

# **PRODUCTS & CUSTOM DEVELOPMENT CAPABILITIES** Delivering Solutions from Discovery to Market

Trusted Products to eXpedite Your Discovery & Development - Advance Confidently





DiscoverX

### ACCELERATE YOUR DRUG DISCOVERY & DEVELOPMENT PROGRAMS WITH CONFIDENCE



#### Assays, Cells, & Reagents: Ready-to-assay & Optimized Products for Small & Large Molecules Discovery to QC Lot Release

Eurofins DiscoverX<sup>®</sup> is the trusted drug discovery and development product solutions provider. As the products division of Eurofins Discovery, and integral in the Eurofins BioPharma global network, DiscoverX has earned this reputation over the past two decades by contributing to the discovery and development of life-saving therapeutics with trusted and validated cell-based assay products for screening and validation of billions of data points for countless therapeutic programs.

Our scientists built the Eurofins DiscoverX product portfolio featuring fitfor-purpose solutions, from ready-to-use homogeneous assay kits, stable engineered cell lines, membrane preps, recombinant proteins/enzymes, and qualified reagents to support your therapeutic drug programs, no matter what stage you have reached, to accelerate your programs with confidence.

The Eurofins DiscoverX portfolio of high-quality products and custom assays enables you to expedite your research and move your candidate through the drug discovery pipeline faster – erasing months to years off your timeline.

#### **Capabilities Highlights**

- Enabling Technologies & Robust Assays Improve productivity & effectiveness of your target validation, screening, lead optimization, & structure-activity relationships campaigns
- **Comprehensive Portfolio** Offering the largest portfolio of cell-based functional & binding assays, cell lines, & proteins/enzymes covering the top therapeutic target classes, including GPCRs, kinases, checkpoint inhibitors, cytokine receptors, ion channels, & more
- Support Every Step of the Way –End-to-end support for your programs from discovery, through development, to commercial release & stability QC lot release testing



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#### Supporting Your Journey with Cell-based Assays & Capabilities for Characterization, Screening, Profiling, Potency, & Lot Release Programs

Developing small molecule and biologic therapeutics presents unique challenges at each development phase. This development requires the knowledge, experience, and a broad range of assays and reagents to understand the therapeutics' structure, activity, and mechanism of action (MOA). Eurofins DiscoverX<sup>®</sup> provides the most comprehensive portfolio of stable cell lines, validated functional and binding assay kits, recombinant proteins, and optimized reagents with these qualities developed and manufactured to support your drug discovery and development journey every step of the way. Several customized solutions can be delivered for program-specific needs by utilizing our deep expertise in cell line engineering, assay design, method qualification, and cell and protein production.

At Eurofins DiscoverX, we are committed to enabling and accelerating your multi-modality drug discovery and development programs from Discovery, through Development, and into Commercial Release and Stability. Discover for yourself how Eurofins DiscoverX enables you to accelerate your therapeutics development. Progress forward, confidently.



### ENZYME FRAGMENT COMPLEMENTATION ASSAY TECHNOLOGY

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#### Flexible Assay Technology for Studying Diverse Applications

Eurofins DiscoverX<sup>®</sup> utilizes the patented enzyme fragment complementation (EFC) technology for most of our cell lines and assays. This patented technology provides drug discovery and development researchers the means to interrogate biomolecular reactions for advancing therapeutic drug screening and development programs. EFC is a homogeneous detection assay system that enables you to measure and rank ligand potencies, discover the MOA, perform binding and functional screens, identify novel compounds, and much more.

EFC has been used as a robust and reliable assay technology for decades in >1M programs including >250 stability and commercial release programs. Eurofins DiscoverX has developed numerous assay formats to interrogate the desired MOA of therapeutics such as PathHunter®, HitHunter®, KILR®, InCELL, and SPRINTer™. These assay formats are used from discovery through development into commercial lot release testing and stability studies of many small molecule and biological therapeutics on the market today and within clinical trials.

#### **Directly Measure Relevant Target Biology**

- Homogeneous Format Add-&-read assay format without the need for washing, centrifugation, or filtration
- Robust Enzymatically-amplified assays with large signal-to-background ratios & high precision with Z' factors > 0.7 & lot-to-lot reproducibility
- Qualified & Validated Extensively optimized for hundreds of targets used for screening billions of data points, & cited in thousands of peer-reviewed publications
- Scalable Easily scalable & HTS-friendly from 96- to 3456-well microplate format

#### **Highlights of EFC-Based Assays**

Homogeneous	Sensitive Detection	Robust	Luminescence Readout
<ul> <li>Simple add-&amp; read assay format</li> </ul>	<ul> <li>Enzymatically amplified assay</li> </ul>	Large dynamic range	<ul> <li>Easily quantified luminescence readout</li> </ul>
<ul> <li>No media change, shaking, or filtration</li> </ul>	<ul> <li>High precision</li> <li>&amp; accuracy</li> </ul>	High-assay reproducibility	<ul> <li>Compatible with most readers</li> </ul>

#### **Functional Assays for Popular Target Classes**



#### **EFC Technology Principle**



EFC is based on two recombinant  $\beta$ -galactosidase ( $\beta$ -gal) enzyme fragments that act as an enzyme acceptor (EA) & an enzyme donor (ED). Separately, the fragments are inactive, but when combined, they form an active  $\beta$ -gal enzyme that hydrolyzes its substrate to produce a chemiluminescence signal.

### **ENZYME FRAGMENT COMPLEMENTATION ASSAY TECHNOLOGY** (CONTINUED)

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#### Assay Formats for Your Modality & Stage of Development

EFC 2

PathHunter® Cell-based Assays

FEC

ED

**Protein/Protein Interactions** 

Detect interacting proteins (e.g. GPCRs/

Internalization & Trafficking

Measure receptor internalization or track

**KILR® Cell-Based Assays** 

**Quantify Cytotoxicity** 

proteins to different cellular locations

(e.g. nucleus, membrane, endosome)

arrestin, NHRs/co-factors, RTKs/SH2)

#### **Quantification & Degradation**



Measure levels of intracellular proteins including degraded proteins

Secretion & Translocation



Study secretion out of the cell or translocation across a membrane to another cellular compartment (e.g. cytoplasm to nucleus)

#### SPRINTer<sup>™</sup> Cell-based Assay

#### **Targeted Protein Degradation**



Detect protein turnover induced by targeted degrader molecules such as PROTACs

#### InCELL Hunter<sup>™</sup> Cell-based Assays

**Compound Target Engagement** (Protein turnover based) Binding ED EFC No Compou Binding Protein Degradation 1

Detect binding to intracellular protein targets through a protein turnover stabilizationbased assay

Learn more at:  $\rightarrow$  discoverx.com/efc







Directly measure antibody- or complement





Detect binding to intracellular protein targets through a protein thermal stability cell-based assay

**Receptor Dimerization** 



Quantify ligand-induced receptor dimerization (e.g. RTKs, ILs)

#### **Downstream Response Evaluation**



Evaluate receptor downstream responses of your drug molecule's MOA targeting TNFa, PD-1, IL-6, CD40, RANK & other receptors.

#### HitHunter<sup>®</sup> Biochemical Assays



Quantify specific cellular analytes (e.g. cAMP, cGMP)



### **ASSAY READY KITS**

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#### Cell-based Assay Kits from Early Discovery to Pre-clinical & Clinical Development to Commercial Release & Stability Programs

Eurofins DiscoverX<sup>®</sup> delivers >1,200 optimized assay kits provided as ready-to-use (RTU) assays with frozen-ready cells, thus eliminating the need for continuous cell culture to perform cellbased functional or binding assays conveniently and confidently. These assay kits are provided in various phase-appropriate formats, from basic research and drug discovery through clinical development, and into commercial release and stability programs.

The extensive menu of target-based assays covers a broad range of target classes including GPCRs (G protein-coupled receptors), kinase, checkpoint, and cytokine receptors; intercellular signaling targets; nuclear and epigenetic proteins; and other targets. Assayready kits contain all the necessary reagents to perform functional or binding whole-cell assays in just a few hours, including frozen, RTU pre-validated cells, optimized detection reagents, and media, 96-well plates, and detailed protocols.

#### **Assay Ready Kit Formats**

#### eXpress<sup>™</sup> Assay Kits

- Fast Analysis Provide quick analysis and implementation utilizing frozen, RTU engineered cells with all required reagents and a detailed protocol
- Hit-to-lead & Lead Optimization Designed For

#### **Bioassay Kits**

- Phase Appropriate Use for characterization, MOA confirmation, detection of neutralizing antibodies, and potency testing in commercial release and stability applications for biologics drug development programs
- Long-term Use & Method Transfer For use in late discovery, throughout clinical development, and ongoing for commercial release and stability studies

#### **Product Highlights**

- **Complete Kits** >1,200 available kits with cryopreserved RTU cells & all the optimized reagents you need to get you started quickly
- Rapid & Reliable Results Analyze multiple targets or screen & profile small & large molecules in-house using simple step-by-step, homogeneous, no-wash protocols for reliable, fast results
- Scalable & Standard Instrumentation HTS compatible, scalable format for increased efficiency & compatible on any standard luminometer with a chemiluminescent read-out
- Phase-appropriate Formats Utilize quick analysis eXpress assay kits for early discovery studies, or qualified bioassays for QC lot release testing & stability studies

screening applications, proof-of-concept, MOA confirmation, and rank-ordering studies. Intended for drug discovery and basic research phases. Not recommended or supported for use in pre-clinical development phases, including characterization or potency testing in QC lot release programs.

- **Qualified or Target-Based** Available as both targetbased and innovator drug-qualified assays
- ICH-like Development Qualified-based bioassays are developed and optimized with the marketed therapeutic following International Council for Harmonization (ICH) guidelines to meet market requirements and regulatory expectations



Minimize assay development time and eliminate lengthy, expensive, and time-consuming cell culture with quick analysis eXpress assay kits or qualified, MOA-based bioassays that are ready-to-use and ensure robust and reliable performance every time.

### **BIOASSAY KITS**



#### Ready-to-use, Cell-based Assays for Biologics Therapeutic **Development. Including Characterization. MOA Confirmation.** NAbs Detection, Stability Studies, & Potency Testing

Bioassays are analytical methods used to measure a drug's biological activity or potency using a biological system representing the MOA of that drug. Eurofins DiscoverX® offers an extensive portfolio of cell-based, mechanistically relevant bioassays optimized and gualified using ICH (International Council for Harmonization) guidelines with marketed innovator biologic drugs or reference standards. These robust, quantitative, readyto-use cell-based assays use a simple, homogeneous protocol. They are easily implemented for characterization, potency measurement, neutralizing antibodies (NAb) detection, stability studies, and many other additional applications to interrogate biological functions and accelerate your biologics development program from discovery to post-market QC lot-release testing.

Bioassays are ideal for determining drug potency and stability using a simple, homogeneous protocol that reflects the drug's clinical MOA. These rapid cell-based assays bypass the need for expensive and time-consuming cell culturing or assay development, potentially reducing timelines and errors.

#### **Product Highlights**

- **Biologically Relevant** MOA-reflective, functional assays for monitoring & testing of biologic therapeutics
- Qualified Qualified with marketed biologic drugs or reference standards using ICH guidelines
- Robust & Reproducibility High intra- & inter-lot reproducibility with assay linearity for stability & potency testing in QC lot release applications
- Simple Protocol, Fast Results Homogeneous • protocol amenable to implementation in multiple labs & high-throughput format for increased efficiency

#### Advantages of Bioassay Kits

Benefits	Outcomes	Implementation	
<ul> <li>Accelerate potency testing &amp; QC lot release testing for commercialization &amp; stability studies</li> </ul>	Increase speed of programs 9 to 18 months	<ul> <li>Simple, homogeneous protocol that yields results in &lt; 24 hours</li> </ul>	
Eliminate assay development timelines	<ul> <li>Obtain biologically relevant data with assays reflective of the target biology</li> </ul>	<ul> <li>Seamless method transfer for faster implementation at CMOs, CDMOs, or CROs</li> </ul>	
Reduce validation times	Measure therapeutic potency	<ul> <li>Virtual &amp; in-person/in-lab support of development programs</li> </ul>	
<ul> <li>Provide accurate &amp; precise intra- &amp; inter-assay data with superior linearity &amp; reproducibility</li> </ul>	Interrogate appropriate MOA	<ul> <li>Provide accurate &amp; precise intra- &amp; inter-assay data with superior linearity &amp; reproducibility</li> </ul>	
<ul> <li>Method transfer support by a global team of trained scientific experts</li> </ul>	Attain high lot-to-lot reproducibility	<ul> <li>Amenable to miniaturization to run in high-throughput 384 well format</li> </ul>	

#### Well-structured Development **Process Delivers Robust & Reproducible Assays**



Optimize assay parameters (thaw-and-use cells only)

Assay Optimization

Refine conditions with originator drug or reference standard

**Testing Innovator Drug** 

Establish robustness, precision, accuracy and linearity of assay

**Assay Qualification** 

#### MOA-reflective Bioassays Deliver Highly Specific Responses





Bioassays measure highly target-specific response & enable interrogation of the therapeutic drug's MOA.

Α

400000

320000

240000

160000

80000

10<sup>-11</sup> 10<sup>-10</sup> 10<sup>-9</sup> 10<sup>-8</sup> 10<sup>-7</sup> 10<sup>-6</sup> 10<sup>-5</sup> 10<sup>-4</sup>

RLU

#### **Perform Potency & Stability Testing**





Measured

78.4

109.4

98.9

RP (%)

(%)

78.4

76.5

98.9

Expected

100

143

100

RP (%)

Relative Bias/

Inaccuracy (%)

-21.6

-23.5

-1.1

**Dilutional Linearity** 

Potency testing is an integral part for the assessment of a drug's specific ability to produce a given result. Bioassays are the primary tool used for measuring drug efficacy during potency testing, enabling researchers to determine how a particular drug dose will react in a given biological system.

Stability testing using Eurofins DiscoverX® bioassays. A. Heat-stressed samples of an anti-PD-1 antibody were tested to evaluate if the PathHunter® PD-1 Signaling Bioassay will differentiate the stressed material from the reference sample. B. To demonstrate stabilityindicating, further qualifications were performed with Nivolumab (Opdivo®). Results indicate that only the heat-treated sample showed significant reduction activity, while the freeze-thawed sample displayed no differences with respect to the untreated reference material.

#### Save Over 12 Months of Assay Development Time

Reference

- 65 °C: 5 min

Nivolumab

Heat Stressed-I

Heat Stressed-II

Freeze-Thawed

Samples

A quantitative and robust bioassay that reflects the drugs' MOA is critical to any development program. Eurofins DiscoverX offers bioassays that can be implemented to accelerate your biologics development program from discovery to post-market. For characterization and QC lot-release testing, where assay reproducibility is paramount, ready-to-use (RTU) bioassays help you save over 12 months of assay development time.



#### **Typical Bioassay Development Timeline**

[Anti-PD1 Antibody], g/mL

### CELL LINES, DETECTION KITS & REAGENTS



#### **Stable Engineered Cell Lines**

Engineered cell lines are essential for in vitro cell-based assays replicating biological systems' physiology. Cell lines are developed reflecting the target's MOA with a drug interaction in a standard cell line background. Cell lines can be propagated repeatedly and kept in culture for extended periods of time. These cells provide the ability to deliver more physiologically relevant results in a cost-effective manner reproducibly.

Eurofins DiscoverX<sup>®</sup> provides the most extensive collection of >1,000 fully qualified, functional cell lines that enable unique drug discovery and development solutions at every stage of your program. Cell lines offered cover all major drug target classes, including GPCRs, cytokines, kinases, checkpoint inhibitors, ion channels, and nuclear proteins such as transcription factors, NHRs, and epigenetic proteins.

With over two decades of experience in generating stable cell lines, Eurofins DiscoverX provides cell lines with unsurpassed quality and industry-validated

#### **Product Highlights**

- Robust Performance Rigorously & continuously validated for accurate pharmacology through Eurofins Discovery with billions of data points screened
- Versatile Use Interrogate diverse MOAs with broad applications ideal for small molecules & biologics screening or profiling
- Diverse Select relevant cell models from over 50 cell types such as HEK 293, CHO-K1, U2OS, & more
- Established Implemented in 200+ global programs for potency, stability, & NAb testing

performance. These cell lines have been used to screen billions of data points to help bring many therapeutics to the market, with many more in the pipeline.

Use the appropriate application-specific detection kits with your cell line model for a complete functional cell-based assay to interrogate the MOA of your small molecule or biologic, measure and rank ligands' potencies, perform binding and functional screens, implement as a lot-release assay, and much more.

#### **Optimized Detection Kits & Reagents**

Eurofins DiscoverX detection kits were developed in tandem with our vast offering of cell lines and their differing MOAs and targets for a sensitive, quantitative readout of your therapeutic molecule. Whether your therapeutic is a biologic, peptide, a small molecule, or a cell therapy, these detection kits provide accurate pharmacology and reproducible results. Choose from various detection kits and reagents with chemiluminescent and fluorescent readouts to suit the diverse needs of your drug discovery and development programs.

The homogeneous, one-step addition detection kit protocols are easy-to-run and scalable for 96 well formats through high-throughput screening (HTS) of 384, 1536, or 3456 assay formats. They include options for running in agonist, antagonist, inverse agonist, and allosteric modulator modes. When used in conjunction with Eurofins DiscoverX cell lines, the detection kits are fully optimized for identifying various assayable events, such as detecting cell-based protein-protein interactions, compound-protein binding, cell death, translocation, and more.

#### **Product Highlights**

- Superior Results Robust assays with sensitive detection & reproducible results
- Homogeneous Easy-to-run, no wash protocols with luminescent & fluorescence read-outs that can be read with any standard plate reader
- Flexible Applicable for studying proteinprotein interactions, receptor dimerization, protein translocation, receptor activation, protein trafficking, receptor internalization, small molecule accumulation, & more
- Scalable High-throughput screening capable & scalable from 96- to 3456- well formats

Eurofins DiscoverX has over two decades of experience developing and optimizing detection kits and reagents to support our engineered cell lines. Utilize Eurofins DiscoverX's optimized detection kits and reagents with PathHunter<sup>®</sup>, KILR<sup>®</sup>, cAMP Hunter<sup>™</sup>, and InCELL cell lines for highly sensitive and reproducible results you can rely on.

### **RECOMBINANT PROTEINS/ENZYMES** & MEMBRANE PREPARATIONS



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#### Offering Industry's Largest Portfolio of Purified Recombinant Kinases & Other Proteins for Screening Inhibitors

Eurofins DiscoverX<sup>®</sup> offers one of the most extensive offerings of recombinant enzymes developed and manufactured for drug discovery. DiscoverX is the new home to the original kinase enzyme and drug discovery business of Upstate Biotech (now part of MilliporeSigma). As the original kinase company, Eurofins DiscoverX has been supporting kinase drug discovery for >20 years with the most comprehensive offering of kinase targets across a variety of formats including active, inactive, mutants, and more. Additionally, these proteins are continuously used and validated by Eurofins Discovery service (e.g. KinaseProfiler<sup>™</sup>).

In addition to the extensive portfolio of kinases, Eurofins DiscoverX also offers a wide variety of other druggable cellular enzymes including phosphatases, ubiquitins, and epigenetic proteins.

#### Purified GPCR & Ion Channel Membrane Preps for Binding & Functional Analysis

Membrane preps are useful for studying the role of membrane proteins in diseases and their response to therapeutics. Eurofins DiscoverX GPCR and ion channel membrane preps are derived from stable cell lines expressing optimal protein levels to be assayed. They are designed for determining membrane protein binding affinities through saturation and competitive radioligand binding analysis and can be used for rank ordering and screening of small molecule or protein therapeutics. For GPCRs, these membrane preps can also be used to perform GTPγS functional studies to evaluate GPCR activity in response to the addition of a ligand or therapeutic.

#### **Product Highlights**

- Comprehensive Portfolio Over 520 active, inactive, unactive, & mutant kinases, phosphatases, & epigenetic & ubiquitin proteins, including many exclusive enzymes along with the PI3K & the PIKK group (ATM, ATR, mTOR, & DNA-PK)
- **Optimal Expression Systems** Enzymes produced in their optimal system (insect, mammalian, or bacterial) to give the correct characteristics for activity & inhibition
- High Quality Rigorous quality-control procedures ensure the highest purity, specific activity, & lot-to-lot consistency
- **Multiple Sizes** Multiple pack sizes & bulk sizing available to provide you with flexible options from a one-time experiment to a full-blown HTS campaign

#### **Product Highlights**

- Robust Performance Large signal-tobackground ratios with specific & high ligand binding capacity
- Reproducible Produced from stable clonal cell lines for superior protein expression & lot-to-lot consistency
- Simple Removes the need for cell culture
- Versatile Use Applicable for saturation & competitive radioligand binding, therapeutic small molecule & antibody screening & ranking, & GTPγS functional studies

#### **Competitive Ligand Binding Assay Principle**



Unlabeled Ligand

### TOOLBOX PRODUCTS: BUILD YOUR OWN ASSAY TOOLS

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# Complete Set of Tools to Build Your Own Cell Lines & Cell-Based Assays

Do-It-yourself toolbox products allow you to develop in-house cell lines and cell-based assays for your target and application of interest. Obtain the benefits of using optimized toolbox products for creating your ideal cell line or assay to save you the effort and time required for assay development.

Take advantage of Eurofins DiscoverX<sup>®</sup>'s proprietary Enzyme Fragment Complementation (EFC) technology to develop your own stable cell lines and cell-based assays to study protein-protein interactions, compoundtarget engagement, cytotoxicity, receptor dimerization and signaling, protein translocation, and much more. Gain an in-depth understanding of the assay principle for consideration of creating optimized assays for multiple applications. Reach out to scientific experts to guide your experimental design through analysis of your results. Design your workflows and utilize engineered parental cell lines, retroparticles, and plasmid vectors to introduce your target of interest and create cell-based assays for multiple applications.

#### **Product Highlights**

- Simple Protocols Detailed, step-by-step instructions with flow-charts & infographics to easily create assays
- Flexible Solutions Utilize any of our cell-line expression vectors to introduce mutants, make modifications, or study unique orthologs or isotypes
- Any Cell Background Make your own stable β-arrestin recruitment or cytotoxicity cellbased assays in any dividing cell type with PathHunter<sup>®</sup> or KILR<sup>®</sup> retroparticles
- Complete Kit Ready-to-use InCELL Pulse™ starter kit includes all the reagents you need to get you started to create your own target engagement assays for your target of interest



#### **Generate Your Own Assays with Parental Cell Lines or Retroparticles**

Design an EFC-based PathHunter SH2recruitment assay with your receptor of choice and an engineered parental cell line.

Create an EFC-based PathHunter internalization assay with your target protein of choice and an engineered parental cell line.

Generate a GPCR  $\beta$ -arrestin cell-based assay to evaluate ligand-induced  $\beta$ -arrestin recruitment to any GPCR in any dividing cell type.

Learn more at: 

discoverx.com/product-category/toolbox-products/

### POTENCY & QC LOT-RELEASE TESTING PRODUCT SOLUTIONS

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#### Providing Functional, MOA-based Bioassays with Superior Lot-to-lot Reproducibility

Cell-based potency assays are critical tools to measure the efficacy of a drug during potency and stability testing. Potency assays are initiated in the early drug development stage to measure the biologic's intended biological effect and MOA being analyzed. Quality control (QC) lot-release testing, intended for late-stage drug release programs, involves assays that ensure consistency with high lot-to-lot reproducibility. Given that the process of drug discovery and development is time consuming, complex, and expensive, implementing a physiologically relevant assay platform from the early development phase to late-stage drug release programs such as QC lot release can prove to be highly valuable.

Eurofins DiscoverX<sup>®</sup> offers the largest available portfolio of qualified, MOA-reflective cell-based assays (bioassays) that are phase-appropriate and meet the requirements of specific therapeutic development stages, including potency and QC lotrelease testing. The bioassays are derived from stable cell lines and

#### **Solution Highlights**

- Physiologically Relevant Bioassays qualified with marketed biologic drugs or reference standards using ICH guidelines
- Phase-appropriate Solutions Complete ready-to-use, functional cell-based assay kits of unsurpassed quality for potency & QC lotrelease testing
- **Deep Expertise** Over two decades of experience in developing cell-based assays to support your specific therapeutic development stage
- Full Support Dedicated team for end-to-end assay transfer & long-term support of your commercial release & stability programs at CRO/CDMO sites

provide a simple, thaw-and-use approach that alleviates assay passage-to-passage variability associated with cells derived from continuous cell culture. Packaged with ready-to-use cryopreserved cells, plates, and all the reagents and documents needed, Eurofins DiscoverX bioassay kits offer the ideal solution for your therapeutic development programs. These kits are rigorously tested to meet ICH (International Council for Harmonization) requirement guidelines and qualified with marketed biologic drugs or reference standards, allowing you to confidently de-risk your potency testing program and accelerate your therapeutic development timelines.



#### Global Programs Using Eurofins DiscoverX Bioassays for Potency, Stability, & NAb Testing for Drug Release

Learn more at:  $\rightarrow$  discoverx.com/application/potency-commercial-release-stability/

### IMMUNO-ONCOLOGY PRODUCT SOLUTIONS

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# Accelerate Cancer Immunotherapeutic Discovery & Development with Cell-based, Clinically Relevant Assays

Immuno-oncology (IO) is a class of treatment modality designed to augment the body's natural immune defense against cancer. The IO space is currently dominated by therapeutics development programs targeting immune checkpoint modulators and cytokines as these molecules hold significant promise in cancer therapy. Another key modality is the modulation of Fcmediated effector mechanisms of therapeutic antibodies, including ADCC, ADCP, CAR-T, CAR-NK, CDC, and other cytotoxicity-focused applications.

Eurofins DiscoverX<sup>®</sup> offers the most comprehensive product portfolio of cell lines, cell pools, eXpress<sup>™</sup> assay kits, and bioassay kits to enable fast, effective, and clinically relevant understanding of IO targets, their pathways, and mechanisms to empower quicker development of IO therapeutics. Continuous culture cell lines allow for full-scale interrogation, screening, and profiling of IO therapeutic MOAs while the ready-to-use qualified bioassays are developed to meet the industry requirements and regulatory expectations. Eurofins DiscoverX offers fast and seamless implementation for IO therapeutic MOA confirmation, stability studies, and potency testing in QC lot release programs as a thaw-and-assay platform.

Learn how you can rapidly screen and develop small molecules, biologics (peptides, antibodies, or bispecific antibodies), or cellular therapies for your IO drug discovery and development program.

#### **Product Highlights**

- MOA-reflective Assays Designed for regulatory acceptance, these assays are intended to interrogate specific target biology for fast implementation through discovery, validation, characterization, & development stages of an intended therapeutic
- Broad Coverage of Checkpoint Modulators Industry's most comprehensive menu of stable cell lines & ready-to-use bioassays for targets including PD-1, SIRPα, CTLA4, OX40, ICOS, & many others
- Comprehensive Cytokine Receptor Assays Functional assays for >85% of human interleukins (IL) receptors as well as cytokine– like interleukins, GM–CSF, interferons, chemokines, TNFα, TGF-β, & Ig superfamily receptor types
- Specific Cytotoxicity Assays Specifically measure direct target cell death in co-cultures using relevant immune effector cells with KILR® cytotoxicity assays for ADCC, ADCP, CAR-T, T cell redirection, & adoptive T cell therapy



Immuno-oncology Product Solution Assay Principles

Learn more at: 

discoverx.com/therapeutic-area/oncology-immuno-oncology/

Whether you are developing small molecule or biologic therapeutics, Eurofins DiscoverX provides you with a variety of drug discovery and development products based on the Enzyme Fragment Complementation platform for multiple applications to meet your specific IO research needs.





#### **Specifically Measure Direct Target Cell Death**

Cytotoxicity assays are required to measure target cell death via several MOA. These MOAs include antibody-dependent cellmediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC), antibody-dependent cell phagocytosis (ADCP), cytotoxic T-cell lymphocyte mediated death (CTL), bi-specific antibodymediated T-cell redirection, chimeric antigen receptor T-cell (CAR-T), and adoptive T-cell therapies. Such assays are designed to capture a therapeutics' ability to cause targeted cell death via one or more primary MOAs, and to predict or mimic a physiological response. Cancer immunotherapy (immune-oncology) therapeutics are designed to treat cancers by boosting the body's immune system to fight and kill the cancer cells. Assays for these drugs need to detect target cancer cell death when co-cultured with immune effector cells or in the presence of the complement system.

#### **Product Highlights**

- Ultra-specific & Sensitive Detect cytotoxicity only from lysed target cells & as few as 75 dead cells with high reproducibility
- Ultimate Flexibility Ability to use with different effector cell types & run cytotoxicity assays from 30 minutes to 72 hours
- **Biologically Relevant** Reflective of the true MOA of the therapeutic or ligand
- Multiple Applications Analyze ADCC, ADCP, CDC, CAR-T, ADC, CTL mediated death, bispecific antibody-mediated T-cell redirection, & adoptive T-cell therapies

The Eurofins DiscoverX® KILR (Killing Immune-Lysis Reaction)

cytotoxicity assay platform provides a simple, non-radioactive, and dye-free method to specifically measure target cell death that avoids the drawbacks of the other commonly used cytotoxicity assays. This homogeneous, plate-based assay platform has broad applications from screening to QC lot-release testing, particularly for immuno-oncology drug development applications such as ADCC, ADCP, CDC, CAR-T, and T-cell redirection. The flexibility of the KILR platform allows you to utilize stable cell lines or cell pools in relevant tumor models. To provide additional flexibility and ease-of-use, accelerate your drug development programs by several months with ready-to-use bioassay format, or eliminate donor-to-donor variability observed with PBMCs with the KILR CD16 Effector Cells.

#### **Evaluate Multiple Cytotoxicity Mechanisms**



The KILR cytotoxicity assay platform specifically measures the killing of antigen-expressing target cells in co-culture with effector cells. This robust and flexible platform can be used for the quantitation of direct cell death mediated through multiple MOAs such as ADCC, ADCP, CDC, T-cell redirection, and CAR-T.

### SIGNALING REPORTER ASSAYS

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#### A Simple, Orthogonal Screening Tool for Understanding Therapeutic MOAs

Cell-based reporter assays are well established and used to evaluate the cellular impact of therapeutics targeting a variety of proteins in signaling pathways. Researchers utilize these standard assays to study gene expression at the transcription level, and they offer an orthogonal screening method for understanding a therapeutic's MOA.

The Eurofins DiscoverX<sup>®</sup> PathHunter<sup>®</sup> Signaling Reporter assay platform provides a simple, functional cell-based assay platform for screening small molecules or biologic therapeutics and quantifying the activation and inhibition of various signaling pathways. These assays provide a downstream (transcriptional/translational) read-out complementary to receptor proximalbased assay read-outs to ultimately gain a comprehensive understanding of your drug molecule's MOA targeting NFAT, NF-KB, PD-1, STAT3, CD27, and more.

#### **Product Highlights**

- Greater Understanding Assess both receptor-upstream & -downstream responses for a comprehensive understanding of the drug molecule's MOA
- Versatile Suitable for screening agonists or antagonists, & capable of building assays to interrogate other pathways
- Simple Protocol, Fast Results Easy-to-run, rapid homogeneous protocol amenable to implementation in multiple labs & high throughput format for increased efficiency
- Biologically Relevant MOA-reflective, functional assays for monitoring diverse signaling & testing of targeted therapeutics



#### **Measure Sensitive Responses from Either Distal or Proximal Events**



Perform comparison studies of antagonists using an anti-PD-1 antibody with two different PathHunter PD-1 assays (A. reporter assay & B. signaling assay).

### Quantify Activation & Inhibition of Signaling Pathways

### PROTEIN TRANSLOCATION ASSAY SOLUTIONS

#### Return to TOC

#### Track Cellular Movement of Proteins to Multiple Membrane Compartments

The movement of proteins from the plasma membrane to endosomes, endoplasmic reticulum to the plasma membrane, or cytoplasm to the nucleus is essential for the protein's specific biological role. When natural movements are altered by therapeutic binding, protein mutations, or abnormal signaling, undesirable consequences such as drug tolerance, unwanted side effects, therapeutic toxicity, and diseases may occur. Measuring therapeutic binding that affects translocating proteins provides insight into these adverse effects and ultimately helps to identify safer drugs.

Eurofins DiscoverX<sup>®</sup> PathHunter<sup>®</sup> protein translocation assays provide the ability to study the internalization and cellular trafficking of your protein of interest to and from different cellular compartments and analyze the pharmacological effects of therapeutics on these events. Unlike alternative methods that require specialized equipment, antibodies, or fluorescent tags, these cell-based assays are high-throughput, easy-to-use, quantitative, and highly specific and sensitive.

#### **Product Highlights**

- Simple, Homogeneous Assay Explore protein translocation to multiple cellular compartments using an easy-to-use, non-imaging, high throughput cell-based assay platform
- Pharmacochaperone Discovery Identify small molecule compounds that functionally rescue disease relevant mutant proteins involved in cystic fibrosis, Alzheimer's disease, Huntington's disease, & others
- **Biologics Discovery** Quantify peptide & antibody-based therapeutics targeting receptors that can induce high levels of translocation
- Flexible Solutions Create quantitative, custom cell-based assays to study the translocation of any protein (e.g., GPCRs, RTK, checkpoint receptors, nuclear proteins, ion channels, & more)



#### **Receptor Internalization Assay Principle**

Monitor the internalization of membrane receptors (A) GPCRs or (B) checkpoint receptors or receptor tyrosine kinases) in an imaging & antibody-free, homogeneous (no wash) HTS-friendly assay format. These assays detect membrane receptor translocation to the endosome after ligand binding for all internalization assay principles.

### SPRINTEr<sup>™</sup> ASSAYS TARGETED PROTEIN DEGRADATION PRODUCT SOLUTIONS



#### Return to TOC

# Rapid Cell-based Assays for the Detection of Protein Turnover

Regulated protein degradation is a critical cellular process for endogenous protein homeostasis. Modulating protein turnover by targeting these endogenous pathways is an emerging therapeutic modality referred to as Targeted Protein Degradation (TPD). One modality of TPD uses small molecules such as PROTAC® (Proteolysis Targeting Chimeras) or molecular glues that can redirect the ubiquitin-proteasome mediated degradation pathway and trigger the degradation of specific proteins in a highly selective and effective manner.

This new approach has expanded the druggable target space by allowing drugs to modulate protein turnover or depletion of over-abundant proteins associated with disease states such as cancer (oncoproteins) or Alzheimer's disease (TAU protein).

#### **Product Highlights**

- Homogeneous Simple, scalable, & homogeneous no-wash protocol amenable to highthroughput screening (HTS) formats for increased efficiency
- Robust & Highly Sensitive Accurately detect target protein turnover at micro/nanomolar sensitivities
- Rapid Results Obtain results in as little as 5 hours to select the right candidate & accelerate development programs

Eurofins DiscoverX<sup>®</sup> SPRINTer protein turnover biosensor assays for rapid screening of small molecule therapeutics and quantifying changes in endogenous protein levels in disease-relevant cell models. Detect protein turnover induced by targeted degrader molecules, such as PROTACs, with higher sensitivity and more rapid kinetics than phenotypic endpoint assays (e.g., cell proliferation).



Identify new molecular entities, such as PROTACs, that modulate endogenous protein levels in physiologically relevant cell models using a homogenous assay format.

#### **Rank Order Potencies of Inhibitors and PROTACs**



The SPRINTer K562 (A.) BRD4 & (B.) c-Myc proteins cell lines were used to rank the order of BET inhibitors (OTX015 & JQ1) & PROTACs (dBET1, MZ1 & ARV-825). In the BRD4 cell lines, the BRD4 inhibitors are much less efficacious at mediating BRD4 degradation than the PROTACs. In contrast, BRD4-targeting PROTACs mediated degradation of c-Myc showed slightly slower kinetics, producing more distinct profiles after a 24 hr incubation.

### INCELL ASSAYS TARGET ENGAGEMENT PRODUCT SOLUTIONS

#### Return to TOC

#### Universal Cell-based Compound-target Engagement Assays

Target engagement assays measure compound binding to a specific protein target. In a cellular environment, these assays monitor compound cellular penetration and compound-target interaction to enable the assessment of compound efficacy and confirmation of MOA.

InCELL cell-based compound-target engagement assays provide the ability to confirm compound cell entry and protein target binding, screen and rank inhibitors, validate hits identified in biochemical assays, and measure cellular  $EC_{50}$  values all in the native cellular environment. These simple binding assays require no custom chemical tracers nor antibody reagents and provide a convenient solution when functional assays are difficult or unavailable. Access two leading Eurofins DiscoverX<sup>®</sup> assay platforms, InCELL Pulse<sup>TM</sup> and InCELL Hunter<sup>TM</sup> — both based on the industry validated EFC

#### **Product Highlights**

- Biologically Relevant Obtain quantitative cellular compound entry & target binding data for more confident drug discovery decisions
- Easy-to-Use Simple, homogeneous protocol to easily measure compound binding to your protein target with a chemiluminescent readout
- High-throughput Amenable Easily automate assays to screen multiple compounds accurately
- Quick & Thorough Protocol Rapidly make your own target engagement cell-based assays in less than 2 weeks following the detailed, step-by-step protocol

technology with similar underlying principles, but crucial differences that suit them for different protein targets. The InCELL Pulse platform is built on the principle of protein thermal stability, while InCELL Hunter is built on the principle of protein stabilization related to protein turnover or interaction disruption.

InCELL target engagement assays are a perfect complement to Targeted Protein Degradation (TPD) programs that allow you interrogate and optimize target-binding portion. Discover the power of the InCELL assays and take advantage of stable cell lines, ready-to-use kits, and a do-it-yourself, starter kit perfect for creating your own compound-target engagement assay.



InCELL Pulse & InCELL Hunter Target Engagement Assay Principles

InCELL Pulse compound-target engagement assays are based on a novel cellular application of the EFC technology incorporating compound binding detection based on protein thermal stability.

InCELL Hunter assays are built on the principle of protein stabilization related to protein turnover or interaction disruption. A larger signal corresponds to greater presence of compound-target engagement in the cell.

#### Learn more at: discoverx.com/application/target-engagement/

### **OBESITY & DIABETES PRODUCT SOLUTIONS**

#### Return to TOC

#### Accelerate the Development of Peptide Therapeutics for Obesity & Diabetes with MOA-reflective Assays for Screening, Profiling, Potency, & Lot Release Programs

Obesity and Type 2 diabetes (T2D) are chronic diseases that affect a significant number of people globally. Several advancements in therapeutics to address these diseases have spurred a global surge in drug discovery and clinical development programs, focusing on innovator drugs, biosimilars, biobetters, and small molecules targeting a variety of target receptors.

Eurofins DiscoverX<sup>®</sup> supports this evolving therapeutic landscape with a comprehensive portfolio of assays tailored for various peptide therapeutics directed at targeting GLP-1 (glucagon-like peptide-1), GIP (gastric inhibitory polypeptide), and glucagon (GCG) receptors, as well as numerous additional novel targets including TSH, PYY, Amylin, GPR10, GPR75, and more. These assays support various drug discovery and clinical development stages, as well as commercialization and stability studies facilitating precise bio-identity and potency testing.

Potency Testing Using the cAMP Hunter Assay for Retatrutide

#### **Product Highlights**

- Qualified Bioassays ICH (International Council for Harmonization) based assay qualification using approved therapeutics like Ozempic<sup>®</sup> (Semaglutide), Victoza<sup>®</sup> (Liraglutide), Tirzepatide, & molecules like Retatrutide (under clinical trial)
- Establish Accurate Pharmacology for Regulatory Filings – Evaluate your therapeutics MOA (mechanism of action) for cAMP accumulation, β-arrestin recruitment, & receptor internalization
- Assay Transfer Support Dedicated global team for end-to-end assay transfer of your commercial release & stability programs at CRO/CDMO sites
- Cell Banking Customized, well-characterized thaw-&t-use working cell banks to ensure longterm assay reproducibility &t supply of the bioassay cells



Thaw-&t-use cAMP Hunter™ Retatrutide RA (receptor agonist) Bioassays demonstrate robust, sensitive, &t differential retatrutide responses in cAMP levels reflective of the accurate pharmacology of drug responses at the GLP-1, GIP, a &t glucagon receptors.

#### Potency Testing Using the PathHunter® GLP-1, GIP, & Glucagon Receptors Assays



of β-arrestin recruitment by tirzepatide & retratrutide at respective target receptors with endogenous ligands (exendin-4 for GLP-1, GIP for GIPR, & glucagon for GCGR).

Comparison

Learn more at:  $\rightarrow$  discoverx.com/therapeutic-area/obesity-diabetes

### ION CHANNEL SOLUTIONS

#### Return to TOC

#### High-quality PrecisION™ Cell Lines for Target Discovery, Hit Screening, Lead Optimization, & Safety Studies

lon channels continue to be an important therapeutic target for a wide range of indications, including arrhythmia, hypertension, local anesthesia, pain, stroke, epilepsy, depression, bipolar disorder, cystic fibrosis, cardiac arrhythmias, COPD, autoimmune disorders, and diabetes. They are an appealing target to develop therapeutics against rare channelopathies, since many of these diseases are caused by the mutation of a single gene. Ion channels not only constitute a significant class of drug targets, they are also critical for evaluating drug safety, including being part of the U.S. FDA required safety testing for any drug targeted against human disease.

Eurofins DiscoverX<sup>®</sup>'s comprehensive portfolio of functionally validated ion channel products is comprised of optimized and PrecisION stable ion-channel cell lines for use in cell-based assays, PathHunter<sup>®</sup> pharma-cotrafficking assays for pharmacochaperone discovery, and a hERG ion channel membrane preps for binding studies.

#### **Product Highlights**

- Validated Functionally & pharmacologically validated ion channel cell lines used in Drug Discovery & Safety programs both in house & at customer sites, with many cell lines in use for over ten years
- Superior Performance Proprietary cell line vector technologies for optimum stability, expression, & uniform current
- Versatile Use PrecisION cell lines applicable for manual & automated patch-clamp studies, PathHunter pharmacotrafficking hERG & CFTR cell lines for pharmacochaperone discovery, & PrecisION hERG membrane prep for safety binding studies

#### Perform Pharmacological Profiling & Rank Order Potency



#### **Execute Fluorescent & Electrophysiology Assay Experiments**



Human sodium voltage-gated ion channel characterization data showing (A.) a voltage step & (B.) current-time plot of NaV1.2 to evaluate a pharmacological profile, & (C.) dose-response curves of NaV1.8/ B1 for 3 blocking compounds to determine rankorder potency.

Activation & inhibition profiles of ligand-gated ion channels (A. & B.) acetylcholine via fluorescent &t (C.) glycine via electrophysiology assays.

# GPCR PRODUCT SOLUTIONS



#### Return to TOC

#### Always Find a GPCR Assay for Your Target of Interest

GPCRs represent the largest family of validated therapeutic targets with over 800 known human GPCRs. Therapeutics targeting GPCRs represent over 40% of all currently marketed drug therapeutics acting on GPCRs either directly or indirectly. GPCRs have a broad array of ligands, including growth factors, ions, lipids, nucleotides, hormones, and neurotransmitters. Their physiological and pathological involvements are vast, ranging from regulation of hunger to development of fetal structures, and from roles in cardiovascular disorders to rare diseases. To help researchers fully characterize their specific GPCR of interest, and the small molecules or biologics effecting their activity, Eurofins DiscoverX® encourages exploring all possible signaling scenarios with a variety of available biologically relevant cell-based functional and binding assays, cell lines, detection kits, and membrane preparations.

The target-specific products in the Eurofins DiscoverX portfolio are sensitive, scalable, and robust for detecting receptor-mediated second messenger signals (cAMP and calcium),  $\beta$ -arrestin recruitment, receptor internalization, and ligand binding. These assays also support the characterization of orphan GPCRs without a known ligand or approved drug as part of the comprehensive GPCR solutions portfolio offered.

#### **Product Highlights**

- **Broad Coverage** Over 90% targets covered across the human GPCRome to always find an assay for your target of interest
- Highly Applicable Ideal for the development of small molecule & biologic therapeutics, from target ID through pre-clinical drug discovery programs
- Assay Options Multiple MOA assay types are available (including β-arrestin, cAMP, calcium, internalization, ligand binding & trafficking) offering a diverse array of GPCR assay solutions for maximum flexibility
- Largest Collection Over 1,600 qualified functional & binding assays seen in >800 peer-reviewed publications, giving you the most comprehensive GPCR assay solutions available for the confidence you need

#### **Choose the Solution that Best Meets Your GPCR Program Needs**



Whether you are developing small molecule or biologic therapeutic drugs, Eurofins DiscoverX provides you with a variety of drug discovery products with multiple assay types to meet your specific GPCR research needs.



#### **Highlights of GPCR Product Solutions**

Applications	Benefits	Product Portfolio	Credibility	
Biologically relevant functional assays	<ul> <li>Homogeneous assays with easy-to follow, rapid, no-wash protocols</li> </ul>	Stable cell lines	<ul> <li>Accepted by industry and the</li> </ul>	
<ul> <li>Broad coverage of human GPCRome, including both liganded and orphan GPCRs</li> </ul>	Luminescent and fluorescent     readouts     Ready-to-use assay kits		scientific community with thousands of peer-reviewed publications & billions of	
Ortholog receptor assays	<ul> <li>Sensitive detection and robust dynamic range</li> </ul>	<ul> <li>Flexible toolbox (do-it-yourself) cell-based assay development products</li> </ul>	data points screened	
<ul> <li>Multiple modalities (second messenger, β-arrestin, and internalization) for ligand bias studies</li> </ul>	Low false positive rate	<ul> <li>Membrane preps suitable for radio- and fluorescent ligand binding assays</li> </ul>	Thorough technical documentation	
Pharmacological profiling (e.g., agonist, antagonist, allosteric modulation)	macological profiling (e.g., agonist, gonist, allosteric modulation) • Reproducible • Qualified, optimized bioassays for develo		Custom product development services	
Ability to multiplex various readouts     (in one cell line)	Suitable for miniaturization     and high-throughput screening	Custom product development services	Biologics License Application     (BLA) filings	

#### **GPCR Product Solutions Assay Principles**



### KINASE PRODUCT SOLUTIONS



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#### Kinase Enzymes & Cell-based Functional, Binding, & Activity Assays for Discovery through Development & for QC Lot-release Testing

Kinases play a central role in cell signaling to elicit many physiological responses. Dysregulation of kinase activity leads to many human diseases, especially cancer. A typical signaling pathway involves a kinase cascade to produce a cellular response starting with receptor activation via a ligand-induced activation step. The activated targets elicit cellular responses that include the promotion of cell growth and division, protein translation, or other physiological responses.

Eurofins DiscoverX<sup>®</sup> offers an extensive portfolio of functional and binding cell-based assays, cell lines, and recombinant kinase enzymes to evaluate any kinase target-based signaling activities to aid your efforts from discovery through development into commercialization. Screen for novel kinase inhibitors, perform pharmacological profiling, and evaluate kinase activation from therapeutic binding. Utilize cell-based assays to determine therapeutic MOA and intracellular compound target engagement. Perform kinase activity assays measuring ADP production or substrate phosphorylation with one of the most extensive offerings of recombinant kinase enzymes available.

#### **Product Highlights**

- Comprehensive Portfolio Binding & functional, cell-based assays for receptor dimerization, SH2 recruitment, & target engagement as well as over 420 kinases active, mutant, & inactive recombinant kinases for activity & biophysical testing
- Highly Applicable Ideal for the development of small molecule & biologic therapeutics, from target ID through pre-clinical drug development programs, into therapeutic commercial release
- Clinically Relevant, Cell-Based Assays Leverage & implement any of the Eurofins DiscoverX qualified or target-based bioassays to accelerate your biological candidate, whether it is a novel therapeutic or a biosimilar
- Rigorously Tested Kinase Enzymes Kinase enzymes utilized in KinaseProfiler<sup>™</sup> services for screening millions of compounds over the past 30 years

#### Cell-Based Assays | Activity Assays | Enzymes >1400 Qualified Kinase Products Assay Types Pharmacological Activity and Testing RTK Dimerization Compound Target ADP Accumulation Agonism Kinase Activity Engagement SH2 Recruitment Substrate Phosphorylation • Inhibition • Mechanism of Action Test Assay Quickly Lead Optimization **Build Your Own Assay Screen In-House** Stable Cell Lines Ready-to-Use Kits · Profiling and Toolbox Starter Kits Recombinant Enzymes Screening Services ADP Accumulation Vectors Custom Assays Rank Order Potencies Parental Cell Lines Assay and Proteins

**Choose the Solution that Best Meets Your Kinase Discovery Program Needs** 

Whether you are developing small molecule or biologic therapeutic drugs, Eurofins DiscoverX provides you with a variety of drug discovery products with multiple assay types to meet your specific kinase research needs.

Learn more at:  $\rightarrow$  discoverx.com/target-class/kinase/



#### **Kinase Product Solutions Assay Principles**













EGFR HER2

**ADP Accumulation Activity Assay** 



Enzyme Coupled Conversion

### CHECKPOINT RECEPTOR ASSAYS



#### Return to TOC

# Accelerate Cancer Immunotherapy Drug Development with Easy-to-use, Functional Cell-based Assays

Regulation of immune responses is tightly controlled through a balance of co-stimulatory and inhibitory checkpoint receptors often exploited by many cancers. Therefore, therapeutics that block inhibitory receptors or activate immune-stimulatory checkpoint receptors, such as PD-1 receptor, have proven to be powerful agents to restore anti-tumor immune responses.

Eurofins DiscoverX<sup>®</sup> offers a large, diverse selection of assays for characterization, screening, and potency QC lot-release testing of immunotherapy therapeutics targeting both inhibitory and co-stimulatory checkpoint receptors. Utilize PathHunter<sup>®</sup> functional, MOA-reflective cell-based checkpoint receptor assays to analyze signaling, dimerization, internalization, and clustering/crosslinking of checkpoint receptors. These simple, rapid assays provide a highly sensitive response in a few hours for most targets without primary cells or complex protocols.

#### **Product Highlights**

- Biologically Relevant MOA-reflective, functional assays for monitoring checkpoint signaling & testing of small molecule or biologic therapeutics
- **Comprehensive Portfolio** Large menu of off-the-shelf assays for accelerating assay development & implementation time
- Robust Assays Highly reproducible assays for potency & lot-release applications for immunotherapy drug discovery & development
- Simple Protocol, Fast Results Easy-to-run, rapid homogeneous protocol amenable to implementation in multiple labs & highthroughput format for increased efficiency



Checkpoint receptors are critical for communication & regulation between tumor & immune cells. T-cell receptors recognize tumor antigens presented by antigen-presenting cells like dendritic cells to T-cells, & their receptorligand interactions can lead to activation (through co-stimulatory signals) or suppression (through co-inhibitory signals) of T-cell responses. These responses are often used by tumor cells to evade the host immune system either by suppressing T-cell activation or by suppressing phagocytosis by macrophages.

#### **Exceptional Assay Performance**



PathHunter checkpoint assays have high passage stability & show superior specificity (A. & B. SIRPa signaling cell line) as well as excellent replicate reproducibility (C. PD-1 signaling cell line).

Learn more at: 

discoverx.com/target-class/checkpoint-receptor/

#### PathHunter<sup>®</sup> Checkpoint Assays have Broad Applications for Cell-based Screening, Functional Characterization Studies, & QC Lot-release Testing



#### Anti-receptor & anti-ligand applications.

The PathHunter PD-1 Signaling Assay was used to demonstrate anti-PD-1 & anti-PD-L1 inhibitory & shows inhibition dose response curves for A. anti-receptor & anti-ligand antibodies using the FDA approved anti-PD-1 antibodies Keytruda®, Opdivo®, & B. an anti-PD-L1 antibody. Keytruda & Opdivo are registered trademarks of Merck & BMS, respectively.

### Screening co-stimulatory (agonist) & co-inhibitory (antagonist) responses.

**C.** Path-Hunter ICOS signaling assay with an anti-ICOS antibody to quantitate the agonistic activity of the anti-body targeting the ICOS receptor.

#### Characterizing small molecule inhibitors.

D. PathHunter PD-1 Signaling Assay was used to assess small molecule receptor tyrosine kinase inhibitors, anti-PD-1 (antibody), & a low molecular inhibitor of anti-PD-L1.

#### Antibody-mediated crossing-linking by Fcy

receptors. E. Agonistic antibody Pogalizumabmediated stimulation of OX40 using the Path-Hunter OX40 signaling assay. Soluble Pogalizumab was unable to activate OX40 cells alone. However, co-culturing with human FcyRIIb clustering cells, enables access to more receptors on the cell surface thereby allowing Pogalizumab to exhibit a dose-dependent increase in NIK stabilization as opposed to none-to-marginal response with the soluble antibody.

#### Study antibody-drug conjugates (ADCs).

F. PathHunter internalization assay for the CD33 checkpoint receptor was tested with a commercial antibody to CD33. CD33 antibody was preincubated with a secondary antibody to cluster the CD33 receptor & then added to cells to monitor internalization. With higher cross-linked antibody concentrations, greater amounts of PK-tagged CD33 complemented EA-tagged protein localized to the endosome. G. B-cell maturation antigen (BCMA) receptor internalization was activated with a commercial BCMA antibody.

### CYTOKINES/INTERLEUKINS RECEPTOR ASSAYS

#### Return to TOC

# Comprehensive Portfolio of Cell-based, Functional Assays for Cytokines Receptors

Cytokines are a group of proteins that play a critical role in regulating the immune system and inflammation. The dysregulation of cytokines is associated with a wide range of diseases, including autoimmune disorders, cancer, and infectious diseases. Cytokine receptors are critical for cellular and extracellular communication in mediating immunological responses. Therapeutics that target cytokines or their receptors can modulate the immune response and potentially treat these diseases. While the development of these drugs is complex and time-consuming and requires a deep understanding of the immune system and the role of cytokines in disease pathogenesis, assays are available to advance this discovery faster.

#### **Product Highlights**

- **Biologically Relevant** MOA-reflective, functional assays for monitoring cytokine receptor activation & dimerization
- Qualified Bioassays Accelerate your cytokine therapeutic release program with cytokine receptor bioassays qualified using approved therapeutics like \*Actemra® (tocilizumab), Kineret® (anakinra), Leukine® (sargramostim), Et Humira® (adalimumab)
- Easy-to-run & Scalable Homogeneous, simple, rapid protocol amenable to highthroughput formats for increased efficiency

Eurofins DiscoverX<sup>®</sup> offers a comprehensive portfolio of PathHunter<sup>®</sup> cell-based, MOA-reflective, functional assays to enable the

\* All registered trademarks are the property of their respective owners.

study and targeting of cytokine receptors, covering over 85% of human interleukins (IL-1 to IL-37) and their receptors. These assays are designed to be highly specific and reproducible, include a simple protocol, and have a large signal-to-noise ratio and matrix tolerance. These cytokine receptor assays have enabled their broad application in functional screening, functional characterization, QC lot release assays, and neutralizing antibody studies.



#### Analyze Multiple Interleukin Receptor Families with Highly Specific Assays

Representative examples of assays for interleukin receptors from 6 different interleukin receptor families. Each plot shows a dose response for the relevant ligand(s) in each assay from the indicated family. Data plotted are mean RLU & standard deviation from at least triplicate wells for each dose. These assays are characterized by robust assay windows & low CVs

Learn more at:  $\rightarrow$  discoverx.com/target-class/cytokine-receptor/

### EPIGENETIC & NUCLEAR PROTEIN PRODUCT SOLUTIONS

#### Return to TOC

#### **Epigenetic Protein Product Solutions**

Epigenetics involves the study of heritable or acquired changes in gene expression caused by non-genetic mechanisms without alterations in gene structure or sequence. Basic epigenetic mechanisms such as histone modifications, DNA methylation, and chromatin remodeling are essential in the regulation of many physiological processes. Alterations to the mechanisms -- either by modifications to DNA and histone components of nucleosomes, or by expression of noncoding RNAs (ncRNAs) - can have implications in a number of cancers, immunological, and neuro-degenerative conditions.

Eurofins DiscoverX<sup>®</sup> offers epigenetics recombinant proteins and InCELL Hunter<sup>™</sup> cell-based assays for studying the modulation of epigenetic mechanisms and identifying small molecule inhibitors and modifiers of DNA methyltransferases and bromodomains. Utilize InCELL Hunter cell-based compound-target engagement assays to confirm small molecule compound cell entry and epigenetic target binding, screen and rank inhibitors, validate hits identified in biochemical assays, and measure cellular EC<sub>50</sub> values all in the native cellular environment.

# Nuclear Protein Cell-based Assays to Evaluate Activation & Translocation of Nuclear Proteins

Nuclear proteins are key targets for drug development due to their ubiquitous roles in controlling cellular behavior and pathway expression. The translocation of many nuclear proteins into and out of the nucleus is a highly controlled mechanism that can dictate protein function. Controlling this translocation behavior using therapeutics, or ensuring that a potential drug does not cause undesired effects on translocation, are importantapplications for measuring nuclear translocation.

Eurofins DiscoverX<sup>®</sup> provides PathHunter<sup>®</sup> nuclear translocation and protein interaction cell-based, functional assays to investigate protein translocation events and activation of nuclear proteins. Nuclear translocation assays allow for studying the trafficking of your protein of interest to and from the nucleus and analyzing the pharmacological effects of therapeutics on these events. Protein interaction assays can be used to evaluate the interaction

#### **Product Highlights**

- **Biologically Relevant** Obtain quantitative cellular compound entry & epigenetic target binding data for more confident drug discovery decisions
- Easy-to-use & Scalable Simple, homoge-

neous, & high-throughput amenable protocol to easily measure compound binding to your epigenetic target with a chemiluminescent readout

- Target Specificity & Selectivity Ability to screen & differentiate multiple target-selective stereoisomers of BRD4 & determine target specificity
- High Quality Proteins Access epigeneticsrelated recombinant proteins produced using optimal expression systems with high quality & purity

#### **Product Highlights**

- Homogeneous, HTS-compatible Assay An easy-to-use, sensitive, & high-throughput cell-based assay platform without the need for antibodies, fluorescent tags, or specialized equipment
- Flexible Solutions Create your own quantitative, functional cell-based assays to study nuclear translocation of any desired target protein
- Diverse Therapeutic Discovery Quantify small molecules, peptides, or antibody-based therapeutics targeting nuclear proteins

of nuclear hormone receptors (NHRs) and their cofactors, including therapeutics that affect this protein-protein interaction. Among the advantages of the Eurofins DiscoverX platform is that, unlike other assays, these cell-based assays do not require antibodies, fluorescent tags, or specialized equipment, and they provide an easy-to-use, high-throughput capable, and quantitative measurement of protein-protein interaction.

### SIGNALING PATHWAY PRODUCT SOLUTIONS

#### Return to TOC

#### A Simple, Orthogonal Screening Tool for Understanding Therapeutic MOAs

Cellular pathway signaling constitutes key mechanisms that transfer biological information within cells for intracellular responses crucial in many physiological processes, including cell proliferation, differentiation, metabolic control, and apoptosis. Cell signaling pathways are activated when ligands (e.g., cytokines, growth factors, or hormones) bind to specific receptors on the cell surface. Detecting specific stimuli via intracellular signal pathways becomes paramount in interrogating the MOA of the target ligand/receptor interaction for advancing drug discovery and development in many pathophysiologic and pharmacologic mechanisms.

Eurofins DiscoverX<sup>®</sup> offers a comprehensive collection of cell-based pathway indicator assays designed to detect activation or inhibition of complex signal transduction pathways in response to a small molecule or biologic. The

#### **Product Highlights**

- Homogeneous Assays Simple, no wash HTS-friendly protocols with a sensitive chemiluminescent read-out
- Multiple Assay Types Binding and functional (direct and reporter-based) cell-based assay with no need for antibodies, fixing, or imaging
- Fast, Superior Results Rapid assay with short compound incubation times, high signal-to-background, and no false positives
- High Specificity Whole cell, non- ELISA assays with increased target specificity

assays are based on the established PathHunter® technology, and feature indicator cell lines used in pathway assays that enable you to measure distinct events within a variety of pathways associated with immune response, compound toxicity, cholesterol metabolism, antioxidant function, DNA damage, and more.



#### Signaling Pathways Assay Principles

PathHunter signaling pathways assays for studying nuclear protein translocation to identify, screen, perform lead optimization, and even safety testing of therapeutics. These assays monitor the activation or inhibition of a particular signaling pathway coupled with the movement of proteins from the cytosolic compartment to the nuclear compartment. Assays shown here measure (A.) TORC1 or TORC2, (B.) p53 (DNA Damage), (C.) SREBP2, and (D.) NRF2 translocation from the cytosol to the nucleus. Other signaling pathway assays measure apoptosis via protein destabilization, protein transcription, receptor dimerization, protein degradation, and more.

### CELL BANKING & CUSTOMIZED SCALE-UP CELL PRODUCTION

#### Return to TOC

# Ensure Long-term Critical Reagents Supply & Assay Reproducibility

Cell banks provide researchers with consistent and reliable cell populations for a myriad of applications from drug discovery to commercialization and stability studies, including high-throughput screening, preclinical studies, lot release testing, and therapeutic manufacturing.

Eurofins DiscoverX<sup>®</sup> also offers custom scale-up cell production capabilities to provide instant ready-to-use cell vials catering to the specialized needs of drug developers and biotechnology companies by facilitating the transition from laboratory-scale cell cultures to large-scale production. Through meticulous process optimization and robust manufacturing, custom scale-up enables efficient and scalable production of cells for diverse applications.

#### **Product Highlights**

- Customized Production Ready-to-use cell vial lots manufactured for your program requirements
- Extensively Tested Well-characterized & QA-released banks to ensure long-term reproducibility for your bioassays implemented in lot release
- **Proven System** Dedicated, two-tiered analytical cell banks for critical reagents (bioassay cells) supply assurance
- Long-Term Storage Two-site secure storage to ensure a continuous supply of bioassay cell

lots for the lifetime of your therapeutic

Testing	Clone	Master Cell Bank	Working Cell Bank	Bioassay Cells	Custom Lot Production
Functional Performance	$\checkmark$	$\checkmark$	$\checkmark$	√ (Bioassay QC criteria)	$\checkmark$
Sterility & Mycoplasma Testing	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Passage Stability	$\checkmark$	$\checkmark$	√ Optional		
Identity & Purity	$\checkmark$				

#### **Characterization & Testing of Cells**

\* Optional cell testing: Viral & bacterial pathogens, cell line identity, compendial mycoplasma testing, & direct inoculation sterility testing available upon requestIta nossin defactudem mori con di et Cupie publii it.

#### **Custom Cell Scale-up Production Capabilities**



Examples of customized cell scale-up production options and a typical custom cell scale-up project.

Learn more at:  $\rightarrow$  discoverx.com/product-category/cell-banks-for-bioassays/

### CUSTOM DEVELOPMENT CAPABILITIES

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## Custom Assays, Cell Lines, Cell Banks, Membrane Preps, & Protein/Enzyme Development

Cell-based assays are valuable tools employed throughout the drug discovery and development phases and into commercial release and stability testing. Implementing cell-based assays for in-house custom assay development can be challenging, from establishing physiological relevancy to method qualification, validation, post-implementation, and support. Phaseappropriate assays can be technically challenging, expensive, and resourceintensive, delaying moving programs forward to the clinic.

Eurofins DiscoverX<sup>®</sup> offers the industry's most extensive off-the-shelf menu available of cell-based assays and recombinant proteins that can be implemented for your programs. Several customized solutions can be delivered for program-specific needs by utilizing our deep expertise in cell line engineering, assay development, and protein production. These solutions include varying targets in different cell backgrounds, unique MOA, producing active recombinant proteins (GPCRs, ion channels, transporters, kinases,

#### **Capabilities Highlights**

- **Development Expertise** Decades of cell line engineering & cell-based assay & recombinant proteins development expertise including enzymes and membrane proteins
- Cell Line Engineering Capability Exogenous expression approaches or gene editing
- **Collaborative** Consultative product development with regular updates through a dedicated project manager
- **Complete Solution** Customized assay development with screening & profiling services within the same team

phosphatases, epigenetic proteins), creating ready-to-use bioassays qualified with your clinical molecule, and more.

Gain from our experience leveraging over 20 years of custom development expertise and a vast history of generating thousands of customized assays and active recombinant proteins including fully-native membrane targets for drug discovery programs at multiple companies globally through screening, lead optimization, and bioanalytical assay development.

#### **Key Customized Development Capabilities**

- Cell line engineering through exogenous expression (constitutive vs inducible) approaches, gene editing (e.g. KO/KI with CRISPR/Cas9), or retroviral or lentiviral transduction
- Bioassay development and International Council for Harmonization (ICH)-based method qualification
- Screening (high- and ultra-high throughput), characterization, profiling, Investigational New Drug (IND)-enabling studies and comparability studies
- Analytical Master Cell Bank (MCB) (critical reagents; bioassay cells) 2-tiered production
- Bioassay method transfer to QC testing sites
- Dedicated large lot or multiple lot production of ready-to-use cryopreserved cells
- Protein development and production, including recombinant enzymes (active, inactive, unactive) and full-length membrane proteins (pure, functional, stable) in various formats such as micelles of detergent, SMALPs, amphipols, nanodiscs, and proteoliposomes
- Accurate characterizations of recombinant protein functions and interactions, using ligand binding assays, thermal shift assays, and stability tests
- Membrane preparation development and production

#### **Streamlined Approach for Customized Cell Line Generation**



#### **Custom Protein Development & Production Process**



### CDMO/CRO CERTIFICATION PROGRAM FOR CELL-BASED ASSAYS

#### Return to TOC

#### Take Your Cell-based Services to the Next Level: From Assay Qualification to Method Transfer

Biopharmaceutical companies developing and manufacturing biologics, biosimilars, and generics need vital resources and efficiencies from Contract Development and Manufacturing Organizations (CDMOs) and Contract Research Organizations (CROs) that can support their therapeutic programs with robust bioassays. Certified CDMO/CROs are recommended to biopharma clients aligned with their focused downstream therapeutic efforts.

The CDMO/CRO Certification Program from Eurofins DiscoverX® trains, validates, and qualifies trusted CRO/CDMOs to properly and efficiently run Eurofins DiscoverX bioassays supported by seamless method transfer capabilities supported by a global team of Application Scientists.

#### **Program Highlights**

- **Full Support** Supporting CRO/CDMOs every step of the way from assay qualification to method transfer
- Industry Leader Implementing the highest quality bioassays in the industry
- Certification Program Qualifying CRO/CDMOs to run Eurofins DiscoverX bioassays to help CRO/CDMO clients therapeutic efforts ultimately

At Eurofins DiscoverX, you can find the most extensive portfolio of qualified bioassays and custom bioassay development services. With over two decades of experience, biopharma clients seek our advice when moving their drug product downstream and need a CRO/CDMO that can successfully run our bioassays and support the potency lot-release testing of their therapeutic candidates.

#### **CRO & CDMO Service Providers with Certified Experience in Running Eurofins DiscoverX Bioassays**



### **Begin Your CRO Certification**



Contact us at CRO\_Certification@discoverx.com



Attend a 2-day theoretical and wet-lab workshop at your site







**Obtain your CRO Certification** 



Sign agreement letter prior to attending workshop

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Cell-based Products for Basic Research & Discovery through the Commercial Release of Small Molecule & Biological Therapeutics





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