmacologic agents to evaluate biological consequences. By choosing a select group of receptors to study (a predesigned panel), it is possible to better understand the biological and toxicologic effects of your compounds. We have pre-designed several NR panels for you to choose. Of course, you can also customize your own panel of receptors or talk to our experts to assist in developing a plan of study.

In Vitro Hepatotoxicty Services

We also offer screening services for gene expression and in vitro hepatotoxicity testing. Please see the Resources section for additional information.

Custom Assay Development

Having difficulty developing an assay? Interested in an animal model but can't find the appropriate tools? We have vast experience cloning nuclear receptors from a variety of species and developing robust whole cell-based assays. We can develop the assay under a non-propriety agreement for your use in-house or for screening in our labs, including:

- **Custom Nuclear Receptor Assays**
- **Ortholog Nuclear Receptor Assays**
- **Selective Receptor Modulation Assays**
- **Nuclear Receptor Assays in a Specific Cell Line**
- **Nuclear Receptor Assay with a Specific Reporter**
- **Non-Nuclear Receptor Signaling Pathway Reporter**

Gene Expression

Knowing that your compounds regulate the activity of a specific nuclear receptor using our services is a great first step in characterizing and prioritizing potential new drugs. However, this is just a beginning to fully understanding the biologic (or toxicologic) effects that may ensue. Gene expression is a widely used approach for characterizing biological perturbations, defining the molecular mechanisms of diseases and making critical decisions about risks associated with compounds of interest.

Whether your laboratory provides its own samples or you allow our experts to implement the study in our labs, we have a gene expression solution for you. Our highly-trained specialists provide a comprehensive offering of genomic services including RNA extraction, qPCR services, microarray services, and microarray data analysis. We will help you identify the appropriate technology, experimental design, and program goals to ensure that your needs will be met.

qPCR

Quantitative real time PCR (qPCR) is the gold standard for gene expression analysis. Our team of experts in nuclear receptor biology and toxicology will provide the know-how in gene selection, primer design, and mRNA accumulation analysis. QPCR Solutions:

We offer predesigned panels of optimized primers for nuclear receptor target genes including PXR, CAR, and PPARs.

Experience in gene selection for disease and pathway-specific studies including inflammation-, cancer-, diabetes-, and drug metabolism-related gene expression.

We will provide data on mRNA levels relative to a housekeeping gene, statistical analysis, and interpretation in our study report.

Resources

Drug Induced Liver Injury

Drug Induced Liver Injury (DILI) liver toxicity is a major cause of drug failure in clinical trials as well as market withdrawal of approved drugs. In addition, due to species differences in drug metabolism, it is often difficult to extrapolate the results obtained from preclinical animal models to humans. The upcyte® cells are proliferating human hepatocytes that retain important drug metabolizing enzymes, such as cytochrome P450 3A4 (CYP3A4), which make them an attractive model system to examine drug-induced liver injury (DILI). Compounds with well-documented in vivo hepatotoxicity were screened after acute and repeated doses up to 1 week. The evaluation of complex mechanisms of cell toxicity demonstrated that upcyte hepatocytes offer suitable properties to be potentially used for toxicological assessments during drug development.

Endocrine Disruption

Endocrine disruptors (EDCs), environmental and man-made chemicals that interfere with the body's endocrine system, have the ability to impact drug and xenobiotic processing. This in turn can lead to adverse developmental, reproductive, immune, and neurological effects in humans and animals. Endocrine disruptors can be found in many everyday products such as plastic bottles, detergents, and pesticides, and much of the international concern is focused on such synthetic chemicals. Many EDCs work by acting on nuclear receptors, particularly sex steroid receptors (estrogen and androgen receptors) and the related transcription factors. The impact on human health through known and unknown effects of these chemicals makes understanding their nuclear receptor interactions a necessary focus of environmental and chemical testing.

upcyte® technologies

The platform utilizes upcyte® human liver cells to assess chemical and drug-induced toxicity. Unlike transformed hepatic cell lines, upcyte® hepatocytes have drug metabolism and transport activity comparable to primary hepatocytes. These cells are proliferating and able to correctly identify genotoxicants. The upcyte® hepatocytes combine the characteristics and advantages of primary hepatocytes with the added practical advantage of having access to the same donor cells for use in iterative, large-scale testing over extended periods – making them ideal for drug discovery.

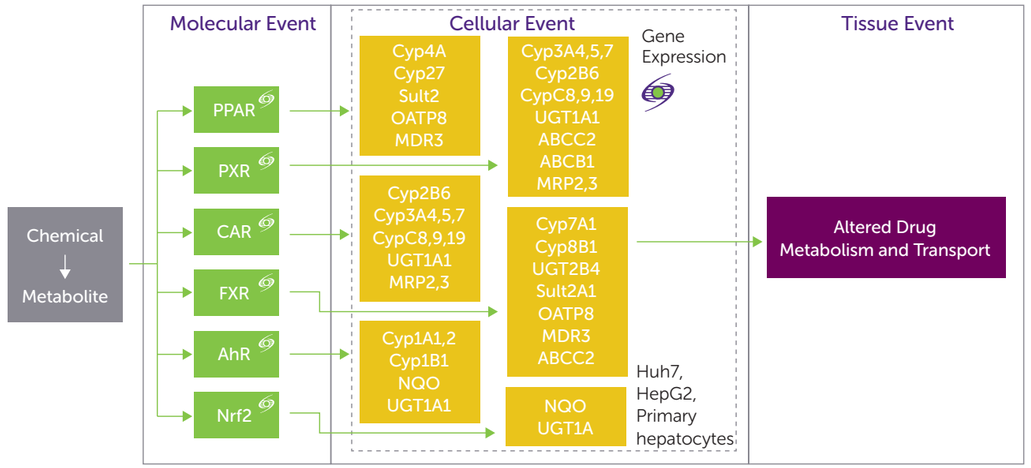
upcyte® technologies has developed a novel technique which allows for the generation of human hepatocyte cultures with the ability to proliferate while maintaining many differentiated functions. upcyte® hepatocytes are used by INDIGO Biosciences through commercial license agreement with upcyte technologies, GmbH (Hamburg, Germany).

1. upcyte® hepatocytes did not form colonies in soft agar and are not immortalized anchorage-independent cells.
2. Confluent cultures expressed liver-specific proteins, produced urea and stored glycogen.
3. CYP activities were low but similar to that in 5-day cultures of primary human hepatocytes. CYP1A2 and CYP3A4 were inducible; moreover, upcyte® hepatocytes predicted the in vivo induction potencies of known CYP3A4 inducers. Placing cells into 3D culture increased their basal CYP2B6 and CYP3A4 basal activities and induction responses.
4. Phase 2 activities (UGTs, SULTs and GSTs) were comparable to activities in freshly isolated hepatocytes.
5. upcyte® hepatocytes were markedly more sensitive to the hepatotoxin, α-amanitin, than HepG2 cells. The cytotoxicity of aflatoxin B1 was decreased in upcyte® hepatocytes by co-incubation with the CYP3A4 inhibitor, ketoconazole. upcyte® hepatocytes differentiated between ten hepatotoxic and eight non-hepatotoxic compounds.
6. In conclusion, upcyte® hepatocyte cultures have a differentiated phenotype and exhibit functional phase 1 and 2 activities. These data support the use of upcyte® hepatocytes for CYP induction and cytotoxicity screening.

In Vitro Hepatotoxicity Platform

Drug-Drug Interactions

Drugs that induce xenobiotic metabolizing enzymes (XMEs) responsible for their own metabolism or that of a coadministered drug are a major source of concern in drug discovery. Human upcyte® hepatocytes are proliferating hepatocytes that retain many characteristics of primary human hepatocytes and are an important model for studying drug-drug interactions (DDI). We conducted a comprehensive evaluation of altered gene expression in upcyte® cells treated with a selection of reference XME inducers. Cells were treated with prototypical agonists of Pregnane X Receptor (PXR, rifampicin), Constitutive Androstane Receptor (CAR, CITCO), Aryl Hydrocarbon Receptor (AhR, MeBio), Farnesoid X Receptor (FXR, GW4064), Liver X Receptor (T0901317), Peroxisome Proliferator-Activated Receptor Alpha (PPARA, GW590735), Nuclear factor (erythroid-derived 2)-like 2 (Nrf2, Sulforaphane) or Liver Receptor-Homology 1 (ML179). Next Generation Sequencing (NGS) was used to quantify the altered gene expression induced by these drugs with a focus on XMEs that can affect DDI Bulk availability of upcyte cells, cells from multiple donors and the characteristic induction of XMEs makes upcyte® hepatocytes suitable for DDI screening, as well as more in-depth mechanistic investigations.



Downstream NR Target Genes

Knowing that your compounds regulate the activity of a specific nuclear receptor using our kits or services is great first step in characterizing and prioritizing potential new drugs. However, this is just a beginning to fully understanding the biologic (or toxicologic) effects that may ensue. upcyte® cells retain nuclear receptor activity similar to those seen in primary human hepatocytes. We have validated primer sets for a variety of liver-specific NRs and can test your compound's ability to functionally affect gene expression. In addition, we can provide comprehensive analysis of gene expression via Next Generation Sequencing (NGS).

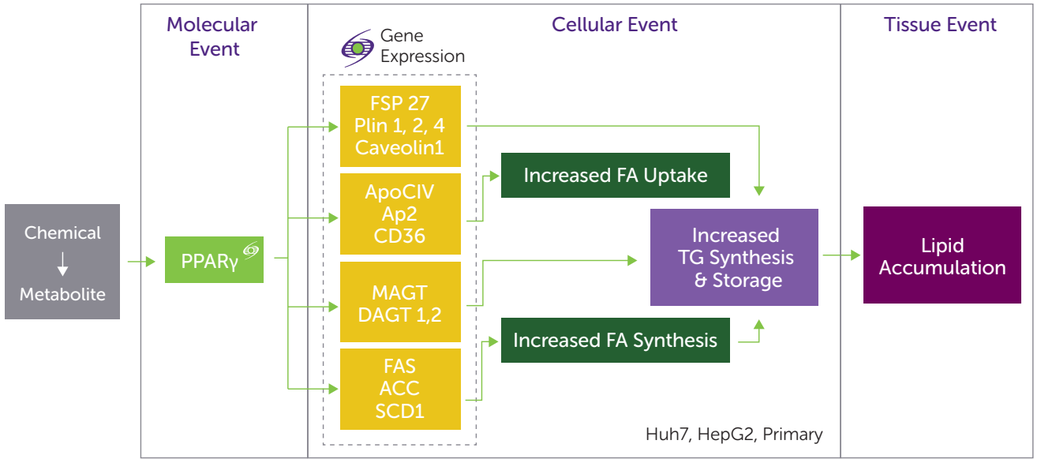
Resources

Hepatocyte CYP Inhibition

Cytochrome P450 (CYP) enzymes play a major role in the metabolism of the majority of xenobiotics. Cells that perform reliably in inhibition assays should have reproducible Phase I and II enzyme activities at levels that allow for a good dynamic range for inhibition. upcyte® hepatocytes have donor-dependent basal enzyme activities and represent a reliable tool for xenobiotic inhibition studies.

Non-Alcoholic Fatty Liver Disease

Non-Alcoholic Fatty Liver Disease is characterized by liver inflammation and the buildup of extra fat in liver cells not caused by excessive alcohol consumption. Nuclear receptors are important transcriptional regulators of lipid metabolism in the liver. The upcyte® human hepatocyte system has emerged as a good alternative to primary hepatocytes to examine liver diseases *in vitro*, including steatosis. The ability of a prototypical agonists of liver NRs to affect triglyceride accumulation in hepatocytes was examined. Prototypical activators of PXR (rifampicin), CAR (CITCO), AhR(MeBio), FXR (GW4064), LXR (T0901317), PPARA (GW590735), Nrf2 (Sulforaphane) or LRH-1 (ML179) were examined. In addition, the gene expression network affected in the steatotic liver and the subsequent effect of FXR activation on gene expression was examined. Together, this data supports the role of these nuclear receptors in affecting gene expression and lipid accumulation in human liver.

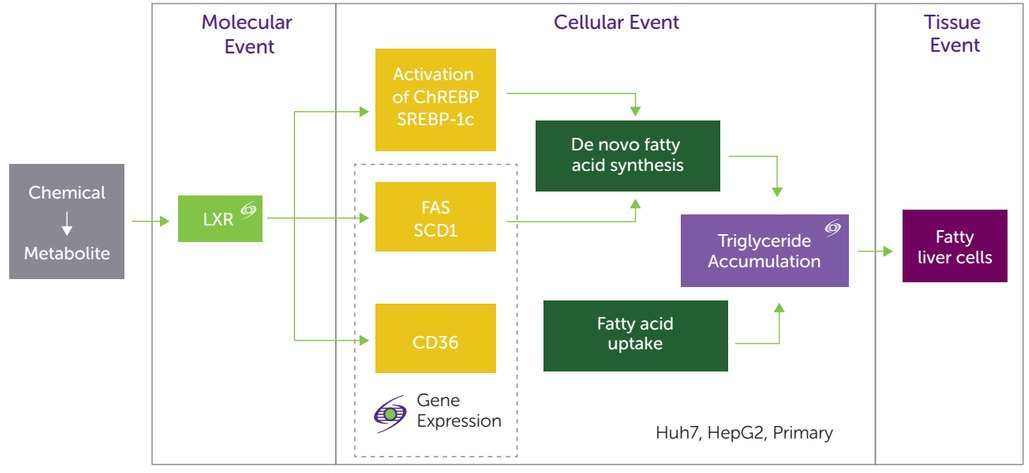


In Vitro Genotoxicity Assay

The use of the current *in vitro* micronuclei (MN) test leads to a substantial number of false positives. Recent data suggest that the species of a cell type is crucial in detecting MN formation. Cells that perform reliably in the *in vitro* MN assay should have Phase I and II enzymes comparable to primary human hepatocytes. As upcyte® hepatocytes fulfill the criteria of Phase I and II enzyme activity comparable to primary hepatocytes and are proliferating cells, they are appropriate for MN tests. These cells are able to correctly identify genotoxins.

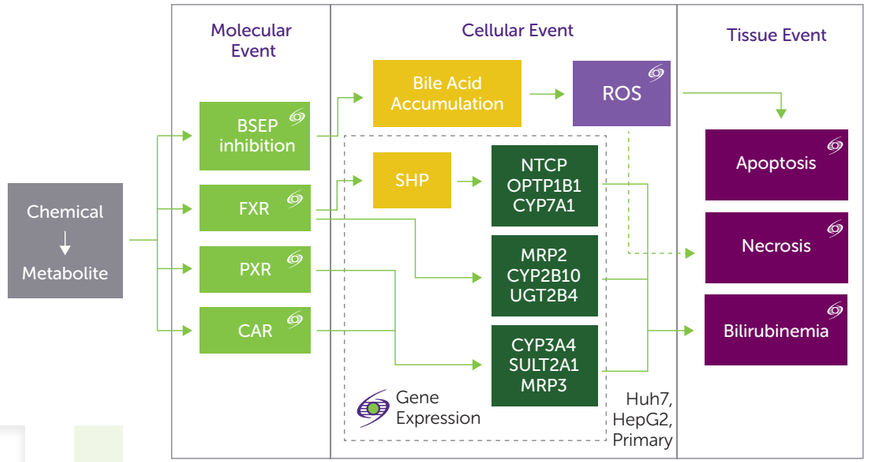
Steatosis

Fatty liver (steatosis) is an abnormal accumulation of certain fats (triglycerides) inside liver cells. In the United States and other Western countries, the most common causes of fatty liver are consumption of large amounts of alcohol, toxins, certain drugs, hereditary metabolic disorders, and metabolic abnormalities, such as excess body weight, insulin resistance (as can occur in diabetes), and high levels of triglycerides (a fat) in the blood.



Cholestasis

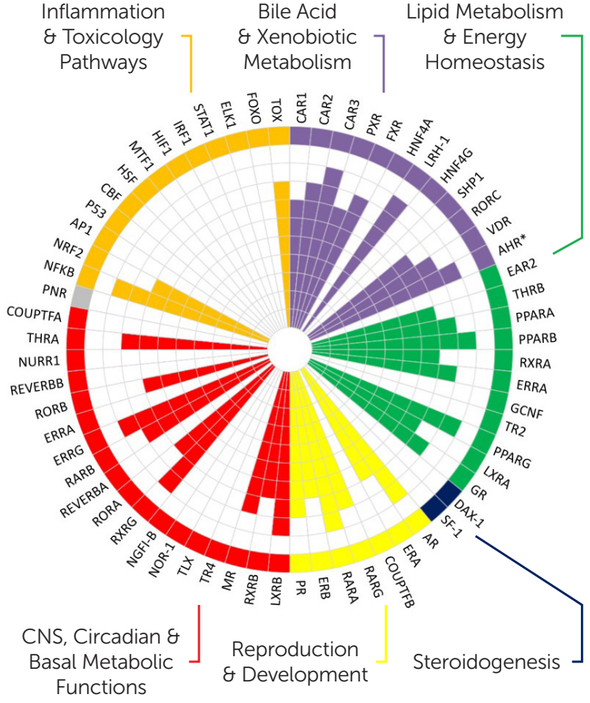
With cholestasis, the flow of bile (the digestive fluid produced by the liver) is impaired at some point between the liver cells (which produce bile) and the duodenum (the first segment of the small intestine). When bile flow is stopped, the pigment bilirubin (a waste product formed when old or damaged red blood cells are broken down) escapes into the bloodstream and accumulates. Normally, bilirubin binds with bile in the liver, moves through the bile ducts into the digestive tract, and is eliminated from the body in stool.



Resources

Nuclear Receptor Profiling

A major focus in the current discovery of drugs targeting nuclear receptors is identifying those with the highest selectivity and therefore lowest potential for off-target and unwanted effects. Due to regulation of metabolic enzymes by several NRs, there is increasing interest in understanding the potential of drug-drug and drug-nutrient interactions of potential drug leads. We provide a comprehensive list of optimized, robust, and selective whole-cell NR assays, ideally suited for examining selectivity as well as potential drug-drug interactions. By relying on our profiling service and our nuclear receptor experts, you can make those critical decisions on your compounds with the highest degree of confidence.



Detailed Reports

- All the raw data for each receptor and mode
- Summary tables and plots of your data for each receptor and mode including non-linear regression analysis, EC50, and peak activity
- Detailed statistical analysis and IBIPlot™ to visualize the chemical-by-chemical profile of activity across all receptors in your study (available upon request)
- All data is secure and confidential

Benefits of Profiling Services

- Ability to study the largest portfolio of optimized, cell-based nuclear receptor assays
- Unlike biochemical and direct binding interaction systems, our assays can be used to study agonists, antagonists, and inverse agonists
- Flexible options with the capability of studying our whole library of assays, choosing from predefined panels, or creating your own
- Rapid turnaround time with a detailed report evaluating your compounds' efficacy, potency, and selectivity

Nuclear Receptor Reporter Assays Predesigned Panels

Defining the system that each nuclear receptor participates in can be approached in several ways, such as sequence similarity, potential disease implication, or transcriptional networks. The latter is particularly helpful since it encompasses NRs to which there are no known endogenous ligands (orphan receptors) or have few selective pharmacologic agents to evaluate biological consequences. By choosing a select group of receptors to study (a predesigned panel), it is possible to better understand the biological and toxicologic effects of your compounds. We have pre-designed several NR panels for you to choose. Of course, you can also customize your own panel of receptors or talk to our experts to assist in developing a plan of study.

Pathway Panels

Endocrinology & Steroid Receptor: ERα (NR3A1); ERβ (NR3A2); MR (NR3C2); AR (NR3C4); PGR (NR3C3); ERRγ (NR3B3)
Metabolic Disease: PPARα (NR1C1); PPARδ (NR1C2); PPARγ (NR1C3); GR (NR3C1); LXRα (NR1H3); LXRβ (NR1H2); FXR (NR1H4); VDR (NR1I1); TRα (NR1A1); LRH-1 (NR5A2)
Retinoid Panel: RXRα (NR2B1); RXRβ (NR2B2); RXRγ (NR2B3); RARα (NR1B1); RARβ (NR1B2); RARγ (NR1B3); RORα (NR1F1); RORγ (NR1F3)
Toxicology Panel: PPARα (NR1C1); FXR (NR1H4); CAR (NR1I3); TRα (NR1A1); AhR; Nf-kB; Nrf2

Functional Classification Panels

CNS, Circadian and Basal Metabolism: LXRB, MR, RARB, RORA, RORG, RXRB, TRA, TRB
Lipid Metabolism and Energy: ERRA, GR, LXRA, PPARA, PPARD, PPARG, RXRA, TRB
Reproduction and Development: AR, ERA, ERB, ERRG, PGR, RARA, RARG, RXRA, RXRG
Xenobiotic and Bile Acid Metabolism: AhR, CAR1, CAR2, CAR3, FXR, LRH-1, PXR, RORG, VDR

Potential Indication Panels

Xenobiotic Metabolism: AhR, CAR1, CAR2, CAR3, PXR, NF-kB
Diabetes: GR, LXRA, LXRB, PPARG, RXRA, RXRB, RXRG, TGFβ
Osteoporosis: AR, ERA, ERB, ERRA, ERRG, PGR, VDR
Dyslipidemia: FXR, LRH-1, LXRA, LXRB, PPARA, RORA, TRA, TRB, VDR
Obesity: ERB, GR, PPARD, PPARG, TRA, TRB, TGFβ
Atherosclerosis: AhR, LXRA, LXRB, PPARA, RORA
Cancer: AhR, AR, ERA, ERB, ERRG, LRH-1, Nrf2, PPARD, PPARG, RARA, RARB, RARG, RXRA, RXRB, RXRG, VDR, TGFβ
Inflammation: AhR, GR, Nrf2, PPARA, PPARD, PPARG, RORA, RORG, TGFβ
NASH: FXR, LXRA, LXRB, PPARA, PPARD, PPARG, CAR, PXR

Resources

Discovery Toxicology

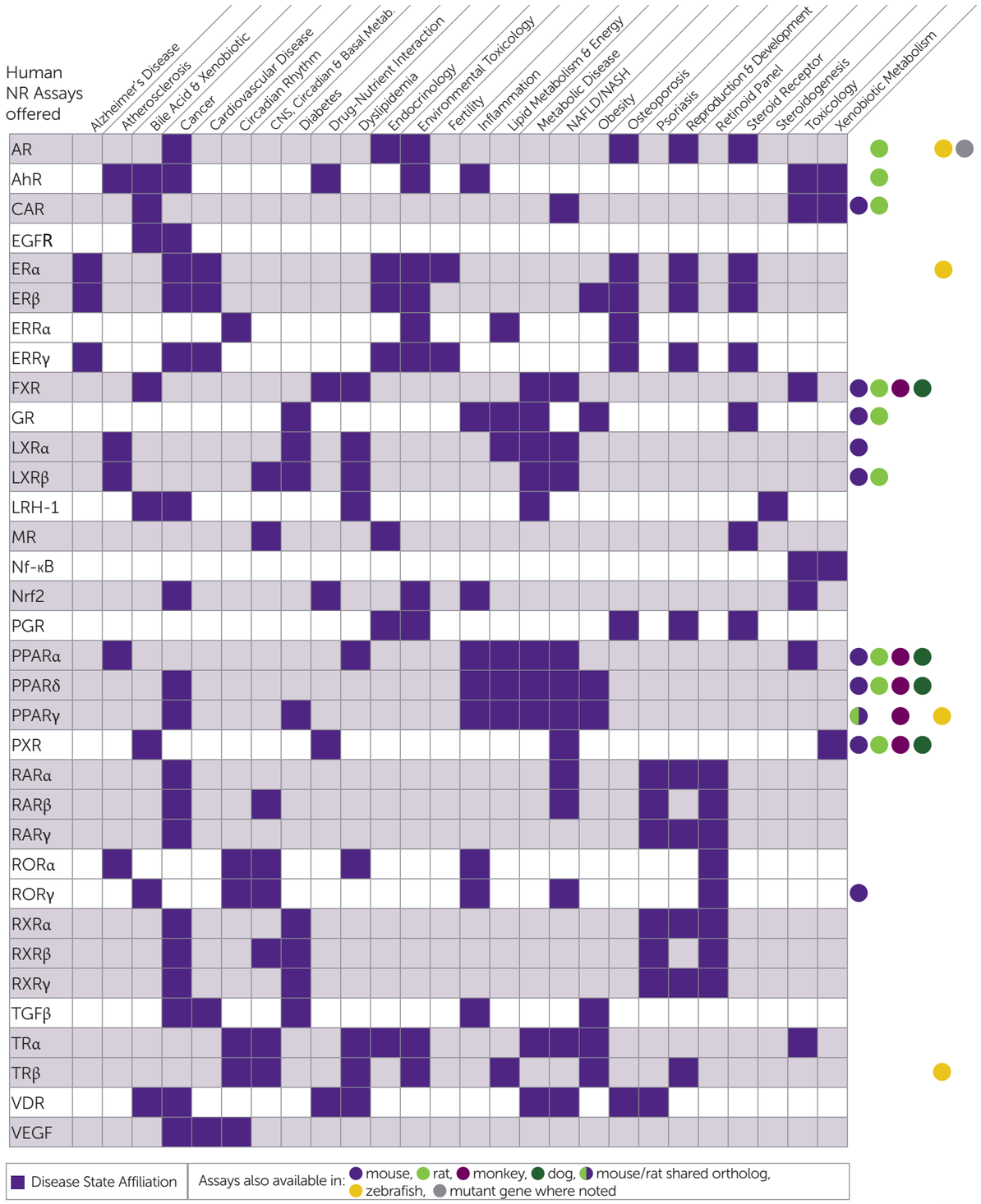
As toxicity continues to be a primary cause for compound attrition and long development cycle times, companies have increasingly integrated safety assessment principles into earlier phases of the drug discovery process, and a new discipline has emerged called "Discovery Toxicology."

INDIGO's approach to Discovery Toxicology is to provide research services to assist in prioritizing drug leads, found either through our Drug Discovery services or products, or through your own efforts. We provide a series of in vitro assays in the broad categories of Prospective Screens, Safety Pharmacology, and Retrospective Screens.

Human Nuclear Receptor Assay Screening Services

Drug Discovery	Prospective Screens	Safety Pharmacology	Retrospective Screens
Utilizing high-throughput screening (HTS) assays to identify compounds that regulate the drug target of interest	Informative in vitro screens that can predict a toxicological event. The earlier in the discovery process this occurs, the better.	Examination of efficacy and selectivity of drug leads as well as potential for regulating networks of targets associated with disease.	In the iterative process of drug discovery, it is often necessary to understand and interpret adverse events found in animal models and to integrate into lead optimization.
INDIGO Solution			
HTS screening services for human nuclear receptors	• Drug-Drug Interaction Screens • Toxicology Pathway Screens • Phenotypic Screening	• Comprehensive Nuclear Receptor portfolio • Disease and pathway specific panels of NR and non-NR assays	Non-human ortholog assays for most NRs

Nuclear Receptor Potential Indicators



Your distributor in Switzerland

LubioScience GmbH
Baumackerstrasse 24
8050 Zürich

+41 (0)41 417 02 80

info@lubio.ch
www.lubio.ch

INDIGO BIOSCIENCES
3006 Research Drive, Suite A1
State College, PA 16801 USA

+1 (814) 234-1919

+1 (814) 272-0152

indigobiosciences.com

For general product inquiries and product purchases,
please contact a Customer Service Representative:

+1 (814) 234-1919

customerserv@indigobiosciences.com

For technical inquiries relating to products,
please contact a Technical Service Representative:

+1 (814) 234-1919

techserv@indigobiosciences.com

For screening services,
please contact a Customer Service Representative:

+1 (814) 234-1919

customerserv@indigobiosciences.com