

CEREP SERVICES

Cerep offers preclinical drug discovery services for *in vitro* pharmacology, *in vitro* ADME-Tox & *in vivo* pharmacokinetics, and provides solutions allowing faster and cost-effective drug discovery by identifying at early stages the most promising drug candidates as well as eliminating those compounds likely to fail in development.

Cerep has developed unique know-how based on technologies of *in vitro* screening and of profiling using its proprietary database BioPrint[®], which allows the modeling of clinical effects of drug candidates from their molecular properties.

In 2010, services provided are clearly distinguished in two categories:

- ▶ Screening – profiling on standard assays/platforms and compound management ;
- ▶ Custom services encompassing assay development, adaptation to new technologies/biological models, profile design, data interpretation/consultancy supported by BioPrint[®] if appropriate.

Standard services are detailed in our 2010 catalog and Cerep custom offer is described using case studies and tool boxes in a Custom Research services brochure to be made public during the first half of 2010.

The strength of our services also originates from our in-house production of biological material or from established partnerships with renowned reagents providers (such as PerkinElmer).

Cerep's technologies benefit to more than 460 pharmaceutical and biotechnological companies worldwide including most of the top pharmaceutical firms.

Cerep's next objective is to open satellite laboratories, closer to where compounds are synthesized and drug candidates optimized, thus further decreasing turnaround time for data generation and delivery to discovery teams. According to plans, Cerep is proud to announce the opening of the first of those satellites in Shanghai, China.

The success of this endeavour can only be achieved through the provision of consistent high quality data – reason for Cerep's permanence – wherever the screening is performed.

BROAD PROFILING/SCREENING SERVICES

Cerep continues to expand and diversify the assay families in our catalog, with around 100 assays added each year. We now offer 14 PDE's, 24 phosphatases, 143 cellular functional GPCRs, 270 kinases, including 16 cellular kinase assays ...

Cerep's broad profiling/screening services can help you navigate toward more efficient drug discovery. They include:

- ▶ Assay design
- ▶ Assay development/transfer
- ▶ Compound management
- ▶ High throughput screening
- ▶ High throughput profiling
- ▶ Fast turnaround selectivity screening

Cerep's platforms cover a wide range of target classes including ADME-Tox related targets; peptide and non peptide GPCRs; various enzymes, transporters, nuclear receptors and ion channels; employing methods and assay types such as radioligand binding assays, calcium mobilization and cAMP measurement using TR-FRET, transporter/uptake assays, and bioluminescent and other fluorescent-based assays

More than a hundred assays are developed each year, selected through various families to offer the most representative targets. They are either integrated in the Cerep catalog or are exclusively available to sponsor.

Advantages of our broad profiling services include:

- ▶ Reproducibility – year after year – 21 years of experience.
- ▶ Low rejection rate allowing rapid delivery of results and rigorous quality control process
- ▶ Practical and operational innovation providing efficient custom oriented services (highly flexible and specialized teams and a lean organization)
- ▶ Excellent scientific support.

■ ASSAY DESIGN AND DEVELOPMENT

Our customized assay development services include a full range of assays and technologies adapted to clients' specific projects and needs. Whether performing a million-compound primary screening, or secondary profiling of hits or lead candidates, you need tools that support the prediction of human biology. Cerep has an extensive and integrated suite of core competencies that will be valuable to your drug discovery programs.

■ TOOL-BOX SOLUTIONS

The tool boxes shown below provide information about Cerep's know-how and expertise to develop assays. **They are extendable to other studies, targets and technologies depending on your needs.**

Please consult us for a specific solution adapted to your specific request.

► Tool-box for GPCR assay development

Studies ↓	Targets →	Gi	Gq	Gs	G12/13/?
Binding Association/Dissociation kinetic		Filtration SPA	Filtration SPA	Filtration SPA	Filtration SPA
Agonist Antagonist Allosteric modulator		Filtration SPA TR-FRET Alphascreen® Impedance ¹	TR-FRET Fluorescence ¹ Impedance ¹ Luminescence	TR-FRET Alphascreen® ¹ Impedance ¹	Impedance ¹ ELISA
Inverse agonist		TR-FRET Alphascreen® Impedance	Impedance	TR-FRET Alphascreen Impedance	Impedance
Desensitization		Impedance ¹	Fluorescence ¹ Impedance ¹ Luminescence	Impedance ¹	Impedance ¹
Weak agonist/antagonist		Impedance ¹	Impedance ¹	Impedance ¹	Impedance ¹
Transduction mechanism		Impedance ¹	Impedance ¹	Impedance ¹	Impedance ¹
Deorphanization		Impedance	Impedance	Impedance	Impedance
Kinase phosphorylation		Surefire®	Surefire®	Surefire®	Surefire®

¹ Recommended for endogeneous targets

► Tool-box for enzyme assay development

Technology ↓	Target →	Oxido reductases	Transferases	Hydrolases	Lyases	Isomerases
TR-FRET Alphascreen® Impedance			Kinases • ^C TKRs • ^{A,B,C}	PDEs • ^C	AC • ^C GC • ^C	
Fluorometry		CYPs COXs • TXA ₂ synthetase •	COMT •	HDACs • Sirtuins • ^A GTPase • ^A Phosphatases • Proteases • GABA transaminase •		Topoisomerases •
Radiometry		NOS • Tyr hydroxylase •	HNMT • PNMT •	PLC • PLA ₂ •		Polymerase •
Spectrophotometry		HMGC red • LOs • CYPs • MAOs • ^B Myeloperoxidase • Xanthine oxidase •		Proteases • ACH esterase • ATPase • ^B Arginase •	CA •	

All: Inhibition assay on cell-free model

• direct measurement (labeled substrate) • indirect measurement (unlabelled substrate)

^A Activation assays also available - ^B Binding assays also available - ^C Cell-based models also available

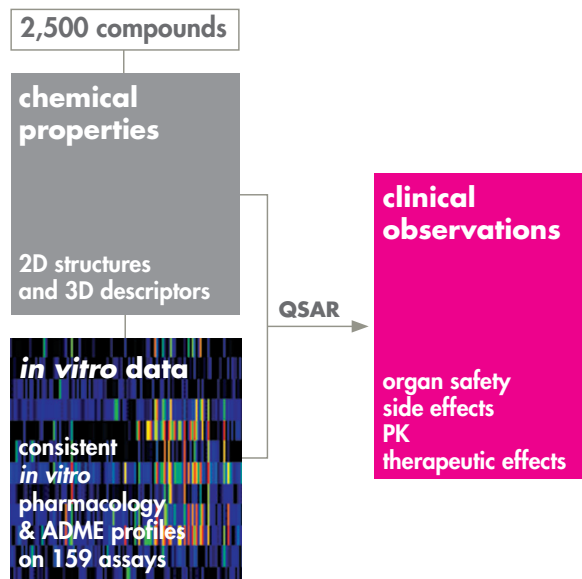
■ BIOPRINT® PROFILE & SERVICES

BioPrint® is a large, homogenous pharmacology and ADME database, which provides a unique resource for supporting decision making in drug discovery. The database is composed of three main data sets:

- ▶ chemical descriptors (structures and chemical information, 2D and 3D descriptors),
- ▶ *in vitro* data also considered as compound descriptors,
- ▶ collected and curated *in vivo* effects of drugs.

Chemical and pharmacophoric descriptors together form a data set for QSAR generation supporting organ safety modeling.

BioPrint® positions a new drug candidate in the context of marketed drugs, anticipating potential *in vivo* liabilities, predicting off-target activities, and ADME characteristics (Drug profile interpretation). In another application, BioPrint® serves to identify secondary targets that are not genetically parented to a test target (Target profile design). Both these applications are available as custom services without need of subscription to BioPrint®.



■ BIOPRINT® PROFILE

The **BioPrint® profile** includes the assays used to explore the properties of about 2,500 BioPrint® compounds (mainly marketed drugs and reference compounds), establishing individual Pharma-ADME fingerprints for each compound.

Offered on a standard basis, this profile is mainly based on target diversity and includes today 105 binding assays (non-peptide, peptide and nuclear receptors, ion channels and amine transporters), 34 enzyme assays (including 10 kinases, 10 proteases and 5 phosphodiesterases), as well as 20 ADME-Tox assays (Solubility, Absorption, LMS and CYP-mediated drug-drug interaction). More than 70% are human targets.

The 159 assays of this profile represent a rationalized panel from a larger assay collection in the database, selected for highest information content.

■ BIOPRINT® DRUG PROFILE INTERPRETATION

Any compound in drug development, when run as a test compound on the BioPrint® profile, can be placed in the context of already marketed drugs, when similar *in vitro* profiles exist in the database. Hypotheses on clinical behavior of the test compounds can be drawn by comparison with data on BioPrint® compounds that have been collected and analyzed over the last ten years, including:

- ▶ **Clinical effects of drugs** with a similar profile or sub-profile.
- ▶ **Adverse Drug Reactions (ADRs) correlated with *in vitro* assays:** more than 5,000 significant statistical associations have been identified between the activity of molecules on a specific target and the occurrence of an ADR in man.
- ▶ **Probability of occurrence of clinical effects or ADRs** estimated with multivariate models using the complete *in vitro* profile: today more than 170 ADRs have been modeled.

■ BIOPRINT® TARGET PROFILE DESIGN

Any target, run as a test target on the BioPrint® compound library, can be compared to any other target in BioPrint®, based on its pharmacological profile (compounds that interact with a given target). Analysis of cross-reacting compounds between targets (number and intensity of common hits), allows to identify targets that are “pharmacophorically related” to the test target. Interestingly, a profile of pharmacophorically related targets can differ significantly to a list of genetically related targets.

BioPrint® target profile design represents highly valuable information, when setting up secondary screening tests, anticipating secondary targets and effectively supporting lead optimization to monitor potential secondary target related liability issues. If the test target is already part of BioPrint® assays, BioPrint® target profile design is limited to data-analysis and establishment of a profile of secondary targets. If the test target is not part of the BioPrint® assay panel, Cerep can develop the assay and run the BioPrint® compounds on an exclusive or shared data basis.

PRICING & PRIVILEGED PARTNERSHIPS

Over the past years, Cerep has maintained prices (not even increasing them at the level of inflation) or rather decreased its prices: for example in 2010 ADMET-PK and kinase assay prices have decreased on average by 30%, cellular functional GPCR assay prices have decreased on average by 20%, ...

Cerep strives sharing economy of scale and productivity gains with clients for example:

- ▶ when better conditions are negotiated with reagents/consumables suppliers,
- ▶ by entering into collaborations such as with PerkinElmer allowing optimized, streamlined project resources management,
- ▶ when new cost effective processes are implemented in the supply chain management, and,
- ▶ of course according to specific project specifications: the more compounds or concentrations tested in single experiment the lower the cost.

Significant discounts from catalog prices are available based on: Number of test concentrations submitted for a single study, number and type of assays selected for a single study and repeated recurring use of Cerep's standard or customized profiles.

PRIVILEGED PARTNERSHIPS

Depending on the amount of business you had with Cerep in 2009, and that you are ready to commit in 2010, you automatically benefit from the following advantages and will obviously keep your agreed conditions whenever they are better than those outlined below:

Amount of business ¹	Client category	Maximum price per well	Maximum price per well	Maximum price per compound ²	Discount from catalog price
		BINDING ASSAYS ³	BIOCHEMICAL KINASE ASSAYS	CELLULAR FUNCTIONAL GPCR ASSAYS	ALL OTHER ASSAYS ³ & STANDARD PROFILES
▶ \$ 60,000	BRONZE	\$ 54	\$ 15	\$ 55	15 %
▶ \$ 150,000	SILVER	\$ 50	\$ 12.5	\$ 46	20 %
▶ \$ 450,000	GOLD	\$ 44	\$ 10.5	\$ 39	25 %
▶ \$ 900,000	PLATINUM	\$ 40.5	\$ 9.5	\$ 35	30 %
▶ \$ 2,500,000	PREMIUM	\$ 37	\$ 8	\$ 31	35 %

¹ Amount of business with Cerep in 2009 and/or committed in 2010.

² For both agonist and antagonist effects (n=1).

³ Excluding assays indicated ☒ Please inquire for applicable discounts.



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■ QUESTIONS OR CONCERNS?

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