DiscoverX

SAFETY*scan*™
In Vitro Pharmacological Profiling Services

Functional Data for Improved Off-Target Liability Testing

Designed for lead optimization and safety profiling, DiscoverX's SAFETY*scan in vitro* pharmacological profiling services improve off-target liability testing. We offer functional assays with human targets for safety screening, improving upon traditional rodent-based binding assays. In addition, SAFETY*scan* services offer a broad menu, including the targets recommended by major pharmaceutical companies for safety profiling[1]. Assessing the specificity of lead compounds early in development using highly relevant and predictive assays allows more informed decision making about compound safety, ultimately leading to the development of safer and more effective drugs.

SAFETY*scan In Vitro* Pharmacological Profiling Services Highlights:

- Better confidence using human target assays, not rodent orthologs
- Functional data to support SAR analysis in lead optimization
- Cost effective alternative to in house assay development and profiling

Family	Target	Readout
GPCR		
Adenosine	A2A	Calcium mobilization
Adrenergic	α1A-adrenoceptor α2A-adrenoceptor β1-adrenoreceptor β2-adrenoreceptor	Calcium mobilization cAMP formation cAMP formation cAMP formation
Cannabinoid	CB1 CB2	cAMP formation cAMP formation
Cholecystokinin	CCK1	Calcium mobilization
Dopamine	D1 D2S	cAMP formation cAMP formation
Endothelin	ETA	Calcium mobilization
Histamine	H1 H2	Calcium mobilization cAMP formation
Muscarinic	M1 M2 M3	Calcium mobilization cAMP formation Calcium mobilization
Opioid and Opioid-Like	δ-opioid receptor κ-opioid receptor μ-opioid receptor	cAMP formation cAMP formation cAMP formation
Serotonin	5HT1A 5HT1B 5HT2A 5HT2B	cAMP formation cAMP formation Calcium mobilization Calcium mobilization
Vasopressin	V1A	Calcium mobilization

[1] Bowes *et al.*, *Nature Reviews*, **11**: 909-922 (2012)

Family	Target	Readout
Transporters		
Dopamine	DAT	Neurotransmitter uptake
Norepinephrine	NET	Neurotransmitter uptake
Serotonin	SERT	Neurotransmitter uptake
Ion Channels		
GABA Channel	GABAA	Membrane potential
Serotonin Channel	5-HT-3	Ion channel activity
CA^{+2} Channel	CAV1.2	Ion channel activity
K^{+} Channel	hERG	Ion channel activity
Na^{+} Channel	NAV1.5	Ion channel activity
Nuclear Receptors		
Steroid Nuclear Receptors	AR GR	Nuclear translocation Nuclear translocation
Kinases		
TK	LCK INSR VEGFR2	Binding Binding Binding
AGC	ROCK1	Binding
Non-Kinase Enzymes		
AA Metabolism	COX1 COX2	Enzymatic activity Enzymatic activity
Monoamine and Neurotransmitter	AChE MAOA	Enzymatic activity Enzymatic activity
Phosphodiesterases	PDE3A PDE4D2	Enzymatic activity Enzymatic activity

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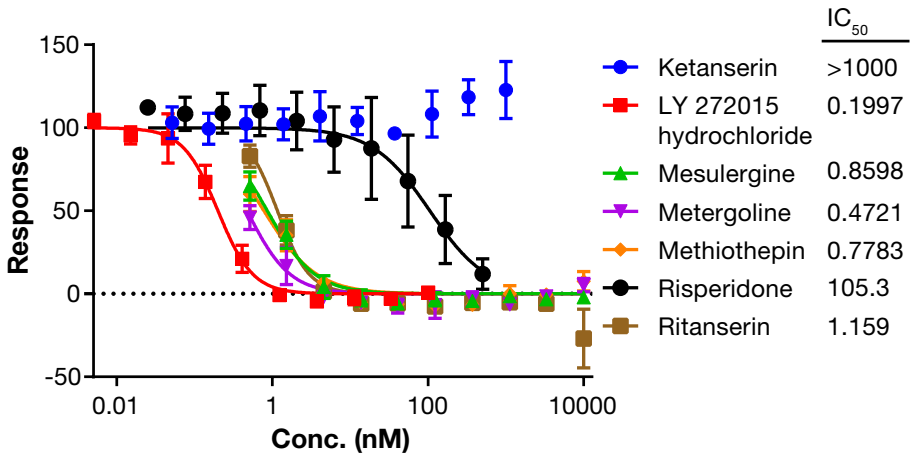
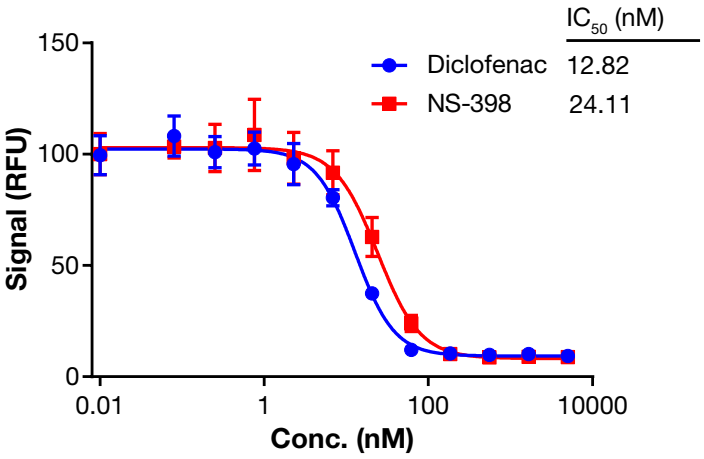
Functional Assays with Human Targets

Inhibition of Serotonin (5-Hydroxytryptamine) HTR2B by Reference Compounds



Cells were stimulated with reference compounds as shown in the figure. Following stimulation, calcium mobilization was detected using the DiscoverX's HitHunter® Calcium No Wash^{PLUS} detection kit (Cat. No. 90-0091) and IC_{50} was determined.

Inhibition of Cyclooxygenase COX2 by Reference Compounds



COX2 enzyme activity was determined by measuring the conversion of arachidonic acid to PPG2 based on fluorometirc readout. COX enzyme was incubated with the compounds at room temperature for 30 minutes before addition of the arachidonic acid (17 uM) and Ampliflu Red (25 uM). Plate was read on a fluorimeter with the emission detection at 590 nm with excitation wavelength 544 nm.

To learn more about the SAFETYscan™ *In Vitro* Pharmacological Profiling Services, please visit www.discoverx.com/safetyscan

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