Safety Pharmacology Solutions

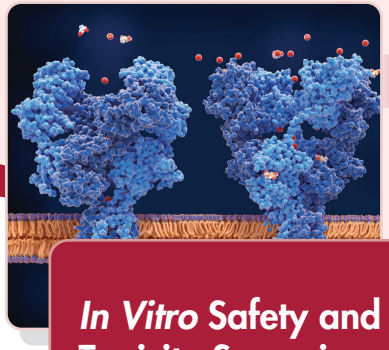
Unlocking the Potential of *In Vitro* Solutions for Safer Pharmaceuticals

Obtain early read on potential drug safety issues

Predicting potential safety liabilities early in drug discovery is paramount for effective lead compound selection. *In vitro* safety screening enables you to assess your compound's risk profile to efficiently select a lead candidate with minimal off-target effects and optimal potency.

Our Solutions for Safety Pharmacology

Our solutions for *in vitro* safety profiling allows you to determine the interaction between your compounds and a broad range of targets that may cause adverse drug reactions in humans.

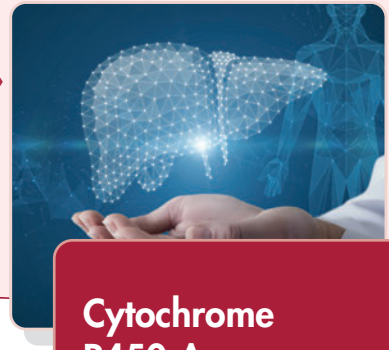


In Vitro Safety and Toxicity Screening

- Enzymatic, biochemical binding, radioligand binding, and functional assays
- A range of available targets including GPCRs, nuclear receptors, cytochrome P450s, ion channels, and more

Cardiac Safety Assessment

- *In vitro* hERG binding assays
- Ion channel screening with patch clamp
- Tissue-based action potential recording using isolated Purkinje fibers
- Organ-based ECG recording using Langendorff preparations



Cytochrome P450 Assays

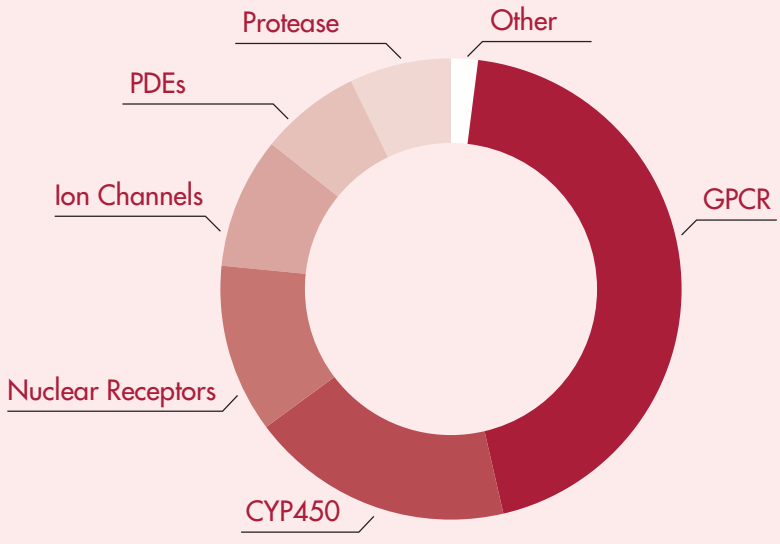
- Small to large scale CYP profiling
- High througput CYP screening
- Tailored solutions

Validated Targets by Family

Our validated targets include receptors, transporters, enzymes, and ion channels.

Early safety profiling includes more than 100 targets across 10 target families for broad coverage of potential adverse drug effects.

All of our selected targets are clinically relevant. Their inhibition was shown to cause potentially serious health problems.



Discover our InVEST™ Targets

In Vitro Evaluation of Safety and Toxicity (InVEST) Made Simple

Our InVEST targets are specifically designed to help you investigate your compound's effects on a large selection of targets. Adding your compound to our monthly screening runs is an efficient and economical way to address your *in vitro* safety screening needs.

InVEST Biochemical

- 70 targets and growing
- Radioligand binding, enzymatic activity, and fluorescent polarization assay formats

InVEST Functional

- A growing panel of more than 30 targets
- Fully customizable target selction

InVEST Cardiac

- Cell-based patch clamp for ion channel screening including hERG, NaV1.5, CaV.2, and nAChR (α4/β2)
- Manual and automated patch formats

InVEST Kinase

- A customizable panel from our selection of over 750 kinase targets

InVEST CYP

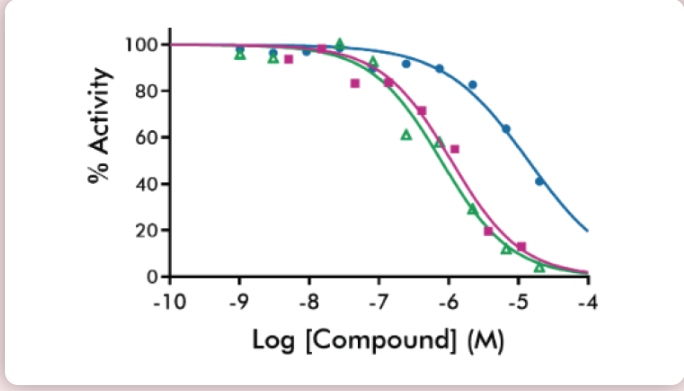
- Compound profiling against the 14 most important CYP isoforms to provide early guidance on a compound's toxicity
- Simple "mix-and-read" fluorescent assay for high-throughput analysis

Why Choose from our InVEST Targets?

- **Efficiency:** selected targets are enrolled in monthly screening runs
- **Robustness:** InVEST target screens are set up as single concentration testing in duplicates
- **Quality Assurance:** IC_{50} values of reference controls are included for each assay
- **Expertise:** direct access to our experts for consultation

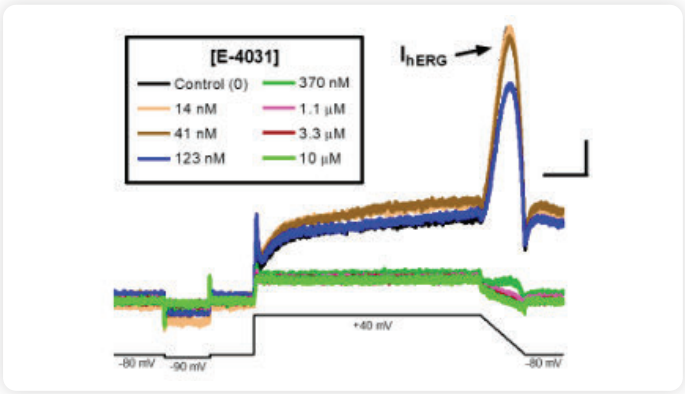
Test your compound against our preselected targets or build your own panel suited to your unique project needs

Sample Data: Enzymatic Activity Assay with a PDE

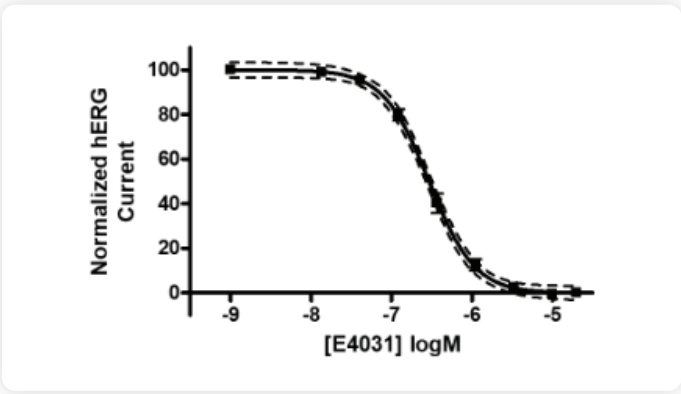


Three reference compounds IBMX, methoxyquinazoline, and Rolipram were tested against the activity of cAMP-specific cyclic phosphodiesterase 4A (PDE4A). Concentration-response curves are shown with semi-log concentrations in singlicates with the following parameters:
- IBMX (blue): IC_{50}= 1.4e-05, hillslope= -0.72
- Methoxyquinazoline (green): IC_{50}= 7.82e-07, hillslope= -0.86
- Rolipram (purple): IC_{50}= 1.1e-06, hillslope= -0.86

Sample data from InVEST Cardiac
Recording of hERG current by manual patch



Example recording of hERG current (I_{hERG}) from CHO hERG-Duo cells (B'Sys) using manual patch.



Concentration-dependent effect of E-4031 on hERG current recorded using manual patch (n=23, 6 independent preparations): IC_{50}=294 nM, Hill Slope=-1.53).

Discover our Targets

InVEST Biochemical

Target Family	Target Name	Assay Format	Species
Cyclooxigenase	COX-1	Enzymatic Activity	Ovine
	COX-2	Enzymatic Activity	Human
Cytochrome P450	CYP1A2	Enzymatic Activity	Human
	CYP2A6	Enzymatic Activity	Human
	CYP2B6	Enzymatic Activity	Human
	CYP2C8	Enzymatic Activity	Human
	CYP2C9	Enzymatic Activity	Human
	CYP2C19	Enzymatic Activity	Human
	CYP2D6	Enzymatic Activity	Human
	CYP2E1	Enzymatic Activity	Human
	CYP2J2	Enzymatic Activity	Human
	CYP3A4 (BOMCC)	Enzymatic Activity	Human
	CYP3A5	Enzymatic Activity	Human
	CYP4A11	Enzymatic Activity	Human
	CYP4F3B	Enzymatic Activity	Human
	CYP19A	Enzymatic Activity	Human
GPCR	Adenosine A1	Radioligand Binding	Human
	Adenosine A2A	Radioligand Binding	Human
	Adrenergic a1A	Radioligand Binding	Human
	Adrenergic α2A	Radioligand Binding	Human
	Adrenergic β1A	Radioligand Binding	Human
	Adrenergic β2A	Radioligand Binding	Human
	Cannabinoid CB1	Radioligand Binding	Human
	Cannabinoid CB2	Radioligand Binding	Human
	Cholecystokinin CCK1	Radioligand Binding	Human
	Dopamine D1	Radioligand Binding	Human
	Dopamine D2S	Radioligand Binding	Human
	Dopamine D3	Radioligand Binding	Human
	Histamine H1	Radioligand Binding	Human
	Histamine H2	Radioligand Binding	Human
	Muscarinic M1	Radioligand Binding	Human
	Muscarinic M2	Radioligand Binding	Human
	Muscarinic M3	Radioligand Binding	Human
	Muscarinic M4	Radioligand Binding	Human
	Muscarinic M5	Radioligand Binding	Human
	Opioid (δ)	Radioligand Binding	Human
	Opioid (κ)	Radioligand Binding	Human
	Opioid (μ)	Radioligand Binding	Human
	Serotonin 5-HT1A	Radioligand Binding	Human
	Serotonin 5-HT1B	Radioligand Binding	Human
	Serotonin 5-HT2A	Radioligand Binding	Human
	Serotonin 5-HT2B	Radioligand Binding	Human
Ion Channel	GABAA (Central BDZ)	Radioligand Binding	Rat
	hERG	Fluorescence Polarization	Human
	NMDA	Radioligand Binding	Rat
	Serotonin 5-HT3	Radioligand Binding	Human
Monoamine Oxidase	MAO-A	Enzymatic Activity	Human
	MAO-B	Enzymatic Activity	Human
Nuclear Receptor	Estrogen-α (ERalpha)	Fluorescence Polarization	Human
	Glucocorticoid	Fluorescence Polarization	Human
	PPARgamma	Fluorescence Polarization	Human
	Progesterone PR	Fluorescence Polarization	Human
Phosphodiesterase	PDE1A	Enzymatic Activity	Human
	PDE1B	Enzymatic Activity	Human
	PDE1C	Enzymatic Activity	Human
	PDE2A	Enzymatic Activity	Human
	PDE3A	Enzymatic Activity	Human
	PDE3B	Enzymatic Activity	Human
	PDE4A	Enzymatic Activity	Human
	PDE4B	Enzymatic Activity	Human
	PDE4C	Enzymatic Activity	Human
	PDE4D	Enzymatic Activity	Human
	PDE4D2	Enzymatic Activity	Human
	PDE5A	Enzymatic Activity	Human
	PDE7A	Enzymatic Activity	Human
	PDE7B	Enzymatic Activity	Human
	PDE8A	Enzymatic Activity	Human
	PDE9A	Enzymatic Activity	Human
	PDE10A	Enzymatic Activity	Human
Protease	ACE1	Enzymatic Activity	Human
	Cathepsin G	Enzymatic Activity	Human
	Thrombin alpha	Enzymatic Activity	Human
Transporter	Dopamine (DAT)	Radioligand Binding	Human
	Norepinephrine (NET)	Radioligand Binding	Human
	Serotonin (SERT)	Radioligand Binding	Human
Other Enzymes	Acetylcholinesterase	Enzymatic Activity	Human
	LCK TK	Enzymatic Activity	Human

InVEST Functional

Target Family	Target Name	Endpoint	Assay Format
GPCR	Adrenergic α1A	Agonist/Antagonist	FLIPR/Ca assay
	Cannabinoid CB1	Agonist/Antagonist	FLIPR/Ca assay
	Dopamine D1	Agonist/Antagonist	Envision/cAMP assay
	Endothelin ETA	Agonist/Antagonist	FLIPR/Ca assay
	Histamine H1	Agonist/Antagonist	FLIPR/Ca assay
	Histamine H2	Agonist/Antagonist	FLIPR/Ca assay
	Muscarinic M3	Agonist/Antagonist	FLIPR/Ca assay
	Opioid (δ)	Agonist/Antagonist	FLIPR/Ca assay
	Opioid (κ)	Agonist/Antagonist	FLIPR/Ca assay
	Opioid (μ)	Agonist/Antagonist	FLIPR/Ca assay
	Serotonin 5-HT2A	Agonist/Antagonist	FLIPR/Ca assay
	Serotonin 5-HT2B	Agonist/Antagonist	FLIPR/Ca assay
	Vasopressin V1A	Agonist/Antagonist	Cell Reporter
Ion Channel	Cav1.2	Inhibitor	Patch Clamp
	hERG	Inhibitor	Patch Clamp
	nAChR (α4/β2)	Agonist/Antagonist	FLIPR/Ca assay
	Nav1.5	Inhibitor	Patch Clamp
Nuclear Receptor	Androgen	Agonist/Antagonist	Cell Reporter
	Estrogen-α (ERalpha)	Agonist/Antagonist	Cell Reporter
	Glucocorticoid	Agonist/Antagonist	Cell Reporter
	Progesterone PR	Agonist/Antagonist	Cell Reporter
Transporter	Dopamine (DAT)	Inhibitor	FLIPR/NT assay

InVEST Cardiac

Category	Target Name	HGNC reference	Synonyms
Calcium Ion Channel	Cav1.2 Ion Channel	CACNA1C	Cav1.2, CACH2, CACN2, TS, LQT8, Voltage-dependent L-type calcium channel subunit alpha-1C
Potassium Ion Channel	hERG Ion Channel	KCNH2	potassium voltage-gated channel subfamily H member 2, Ether-a-go-go-related gene potassium channel 1, Kv11.1
Sodium Ion Channel	Nav1.5 Ion Channel	SCN5A	sodium voltage-gated channel alpha subunit 5, Nav1.5 LQT3, HB1, HBBD, PFHB1, IVF, HB2 HH1 SSS1 CDCD2, CMPD2, ICCD

InVEST Panels

Panels	Panel Size	Description
InVEST44	44	The InVEST44 panel covers a well-published set of 44 targets spanning core biological systems and secondary organs, enabling identification of common off-target interactions for a comprehensive early assessment of a drug candidate's safety.
InVEST CYP	14	The InVEST CYP panel provides profiling against the most important CYP isoforms to deliver early guidance on a compound's toxicity. Our CYP450 inhibition assays are performed with the Vivid™ CYP450 assay technology to detect the activity of CYP enzymes in a simple "mix-and-read" fluorescent assay which is suitable for high-throughput analysis.
InVEST PDE	17	Phosphodiesterase (PDE) screening is performed with an activity assay format based on the hydrolysis of cyclic AMP and cyclic GMP. Inhibition of PDEs prevents the regulation of these second messengers and was found useful in the treatment of a variety of conditions including pulmonary hypertension, acute refractory cardiac failure, erectile dysfunction, etc.

Custom Panel Available: Please Inquire

Ask us about our InVEST Kinase Targets

Reaction Biology Corp.

1 Great Valley Parkway, Suite 2, Malvern, PA 19355

+1.610.722.0247

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REACTION BIOLOGY