Safety Pharmacology Solutions

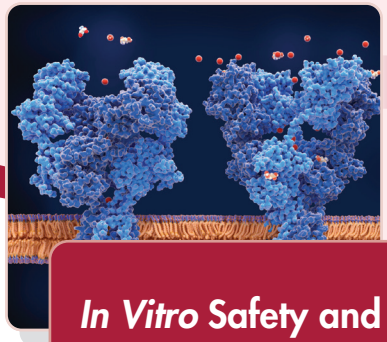
Unlocking the Potential of *In Vitro* Solutions for Safer Pharmaceuticals

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.

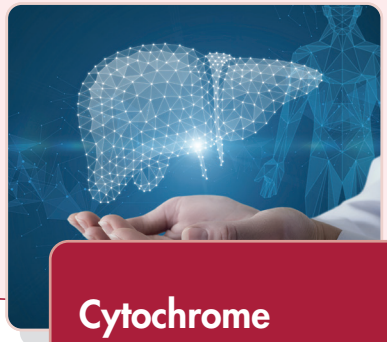


In Vitro Safety and Toxicity Screening

- 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

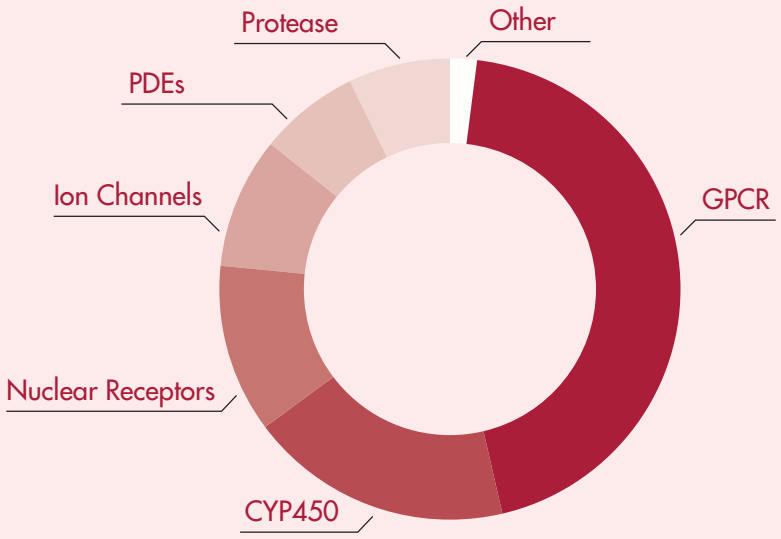
- Small to large scale CYP profiling
- High througput CYP screening
- Tailored solutions

Validated Targets by Family

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

Early safety profiling includes more than 70 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 25 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

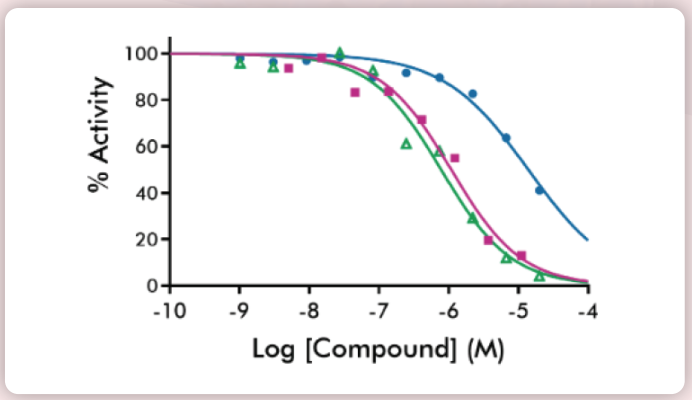
- Compound profiling against the 12 most important CYP isoforms to provide early guidance on a compound's toxicity
- Simple "mix-and-read" fluorescent assay for high-throughput analysis

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

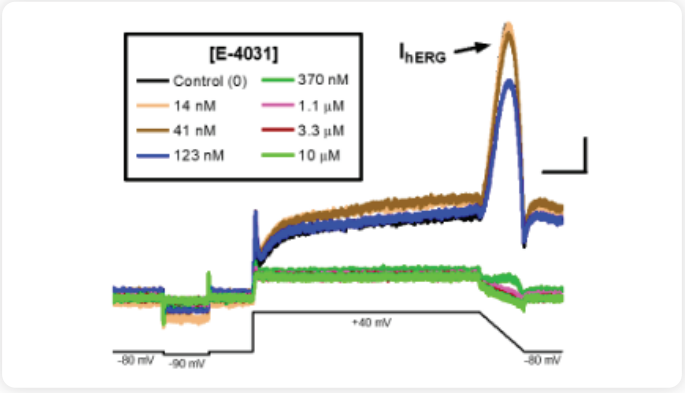
Test your compound against our preselected targets or build your own panel suited to your unique project needs

Sample Data: Enzymatic Activity Assay with a PDE

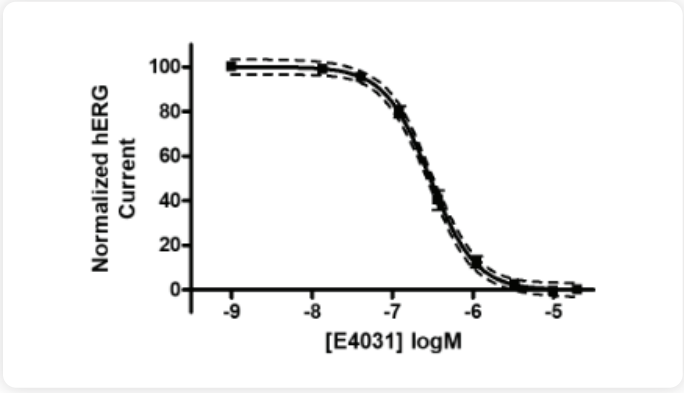


Three reference compounds IBMX, methoxyquinazoline, and Rolipram were tested against the activity of cAMP-specific cyclic phosphodiesterase 4A (PDE4A). Concentration-response curves are shown with semi-log concentrations in singlicates with the following parameters:
- IBMX (blue): IC_{50}= 1.4e-05, hillslope= -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	1A2	Enzymatic activity	Human
	2A6	Enzymatic activity	Human
	2B6	Enzymatic activity	Human
	2C8	Enzymatic activity	Human
	2C9	Enzymatic activity	Human
	2C19	Enzymatic activity	Human
	2D6	Enzymatic activity	Human
	2E1	Enzymatic activity	Human
	2J2	Enzymatic activity	Human
	3A4	Enzymatic activity	Human
	3A5	Enzymatic activity	Human
GPCR	Adenosine A1	Radioligand filter binding	Human
	Adenosine A2A	Radioligand filter binding	Human
	Adrenergic α1A	Radioligand filter binding	Human
	Adrenergic α2A	Radioligand filter binding	Human
	Adrenergic β1	Radioligand filter binding	Human
	Adrenergic β2	Radioligand filter binding	Human
	Cannabinoid CB1	Radioligand filter binding	Human
	Cannabinoid CB2	Radioligand filter binding	Human
	Cholecystokinin CCK1	Radioligand filter binding	Human
	Dopamine D1	Radioligand filter binding	Human
	Dopamine D2S	Radioligand filter binding	Human
	D3 dopamine	Radioligand filter binding	Human
	Histamine H1	Radioligand filter binding	Human
	Muscarinic M1	Radioligand filter binding	Human
	Muscarinic M2	Radioligand filter binding	Human
	Muscarinic M3	Radioligand filter binding	Human
	Muscarinic M4	Radioligand filter binding	Human
	Muscarinic M5	Radioligand filter binding	Human
	Opioid δ	Radioligand filter binding	Human
	Opioid μ	Radioligand filter binding	Human
	Opioid κ	Radioligand filter binding	Human
	Serotonin 5-HT1A	Radioligand filter binding	Human
	Serotonin 5-HT1B	Radioligand filter binding	Human
	Serotonin 5-HT2A	Radioligand filter binding	Human
	Serotonin 5-HT2B	Radioligand filter binding	Human
	Vasopressin V1A	Cell reporter	Human
Ion Channel	5HT3	Radioligand filter binding	Human
	GABAA (Central BDZ)	Radioligand filter binding	Rat
	hERG	Fluorescence Polarization	Human
	NMDA	Radioligand filter binding	Rat
MAO	MAO-A	Enzymatic Activity	Human
	MAO-B	Enzymatic Activity	Human
Nuclear Receptor	Androgen	Cell reporter	Human
	Estrogen-α	Fluorescence Polarization	Human
	Glucocorticoid	Fluorescence Polarization	Human
	PR Progesterone	Fluorescence Polarization	Human
	PPARγ	Fluorescence Polarization	Human
PDE	PDE3A	Enzymatic Activity	Human
	PDE4A	Enzymatic Activity	Human
	PDE4D	Enzymatic Activity	Human
	PDE4D2	Enzymatic Activity	Human
Protease	ACE-1	Enzymatic Activity	Human
	Cathepsin G	Enzymatic Activity	Human
	Thrombin α	Enzymatic Activity	Human
Transporter	Dopamine (DAT)	Radioligand filter binding	Human
	Norepinephrine (NET)	Radioligand filter binding	Human
	Serotonine (SERT)	Radioligand filter binding	Human
Other enzymes	Acetylcholinesterase	Enzymatic Activity	Human
	LCK TK	Enzymatic Activity	Human

InVEST Functional

Target Family	Target Name	Assay Format	Species
GPCR	5-HT2A Human Serotonin	Agonist/Antagonist	FLIPR/Ca assay
	5-HT2B Human Serotonin	Agonist/Antagonist	FLIPR/Ca assay
	α1A Human Adrenoceptor	Agonist/Antagonist	FLIPR/Ca assay
	CB1 Human Cannabinoid	Agonist/Antagonist	FLIPR/Ca assay
	D1 Human Dopamine	Agonist/Antagonist	Envision/cAMP assay
	H1 Human Histamine	Agonist/Antagonist	FLIPR/Ca assay
	H2 Human Histamine	Agonist/Antagonist	FLIPR/Ca assay
	M3 Human Muscarinic	Agonist/Antagonist	FLIPR/Ca assay
	μ Human Opioid	Agonist/Antagonist	FLIPR/Ca assay
	δ Human Opioid	Agonist/Antagonist	FLIPR/Ca assay
	κ Human Opioid	Agonist/Antagonist	FLIPR/Ca assay
	ETA Human Endothelin	Agonist/Antagonist	FLIPR/Ca assay
	V1A Vasopressin	Agonist/Antagonist	Envision/luciferase assay
Transporter	DAT Human Dopamine Transporter	Inhibitor	FLIPR/NT assay
Ion Channels	hERG	Inhibitor	Manual/automated patch clamp
	Nav1.5	Inhibitor	Manual/automated patch clamp
	Cav1.2	Inhibitor	Manual/automated patch clamp
	nAChR (α4/β2)	Agonist	Automated patch clamp

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 CYP

Name	Synonym
CYP19A	Aromatase, CYP19A1, CYP 19A
CYP1A2	Cytochrome P450, family 1, subfamily A, polypeptide 2, CYP 1A2
CYP2A6	Cytochrome P450, family 2, subfamily A, polypeptide 6
CYP2B6	Cytochrome P450, family 2, subfamily B, polypeptide 6
CYP2C19	Cytochrome P450, family 2, subfamily C, polypeptide 19
CYP2C8	Cytochrome P450, family 2, subfamily C, polypeptide 8
CYP2C9	Cytochrome P450, family 2, subfamily C, polypeptide 9
CYP2D6	Cytochrome P450, family 2, subfamily D, polypeptide 6
CYP2E1	Cytochrome P450, family 2, subfamily E, polypeptide 1, CYP 2E1
CYP2J2	Cytochrome P450, family 2, subfamily J, member 2
CYP3A4	Cytochrome P450, subfamily IIIA, polypeptide 4
CYP3A5	Cytochrome P450, subfamily IIIA, polypeptide 5
CYP4A11	CYP4A2, CP4AB, Cytochrome P-450HK-omega
CYP4F3B	LTB4H, 20-hydroxyeicosatetraenoic acid synthase, CYPIVF3

Ask us about our InVEST Kinase Targets

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REACTION BIOLOGY