

Functional, Automatable & MOA-Reflective Cell-Based Bioassays for Accelerating Drug Discovery & QC Lot Release Programs

OUR EXPERTISE IN YOUR HANDS. DISCOVER CONFIDENTLY. Gaurav Agrawal, Ph.D. Scientific Development Manager, Eurofins DiscoverX

Eurofins DiscoverX is a Global Leader in Cell-Based Assays for Screening, Profiling, Potency, & Lot Release Programs



The Eurofins Discovery PRODUCTS COMPANY

From Discovery to Development to Clinic to Post-Market

20+ Years of Enabling Drug Discovery and Development Programs

Image: constraint of the second sec		10+ Druggable target classes	1500+ Stable cell line and membrane preps		20+ Core patents		2000+ Publications across multiple applications	
			55+ Qualified & MOA- based Bioassays	Validated >30 Billion Data screened in assay servisame assays		e d ata Poin ^{services wi}	A Points vices with	
ICH Based Bioassay Qualification Facilitate downstream validation studies	A Bioassay ation downstream studies B Dedicated Scientific Support Experienced team providing scientific support		20+ Successful Assay Transfers At clients/affiliated CRO sites		50+ Global Programs For potency, stability and NAb testing			

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Enzyme Fragment Complementation (EFC) Technology

Enabling Technologies with a Flexible Platform based on a Split β -Galactosidase Enzyme







Homogenous	Robust	Qualified and Validated	Transferrable
 Add-and-read assay format No washing steps No centrifugation step No shaking or filteration 	 Enzymatically-amplified Assay Large signal-to-background High precision and reproducibility 	 Optimized for hundreds of targets Screened billions of datapoints >2K peer-reviews publications 	 Assay protocol is similar across platform Detailed user manuals Assays routinely transferred between multiple sites

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Largest Menu of Cell-Based Assays for Discovery, Potency, & NAb Assay Development



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>800 cell lines to support bioassay development for major drug target classes



Enzyme Fragment Complementation (EFC) Versatile and Robust Platform for Cell-Based Assays

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GPCR Products Portfolio Overview

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- Worlds largest GPCR assay collection available with the widest family coverage
- >90% Assay coverage*
 ~290 unique GPCR targets
- >1600 Functional and binding assays
 Both traditional force-coupled and newer naturallycoupled, functional assays
- Widely recognized product brands

PathHunter[®] HitHunter [®] cAMP Hunter[™] ChemiSCREEN™ ChemiBRITE™



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In addition, Ligand Binding, Trafficking, and GTP_YS Functional Assays available

GPCR Assay Formats

Construction Structure Constructure Constructure





Acetylcholine

Interrogating the three pathways for the same target revealed differences in the mechanism of action of each ligand.

- Carbachol
- ▲ Oxotremorine-M

These assays provide the ability to quantify "bias" for each potential drug candidate to help determine the overall quality of efficacy possessed by each drug.

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From Continuous Culture to Qualified Bioassays



Eurofins DiscoverX Qualified Bioassays are Designed for QC Lot Release Programs

Stable Cell Line Generation and Characterization

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[Anti-CD47], g/ml	-
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Passage	S/B	IC ₅₀ , ng/mL
1	11.5	71.9
14	9.8	55.7
33	14.0	49
45	14.2	49.5

S/B : 17% RSD over 45 passages IC₅₀ : <19% RSD over 45 passages







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Bioassays for Potency and Stability Testing Programs for Drug Release

Industry Requirements Drives Bioassay Development Strategy (Following ICH Based Guidelines)



- Reflective of MOA of the drug/molecule
- Stability-indicating
- Dilutional linearity (50%-150% Range)
 - Robust, precise, accurate
- Reproducible
 - Intra-lot (vial-to-vial)
 - Inter-lot (lot-to-lot)
 - Analyst-to-analyst
- Increasing assay throughput
- Reduce assay variability and failure rate
- Decrease operational costs
- Consistent method execution and seamless transfer between client sites

Assay Automation



Easy-to-Use Assay Protocol



Typical assay protocol for stable cell lines and assay ready kits



Simplified, universal assay format

Easy-to-follow, detailed user manuals Rapid, single addition protocol Homogeneous, no wash format

Sensitive detection with large S:B ratio

Easily quantified luminescence read-out Dose-response curve Utilizes any standard plate luminometer

Flexible Assays Adaptable to Drug Candidates with Different MOAs

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Anti-Receptor



Agonistic Antibody



Anti-Ligand



Clustering and Crosslinking

PathHunter OX40 Signaling Assay Test Molecule: Clustered Agonistic Antibody



Plate-Bound Ligand



Small Molecule Inhibitors



PathHunter PD-1 Signaling Assay Test Molecule: Small Molecule Inhibitors

Everything Necessary for the Assay is Included!

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CNR1 β-arrestin Assay Outline - *Automated steps shown in orange boxes*

Fluent[®] Produces High Inter-Day Assay Precision

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Each replicate dose-response curve across four independent experiments (12 curves)



Inter-day results show high precision in EC₅₀ across four individual experiments performed on four separate days

1	1 2 3	1.1e-8 1.5e-8	1.37e-8				
1	2 3	1.5e-8	1.37e-8			13.5%	
	3	1 56-8		16.9%	1.3e-8		
	4	1.00-0					
	1	1.5e-8	1.43e-8				
2	2	1.2e-8		14.5%			
	3	1.6e-8					
	1	1.1e-8		9.4%			
3	2	1.3e-8	1.23e-8				
	3	1.3e-8					
	1	9.3e-9		13.4%			
4	2	1.2e-8	1.04e-8				
	3	1.0e-8					
Intermediate Precision for EC ₅₀ (Inter-Day): 13.5%							

Key: RSD = Relative Standard Deviation



Qualified Bioassays for Precise Potency Determination for Cytokines and Interleukins

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Global Programs using DiscoverX Bioassays for Potency, Stability and NAb Testing for Drug Release



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SIRPα Bioassay	PD-1 Bioassay	VEGF Bioassay	Insulin Bioassay	CNR1 Bioassay	GLP1R Bioassay	IGF1R Bioassay	Bradykinin Bioassay	PTHR1 Bioassay
Multiple Programs in NA for originator biologics NAb assessment Programs at CROs	Multiple Programs in NA and APAC Clinical Development of Biosimilars	Multiple Programs in NA, EU and APAC Clinical Development of Biosimilars	Multiple Programs in and APAC for clinical Development of Biosimilars	US based Biopharma for originator biologic	Multiple Programs in NA, EU and APAC Clinical Development of Biosimilars in NA	Multiple Programs in NA and APAC for originator biologic	US based CRO for undisclosed client	Multiple Programs in NA, EU and APAC Clinical Development of Biosimilars
ErbB2/ErbB3 Bioassay	FGFR Bioassay	IL-1 Bioassay		* * 4	44. M-	Melanocortin Bioassay	IL-2 Bioassay	IL-23 Assay
Multiple Programs in NA, EU and APAC Clinical Development of Biosimilars	NAb assessment program for US based Biopharma	Multiple Programs in NA for originator biologic		A STATE		European Biopharma for an originator biologic	Multiple Programs in NA and EU for originator biologic	US Based Biopharma for originator biologic
IL-10 Bioassay	GM-CSF Bioassay	IL-31 Bioassay				RANK Assay	MC4R Bioassay	CXCR2 Bioassay
Multiple Programs in NA for originator biologic	Multiple Programs in EU and NA for originator biologic	US based pharma for NAb assessment and potency testing Programs for originator biologic			-	Multiple Programs in and APAC for clinical Development of Biosimilars	Bioassay Program in EU for originator biologic	Bioassay Program in NA clinical development and drug release
AXL Bioassay	CSF2R Bioassay	EGFR/ErbB2 Bioassay	CXCR4 Bioassay	IL7R/CRLF2 Bioassay	CALCRL/RAMP3 Bioassay	KILR CD16 Effectors	FSHR Bioassay	IL7R/IL2R Bioassay
Bioassay Program in NA for originator biologic	Multiple Programs in NA and EU Clinical development and drug release	Multiple Programs in NA and EU Clinical development and release	NAb assessment program for EU based Biopharma	Drug Release Program in EU for originator biologic	Bioassay Program in NA clinical development and drug release	Multiple Programs in NA and EU for Cytotoxicity Release assay	Bioassay Program in APAC for Biosimilar	Bioassay Program in EU for originator biologic

Accelerating Implementation Phase for QC Lot Release with Qualified Bioassays

Typical Bioassay Development Timeline



Eurofins DiscoverX Ready-to-Plate Bioassay Kits Save 9 Months of Assay Development Time

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Delivering Solutions From Discovery To Market

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For further information: <u>www.discoverx.com/bioassays</u> or visit booth #104²²