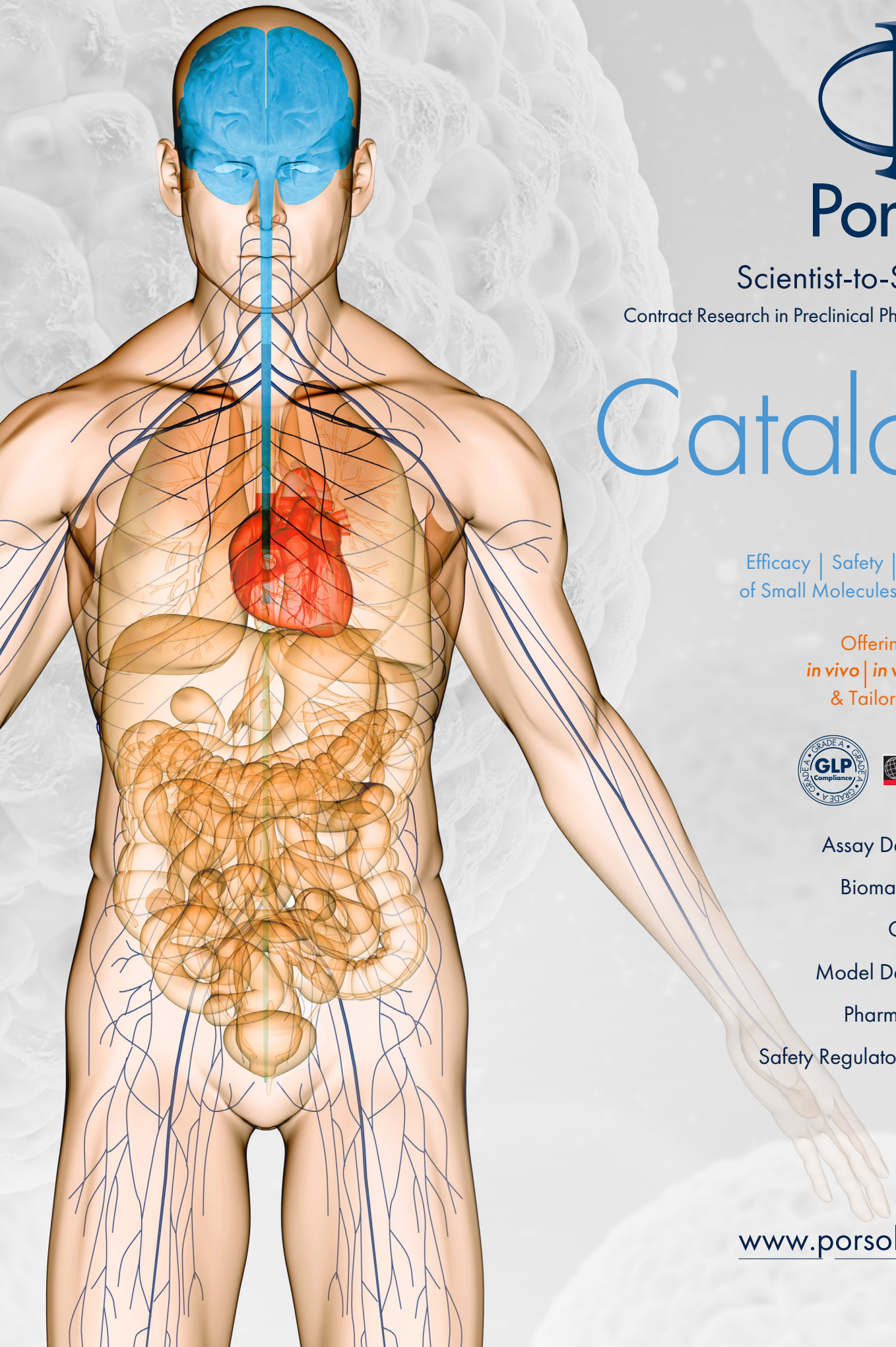


Porsolt

Scientist-to-Scientist

Contract Research in Preclinical Pharmacology

2023

Catalog

Evaluating
Efficacy | Safety | Toxicology
of Small Molecules & Biologics

Offering Discovery
in vivo | ***in vitro*** Models
& Tailored Solutions

GRADE A GLP Compliance GRADE A

aaalac INTERNATIONAL

Assay Development

Biomarker Assays

Cell Biology

Model Development

Pharmacokinetics

Safety Regulatory Package

www.porsolt.com

PORSOLT, A LONG ESTABLISHED, AAALAC ACCREDITED AND FULLY GLP COMPLIANT, PRECLINICAL CRO, HAS BEEN PROVIDING EFFICACY EVALUATION AND SAFETY PHARMACOLOGY SERVICES ALMOST 40 YEARS, COVERING THE DRUG DEVELOPMENT PROCESS FROM EARLY SCREENING THRU REGULATORY SUBMISSION.

PORSOLT PROVIDES PATHOPHYSIOLOGICAL MODELS IN MULTIPLE SPECIES AND CELL LINES, CUSTOMIZED PROCEDURES AND TAILORED SOLUTIONS, INCLUDING IN VITRO ASSAYS, DRUG FORMULATION ANALYSIS AND BIOANALYTICAL SERVICES, FROM HIGHTHROUGHPUT SCREENING, HIGH-CONTENT ANALYSIS AND HIGH-CONTENT HISTOLOGY PLATFORMS, TO MODELS FOR PSYCHIATRIC AND NEUROLOGICAL DISORDERS, PAIN, CARDIAC AND VASCULAR DISEASES, METABOLIC AND EATING DISORDERS, DERMATOLOGY AND ONCOLOGY

Assay & Model Development

Porsolt's vast experience and varied expertise, including newly incorporated in vitro, biomarker and histology capabilities, provides the perfect solution for clients looking for bespoke model development.

Porsolt is uniquely placed to combine in vitro and in vivo models and capabilities from multiple species and disease areas in order to answer the specific questions from our clients.

Whether performing high-throughput screening, high-content analysis, mechanism of action, efficacy or safety testing, Porsolt is the ideal partner for your development programs.

Cell Biology

Porsolt maintains a panel of over 100 validated cell-based assays that allow for the quantification of key phenotypic and molecular events at the single-cell level.

Most of the cellular assays listed below can be adapted to different biological models, or modified for different detection platforms, according to your needs.

Learn about our assay development services:

- Cell proliferation, migration, differentiation (live cell kinetic image analysis – Incucyte®, flow cytometry,Ensight)
- Primary cell isolation, culture and characterization (Immunophenotyping ...) and iPS cell handling (culture and functional assays)
- Biomarker analysis (Luminex, WB, ELISA, CBA, HTRF ...)
- Cell stress, metabolism, inflammation and signaling pathways
- Predictive toxicology (cell death / health, apoptosis)
- Gene expression modulation (siRNA transfection, AAV / LVV transduction)

Consulting

Porsolt's unique expertise and experience, combined with our broad portfolio of services in multiple species, allows us to provide unparalleled consulting and advice on the preclinical process and bespoke model development to address specific questions.

This includes efficacy evaluation, safety pharmacology, discovery and regulatory needs.

Contents 2023

> New developments in progress ?

Follow us on LinkedIn/company/porsolt
and on our website: *www.porsolt.com*

Recent News & Updates

Renewal of Porsolt's GLP compliance

Porsolt's Good Laboratory Practice (GLP) compliance status has been renewed for a further 2 years (until late 2024), with the receipt of an "A" Grade evaluation by the independent ANSM authority.

This uniquely places Porsolt in the preclinical CRO market, recognizes the high standards of work, and confirms its scientists are well versed and trained in GLP guidelines. This experience and approach is extremely valuable for early stage research and mandatory GLP studies.

Porsolt first obtained GLP compliance over 20 years ago, and has maintained this status in every subsequent bi-annual inspection. The quality of preclinical results is crucial for successful drug screening and development. Regulatory authorities require later stage pre-clinical studies to be performed under GLP guidelines, including safety and toxicology studies.

Standalone Histology and Biomarker Analysis Services

Porsolt is continuing to expand our portfolio of services and expert capabilities to capitalize on the wealth of informative data that can be obtained from preclinical studies. Two areas where this is extremely beneficial are Histology and Biomarker Analysis of tissues collected post study.

Histology

Porsolt has significantly invested in cutting-edge equipment and histology capabilities, allowing us to work with multiple tissue types from varied animal species. These capabilities include in-house processing of tissues (paraffin embedded or frozen), specialized staining, immunofluorescence, and immunohistochemistry. Whole slide or high magnification using brightfield and multi-channel fluorescence imaging is combined with acquisition, digitalisation, scanning, with automated and customized image analysis, machine learning, and pathologist review, to produce relevant, descriptive, reproducible, and quantitative data.

Biomarker Analysis with Real Time qPCR

Porsolt's newly developed Real Time PCR (qPCR) capabilities can be used to detect key molecular pathway modulations at early stages and quantitate changes in gene or micro-RNA expression in response to different environmental conditions or drug treatments. This rapid and sensitive analysis can be performed on different types of biological samples from various animal species and enhances the translational value of preclinical studies. Porsolt's scientists design the oligonucleotides based on specific client requests, and these are used in multiplex qPCR reactions to obtain the most information from the client samples.

These techniques enhance the value and provide a more comprehensive picture of pre-clinical, investigative, safety assessment, and toxicology studies, and can be incorporated as part of studies being performed at Porsolt or provided as standalone services for clients interested in sending preclinical and clinical tissue samples for analysis.
Please do not hesitate to contact us to discuss incorporating these services as part of studies performed at Porsolt, or to coordinate the analysis of inhouse samples.

Expansion of Facility

Porsolt has embarked on a further expansion of our facility, with an additional 600 m2 of dedicated animal space. The expansion, slated to be completed in the first half of 2023, complements the additional lab space recently incorporated into the facility. This will also further assist with faster turnaround times for the initiation of projects, as well as meet specific client needs for dedicated colony maagement.

New Tests & Models at a glance

■ CENTRAL NERVOUS SYSTEM

■ DERMATOLOGY

■ GASTROINTESTINAL SYSTEM

■ INFLAMMATION

■ ONCOLOGY

■ PAIN

■ RESPIRATORY SYSTEM

New Capabilities

■ ROUTES OF ADMINISTRATION
Intracaecal, etc.

■ PK STUDIES
Vascular access port for long-term PK studies in rabbits and ferrets

■ BIOCHEMISTRY
Western Blot analysis

Subcellular Fractionation / Enrichment (membrane, cytosol, nuclei)

■ HISTOLOGY
Expanded in-house capacity for tissue sectioning frozen and paraffin embedded
Histology process, FFPE tissue staining and certified board veterinary pathologist analysis / scoring, immunohistochemistry (IHC) & Immunofluorescence (IF)

■ BIOMARKER ANALYSIS
Luminex platform for multiplex detection of proteins (cytokines, chemokines, growth factors, etc.)

■ MULTIPLEXED TISSUE FOR QUANTITATIVE SPATIAL PROTEOMIC ANALYSIS
In development

Models under development

■ CENTRAL NERVOUS SYSTEM

■MEDICAL DEVICES

■ ONCOLOGY

■ PAIN

Recent Posters

EACR 2022

Triple negative breast cancer preclinical models reveal the therapeutic potential of Fingolimod

Tristan Rupp, Océane Pelouin, Laurie Genest, Christophe Legrand, Guillaume Froget, and Vincent Castagné

EACR 2022

Therapeutic potential of Fingolimod and Dimethyl Fumarate in Non-Small Cell Lung Cancer preclinical models

Tristan Rupp, Solène Debasly, Laurie Genest, Lulubelle Ribault, Guillaume Froget, and Vincent Castagné

AcTox 2022

In vitro predictive toxicity screening assays during early stage drug development: Case study data for the validity of 2D and 3D models

Sébastien Brèche, Elise Esneault, Sonia Goineau, Christophe Legrand, Mikael Paquet, Kendall Walker and Florian Simon

SPS 2022

The ferret: The gold standard for emesis assessment

Sonia Goineau, Philippe Guillaume, Guillaume Froget

SFN 2022

Screening cascade for the evaluation of new anti-epileptic drug candidates

Esneault E, Ntchhongoue L.I., Martineau M. and Roux CM.

SFN 2022

Human iPSC microglia for assessing new treatments in neurological diseases.

Walker, K., Bellec-Dyevre J., Cancio C., Paquet M., Esneault E. and Simon F.

Recent Publications

Drug Discovery and Evaluation: Safety and Pharmacokinetics Assays
Book Chapter: Central Nervous System (CNS) Safety Pharmacology studies
Christelle Froger-Colleaux, Elise Esneault, Anne-Marie Hernier, Vincent Castagne
December 2022 (DOI: 10.1007/978-3-030-73317-9_3-1)

Therapeutic Potential of Fingolimod and Dimethyl Fumarate in Non-Small Cell Lung Cancer Preclinical Models.
Tristan Rupp, Debasly S, Laurie Genest, Guillaume Froget, Vincent Castagné
Int J Mol Sci. 2022 Jul 25;23(15):8192. doi: 10.3390/ijms23158192.

A Face-To-Face Comparison of Tumor Chicken Chorioallantoic Membrane (TCAM) In Ovo with Murine Models for Early Evaluation of Cancer Therapy and Early Drug Toxicity.
Tristan Rupp, Christophe Legrand, Hunault M, Laurie Genest, David Babin, Guillaume Froget, Vincent Castagné.
Cancers (Basel). 2022 Jul 21;14(14):3548. doi: 10.3390/cancers14143548.

Anti-CTLA-4 and anti-PD-1 immunotherapies repress tumor progression in preclinical breast and colon model with independent regulatory T cells response.
Rupp T, Genest L, Babin D, Legrand C, Hunault M, Froget G, Castagné V.

Transcranial direct current stimulation (tDCS) reduces motivation to drink ethanol and reacquisition of ethanol self-administration in female mice
Solène Pedron, Stéphanie Dumontoy, Maria del Carmen González-Marín, Fabien Coune, Andries Van Schuerbeek, Emmanuel Haffen, Mickael Naassila & Vincent Van Waes
Scientific Reports volume 12, Article number: 198 (2022) Nature Press

Ulotaront, a Novel TAAR1 Agonist with 5-HT1A Agonist Activity, Lacks Abuse Liability and Attenuates Cocaine Cue-Induced Relapse in Rats
Colleen Synan, Carrie Bowen, David J. Heal, Christelle Froger-Colléaux, Patrick M. Beardsley, Nina Dedic, Seth C. Hopkins, Una Campbell, Kenneth S. Koblana
Drug and Alcohol Dependence, 2021

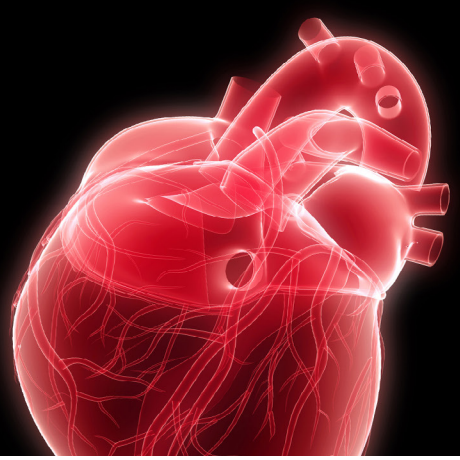
Memory Disorders Related to Hippocampal Function: The Interest of 5-HT 4 Rs Targeting.
Candice M Roux, Marianne Leger , Thomas Freret
Int J Mol Sci. 2021 Nov 8;22(21):12082

Introduction to the EQIPD quality system.
Bespalov, Anton ; Bernard, René ; Gilis, Anja ; Gerlach, Björn ; Guillén, Javier ; Castagné, Vincent ; Lefevre, Isabel A ; Ducrey, Fiona ; Monk, Lee ; Bongiovanni, Sandrine ; Altevogt, Bruce ; Arroyo-araujo, María ; Bikovski, Lior ; De Bruin, Natasja ; Castaños-vélez, Esmeralda ; Dityatev, Alexander ; Emmerich, Christoph H ; Fares, Raafat ; Ferland-beckham, Chantelle ; Froger-colléaux, Christelle ; Gailus-durner, Valerie ; Hölter, Sabine M ; Hofmann, Martine Cj ; Kabitzke, Patricia ; Kas, Martien Jh ; Kurreck, Claudia ; Moser, Paul ; Pietraszek, Malgorzata ; Popik, Piotr ; Potschka, Heidrun ; Prado Montes De Oca, Ernesto; Restivo, Leonardo; Riedel, Gernot ; Ritskes-hoitinga, Merel ; Samardzic, Janko ; Schunn, Michael ; Stöger, Claudia ; Voikar, Vootele ; Vollert, Jan ; Wever, Kimberley E ; Wuyts, Kathleen ; Macleod, Malcolm R; Dirnagl, Ulrich ; Steckler, Thomas.
eLIFE. (2021) Vol. 10.

Neonatal phencyclidine and social isolation in the rat: effects of clozapine on locomotor activity, social recognition, prepul se inhibition, and executive functions deficits.
Al Mahdy Hamieh, David Babin, Evelyne Sablé, Anne Marie Hernier, Vincent Castagné
Psychopharmacology (2021) 238:517–528

Cardiovascular System

Porsolt has an extensive portfolio of cardiovascular procedures, ranging from standard cardiovascular telemetry studies for safety evaluation, to pathophysiological models for specific therapeutic areas. Porsolt also possesses considerable expertise with *in vitro* models, providing clients with a comprehensive assessment of all aspects of cardiovascular function.



in vivo ARRHYTHMIAS & CARDIAC TOXICITY

Digoxin-induced ventricular arrhythmias *(anesthetized animals)*	Guinea-pig	CV 3.5
Torsades de Pointes arrhythmias *(modified Carlsson model)*	Rabbit	CV 3.9

in vivo AUTONOMIC NERVOUS SYSTEM

Postural hypotension *(anesthetized animals)*	Rat	CV 6.3

in vitro CARDIAC ACTIVITY RECORDING

Calcium assay	iPSC-derived cardiomyocytes	PF 1.7
hCav1.2 channel	HEK 293 cells	CV 5.9
hERG channel	HEK 293 cells	CV 5.6
hERG trafficking	HEK 293 cells	CV 5.10
hKir2.1 channel	HEK 293 cells	CV 5.8
hKir2.1 trafficking	HEK 293 cells	CV 5.13
hNav1.5 channel	HEK 293 cells	CV 5.7
Inositol triphosphate receptor channel function	H9C2 cells	PF 3.21
MEA assay	iPSC-derived cardiomyocytes	CV 5.14

in vivo HEMODYNAMICS

ANESTHETIZED ANIMALS

Arterial blood pressure, heart rate and ECG	Rat - Guinea-pig	CV 1.1
Regional blood flow	Rat	CV 1.5
Systemic, cardiac, renal and pulmonary hemodynamics	Dog – Mini-pig	CV 1.7
Systemic and cardiac hemodynamics *(cardiac denervated animal)*	Dog	CV 1.11

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Cardiovascular System

CONCIOUS ANIMALS *(TELEMETRY)*

Arterial blood pressure, heart rate ± ECG	Mouse – Rat – Dog Guinea-pig – Mini-pig	CV 1.4
Left ventricular pressure, heart rate ± ECG	Rat – Dog	CV 1.16
Pulmonary arterial blood pressure, heart rate and ECG	Dog	CV 1.14
Right ventricular pressure and heart rate	Rat	CV 1.15
Endothelial cell activation / Drug-Induced Vascular Injury	HUVECs	PF 1.6

HYPERTENSION

in vitro Endothelial cell activation / Drug-Induced Vascular Injury	HUVECs	PF 1.6
in vivo 5/6 nephrectomy	Rat	REN 3
Arterial blood pressure and heart rate *(anesthetized animals)*	SH Rat	CV 2.1
Arterial blood pressure and heart rate *(telemetry)*	SH Rat	CV 2.4
Bile duct ligation-induced portal vein hypertension *(telemetry)*	Rat	CV 2.7
Chronic *(2K1C)* Goldblatt hypertension *(high renin model)*	Rat	CV 2.5
Chronic DOCA - salt hypertension *(low renin model)*	Rat	CV 2.3
Monocrotaline-induced pulmonary hypertension *(anesthetized animals)*	Rat	CV 2.6
Monocrotaline-induced pulmonary hypertension *(telemetry)*	Rat	CV 2.8

ISOLATED VASCULAR BEDS

ex vivo Isolated mesenteric artery	Dog	CV 8.4
Isolated saphenous vein	Rabbit – Dog	CV 8.2
Isolated thoracic aorta	Rat – Rabbit	CV 8.1

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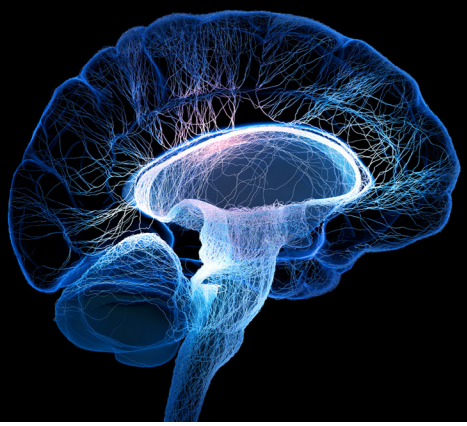
Central Nervous System

Porsolt offers models in all areas of psychopharmacology, epilepsy, sleep-wake, and neurodegenerative disorders. We are uniquely placed to offer a full range of CNS efficacy and safety pharmacology assessments, from basic models and regulatory tests, to the evaluation of abuse and dependence liability and proconvulsant risk using EEG.



CNS GENERAL SCREENING

in vitro	Calcium response (release or sponsaneous oscillation)	Mouse - Rat primary neurons	PF 3.3
	Cytolysis / Viability	Mouse - Rat primary neurons	PF 3.4
	Mitochondrial membrane potential measurement	Mouse - Rat primary neurons	PF 3.4
New!	Neurite outgrowth (scratch assay)	Rat primary neurons	PF 3.44
New!	Neurite outgrowth (scholl analysis)	Rat primary neurons	PF 3.45
in vivo	Accelerating rotarod	Mouse – Rat	CNS 1.17
	Activity meter	Mouse – Rat	CNS 1.2
	Barbiturate interaction (sleep induction)	Mouse – Rat	CNS 1.8
	Beam walking	Mouse – Rat	CNS 1.12
	Ethanol interaction (sleep induction)	Mouse – Rat	CNS 1.9
	Foot-fault	Rat	CNS 1.16
	Grip strength	Mouse – Rat	CNS 1.19
	Neurological score	Rat	CNS 1.15
	Odor discrimination	Rat	CNS 1.18
	Primary observation (Irwin)	Mouse – Rat	CNS 1.1
	Rectal temperature (option: implants)	Mouse – Rat	CNS 1.11
	Removal of adhesive	Rat	CNS 1.14
	Rotarod	Mouse – Rat	CNS 1.5
	Tetrad test	Mouse – Rat	CNS 1.13

COGNITION

in vivo

AGE-RELATED DEFICIT

Delayed alternation (acquisition)	*Aged Rat*	*CNS 6.10*
Delayed alternation (stabilized performance)	*Aged Rat*	*CNS 6.11*
Morris water maze (acquisition and retention)	*Aged Mouse – Aged Rat*	*CNS 6.7*
Operant reversal	*Aged Rat*	*CNS 6.34*
Social recognition	*Aged Rat*	*CNS 6.9*

Y-Maze (Novelty-based spatial preference)	*Aged Rats*	*CNS 6.41*
Y-Maze (Spontaneous alternation)	*Aged Rats*	*CNS 6.39*

EXPERIMENTAL PROCEDURES

Delayed alternation (acquisition)	Rat	CNS 6.13
Delayed alternation (stabilized performance)	Rat	CNS 6.15
Fear Conditioning (context, cue & extinction)	Mouse – Rat	CNS 6.38
Morris water maze (single session)	Rat	CNS 6.16
Morris water maze (acquisition and retention)	Mouse – Rat	CNS 6.17
Operant reversal	Rat	CNS 6.24
Operant Set-shifting	Rat	CNS 6.35
Passive avoidance	Mouse – Rat	CNS 6.19
Social recognition (30 minute retention)	Rat	CNS 6.20
Social recognition (120 minute retention) (delay-induced forgetting)	Rat	CNS 6.21
Y-Maze (Novelty-based spatial preference)	Mouse - Rat	CNS 6.41
Y-Maze - Spontaneous Alternation	Mouse – Rat	CNS 6.39

MODELS OF PHARMACOLOGICALLY - INDUCED AMNESIA

Diazepam - induced amnesia

Passive avoidance	Mouse – Rat	CNS 6.27

MK 801 - induced amnesia

Delayed alternation *(stabilized performance)*	Rat	CNS 6.29
Morris water maze *(acquisition and retention)*	Rat	CNS 6.23
Operant reversal	Rat	CNS 6.31
Passive avoidance	Rat	CNS 6.26
Social recognition *(30 minute retention)*	Rat	CNS 6.33

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Central Nervous System

Scopolamine - induced amnesia

Delayed alternation *(stabilized performance)*	Rat	CNS 6.28
Morris water maze *(acquisition and retention)*	Rat	CNS 6.18
Morris water maze *(single session)*	Rat	CNS 6.3
Operant reversal	Rat	CNS 6.32
Passive avoidance	Mouse – Rat	CNS 6.1
Social recognition *(30 minute retention)*	Rat	CNS 6.5

NEURODEGENERATION-RELATED DEFICIT

> *See "Neurodegeneration" section on page 15*

in vivo

DRUG ABUSE & DEPENDENCE *(Safety and efficacy)*

Drug Discrimination	Rat	CNS 7.8
Flumazenil-precipitated withdrawal *(ECS threshold)*	Mouse	CNS 7.2
Naloxone-precipitated withdrawal *(Saelens)* safety-efficacy	Mouse – Rat	CNS 7.1
Non-precipitated withdrawal *(option: telemetry)*	Rat	CNS 7.3
Opiate tolerance *(hot plate)*	Mouse – Rat	CNS 7.4
Place preference	Mouse – Rat	CNS 7.5
Self-administration *(initiation)*	Rat	CNS 7.6
Self-administration *(substitution)*	Rat	CNS 7.7
Self-administration *(reinstatement)*	Rat	CNS 7.9
Self-administration *(progressive ratio)*	Rat	CNS 7.10

ex vivo

ELECTROPHYSIOLOGY

	Brain slices *(LTP)*	Mouse	CNS 9.9
New!	Brain slices (4-AP-induced seizure)	Mouse	CNS 9.10

in vivo

CONCIOUS ANIMALS *(TELEMETRY)*

Anesthetized animals

New!	Compound Motor Action Potential (CMAP)	Mouse - Rat	CNS 9.8
New!	Nerve Conductance Velocity (NCV)	Mouse - Rat	CNS 9.8
	EEG trace monitoring	Mouse – Rat – Dog	CNS 9.5
	Electrical amygdala kindling	Rat	CNS 9.3
	Quantified EEG	Mouse – Rat - Dog	CNS 9.7
	Sleep/wakefulness cycle	Rat	CNS 9.2

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Central Nervous System

EPILEPSY

in vitro	4-AP calcium spontaneous oscillation modulation	Mouse - Rat Primary Neurons	PF 9.16
	GABA Pathway (calcium spontaneous oscillations)	Mouse - Rat Primary Neurons	PF 9.17
	Glutamate pathway (calcium release and spontaneous oscillations)	Mouse - Rat Primary Neurons	PF 9.18
	Kainate (calcium release)	Mouse - Rat Primary Neurons	PF 9.19
	NMDA antagonists (calcium release)	Mouse - Rat Primary Neurons	PF 9.20
ex vivo	New! 4-AP induced seizure on hippocampal slices	Mouse	CNS 9.10
in vivo	6Hz psychomotor	Mouse – Rat – Gerbil	CNS 5.9
	Audiogenic seizures	Mouse	CNS 5.7
	Bicuculline convulsions	Mouse – Rat	CNS 5.6
	Electrical amygdala kindling (Electrophysiology)	Rat	CNS 9.3
	Electroconvulsive threshold	Mouse – Rat – Gerbil	CNS 5.2
	GBL-induced absence epilepsy (EEG telemetry)	Mouse	CNS 5.12
	Genetic absence epilepsy (WAG)	Rat	CNS 5.14
	Intravenous PTZ seizure threshold	Rat	CNS 5.11
	Kainic acid convulsions	Rat	CNS 5.10
	Kainic acid induced spontaneous seizure	Rat	CNS 5.16
	Maximal electroshock	Mouse – Rat	CNS 5.1
	Pentylenetetrazole seizures	Mouse – Rat – Dog	CNS 5.15
	Pilocarpine induced spontaneous seizure	Rat	CNS 5.17
	Pilocarpine convulsions	Rat	CNS 5.13
	Picrotoxin convulsions	Mouse – Rat	CNS 5.5
	Strychnine convulsions	Mouse – Rat	CNS 5.4

NEUROINFLAMMATION

in vitro	Immune cell phagocytosis (E.Coli particles)	hiPSC derived microglia	PF 9.21
	Immune cell phagocytosis (S.Aureus particles)	hiPSC derived microglia	PF 9.22
	Inflammatory cytokine release (LPS stimuli)	hiPSC derived microglia	PF 9.23

NEURODEGENERATION

in vitro	Glutamate-induced excitotoxicity	Rat cortical or hippocampal neurons	PF 9.33
	Cuprizone-induced demyelination	Mouse	*In development*

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Central Nervous System

in vivo	**ALZHEIMER DISEASE**		
	Streptozotocin *(STZ)* – induced cognitive deficit	Rat	CNS 10.11
	< EXPERIMENTAL PROCEDURES		
	Morris water maze		
	Y-maze (Novelty-based spatial preference)		
	HUNTINGTON DISEASE		
	Motor function and neuroscore Subchronic 3-NPA	Rat	CNS 10.8
	< EXPERIMENTAL PROCEDURES		
	Activity meter		
	Rotarod		
	Lesion volume		
	PARKINSON DISEASE		
in vitro	6-OHDA induced toxicity	hiPSC derived dopaminergic neurons	PF 9.32
	MPP+ induced toxicity	hiPSC derived dopaminergic neurons	PF 9.27
New!	MPP+ induced toxicity	SH-SY5Y cells	PF 9.34
New!	Rotenone induced toxicity	hiPSC derived dopaminergic nerons	In development
in vivo New!	Alpha Synuclein PFF model	Mouse	CNS 10.22
	Cognitive deficit Bilateral striatal 6-OHDA lesion	Rat	CNS 10.9
	L-DOPA dyskinesia Unilateral medial forebrain bundle (mfb)	Rat	CNS 10.5
	Motor deficit Unilateral medial forebrain bundle (mfb) 6-OHDA lesion	Rat	CNS 10.2R
New!	MPTP - induced lesion	Mouse	In development

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Central Nervous System

PSYCHIATRIC DISEASES

ANXIETY

Elevated plus-maze	Mouse – Rat – Gerbil	CNS 3.3
Fear potentiated startle reflex	Rat	CNS 3.13
Four plates	Mouse	CNS 3.1
Light-dark box	Mouse	CNS 3.4
Marble burying	Mouse	CNS 3.7
Novelty-induced hypophagia	Mouse – Rat	CNS 3.5
Stress-induced hyperthermia (group-housed animals)	Mouse	CNS 3.6
Stress-induced hyperthermia (singly-housed animals) (option: implants)	Mouse	CNS 3.17
Vogel conflict	Rat	CNS 3.8

DEPRESSION

Behavioral despair	Mouse – Rat	CNS 2.5
Chronic Mild Stress	Mouse	CNS 2.10
Differential Reinforcement of Low rate *(DRL 30)*	Rat	CNS 2.6
Open space swimming	Mouse	CNS 2.8

PSYCHOSIS

Amphetamine hyperactivity	Mouse – Rat	CNS 4.1
Amphetamine stereotypy	Mouse – Rat	CNS 4.2
Catalepsy	Mouse – Rat	CNS 4.9
Dual-hit neonatal PCP and post-weaning social isolation	Rat	CNS.418
MK-801 hyperactivity	Mouse – Rat	CNS 4.13
PCP hyperactivity	Mouse – Rat	CNS 4.8
Prepulse inhibition *(deficit induced by apomorphine)*	Rat	CNS 4.11
Prepulse inhibition *(deficit induced by MK-801)*	Rat	CNS 4.14
Prepulse inhibition *(deficit induced by PCP)*	Rat	CNS 4.15
Sociability (3-Chamber) Test	Mouse	*CNS 4.19*

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Central Nervous System

STROKE

in vitro	Excitatory neurotransmitter induced excitotoxicity (Glutamate, NMDA, and Kainate)	Rat / Mouse primary neurons	PF 9.29
	Excitatory neurotransmitter induced excitotoxicity (Mitochondrial Membrane Potential) (Glutamate, NMDA, and Kainate)	Rat / Mouse primary neurons	PF 9.30
	Excitatory neurotransmitter induced excitotoxicity (Calcium Response) (Glutamate, NMDA, and Kainate)	Rat / Mouse primary neurons	PF 9.31
in vivo	Intrastriatal NMDA administration	Mouse	CNS 10.14
	Transient focal cerebral ischemia Middle Cerebral Artery Occlusion	Rat	CNS 10.3

< Experimental Procedure

Lesion volume

< Experimental Procedures

Beam walking

Foot-fault

Removal of adhesive

Neurological score

Lesion volume

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Central Nervous System

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
Histology *(IHC-P)*	Neurons *(pan neuron, dopaminergic GABA interneuron, Purkinje)*	Rat - Mouse - Pig
	Glial cells *(astrocytes, microglia, oligodendrocytes)*	Rat - Mouse - Pig
	Aggregated protein α-synuclein	Human-Mouse (cell supernatant and brain)
	Neuron activity proteins *(synapse, myelination)*	Rat - Mouse
	Nerve growth factor *(NPY,TrkA)*	Rat - Mouse
	Ubiquitin system/autophagy (Ubiquitin, P62)	Mouse
	Lysosome (LAMP-1,GCase, PSAP)	Mouse
Staining *(paraffin slices)*	Hematoxylin & eosin, Sirius red, Masson's trichrome,...	Multiple species & tissues
Luminex	Inflammation pathway IL-6, IL-10, MCP-1or IL-8 IFN-γ or IL-1β ,TNF and IL-12p70	Human - Mouse *(cell supernatant)*
qPCR	miR16, miR132, miR124, TNF-α αIL- β,IL-6	Rat (Cortex), Primary Neurons
WB	RAS/Erk Signaling *(Erk, P-Erk, S6, P-S6)*	Mouse *(Pancreas, cerebellum)*
	Alzheimer Pathway *(P-Tau Ser398, P-Tau Ser202 Tyr205, GSK3b & P-GSK3)*	*Rat (Hippocampus)*
ELISA	Amyloid proteins *(β-amyloid)*	*Dog (CSF, plasma)*

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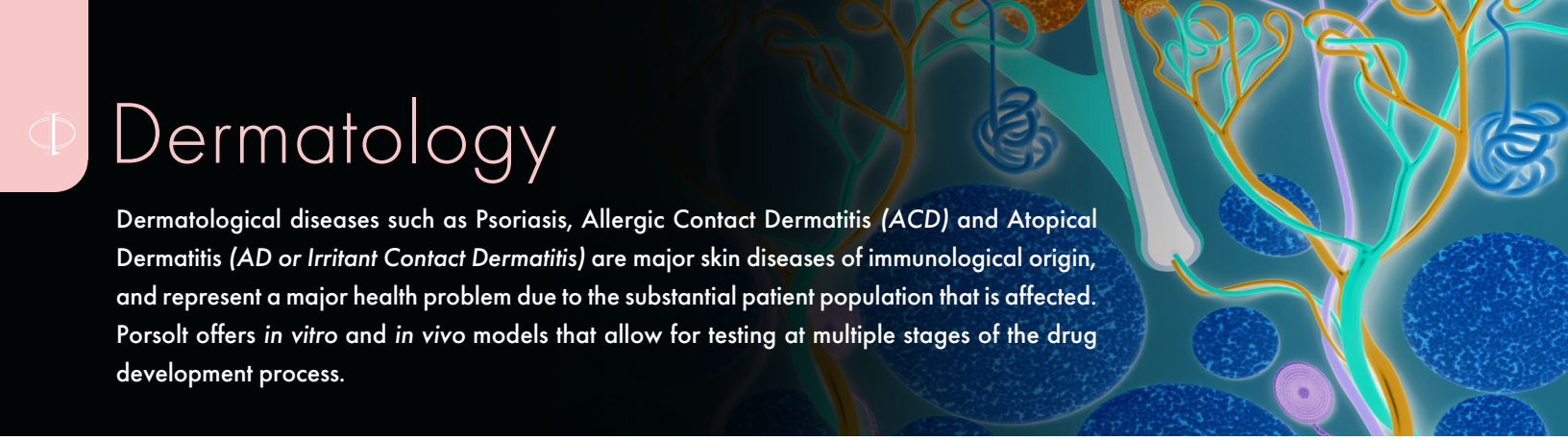
Dermatology



Dermatological diseases such as Psoriasis, Allergic Contact Dermatitis *(ACD)* and Atopical Dermatitis *(AD or Irritant Contact Dermatitis)* are major skin diseases of immunological origin, and represent a major health problem due to the substantial patient population that is affected. Porsolt offers *in vitro* and *in vivo* models that allow for testing at multiple stages of the drug development process.

in vitro

INFLAMMATORY PATHWAY AND ANTI-INFLAMMATORY ACTIVITY

Atopic Dermatitis - Poly *(I:C)* induced cytokine release	NHEK	PF. 4.26
Cannabinoid anti-inflammatory evaluation Cytokine release	NHEK	PF. 4.27
Cytokine release	Keratinocytes Dendritic cells *(Langerhans)*	PF. 4.10
IL-6 induced secretion *(by IL-17)*	NHDF	PF. 4.25
Immune cell activation	Lymphocytes, PBMC Dendritic cells *(Langerhans)*	PF. 5.9
Immune cell proliferation	Lymphocytes, PBMC	PF. 5.8
Immune cells phagocytosis *(E.coli particles)*	Macrophages Dendritic cells *(Langerhans)*	PF. 4.16
TNFα induced cytotoxicity	L929	PF. 4.1

OXIDATIVE DAMAGE AND ANTI-OXIDANT POTENTIAL

Cell viability - protection	HaCaT, NHEK, NHDF	PF. 4.2 & 3.4
Lipid peroxidation induction	HaCaT, NHEK	PF. 4.23
Reactive Oxygen Species induction *(ROS) (multiple inducers)*	HaCaT, NHEK	PF. 4.22

PIGMENTATION

Endothelin signaling pathway - Calcium	Normal human epidermal melanocyte *(NHEM)*	PF. 4.28

PREDICTIVE TOXICITY

Cytotoxicity - Cell viability	Cell lines *(3T3, L929, HaCaT)* NHEK, NHDF	TOX 17&18
Ocular irritation HET-CAM	Chicken egg	PF. 4.14
Skin irritation	Reconstituted human epidermis	PF. 4.15
Skin sensitization	Monocyte cell line *(THP1)*	PF. 4.20

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Dermatology

PROTECTION AGAINST POLLUTION

Indoor dust - Inflammatory cytokine release	Dendritic cells (Langerhans)	PF. 4.24
Urban dust - Inflammatory cytokine release	NHEK Dendritic cells (Langerhans)	PF. 4.10
Urban dust - Lipid peroxidation	NHEK	PF. 4.9
Urban dust - Reactive Oxygen Species induction (ROS)	NHEK	PF. 4.8

SKIN AGING

New!	Wound healing	Elderly fibroblast or keratinocyte donor	PF. 4.12
	Senescence *(oxidative stress induction or high passage senescence)*	Keratinocytes	PF. 4.11
	Total collagen secretion	Elderly fibroblast donor	PF. 4.13

SKIN MICROCIRCULATION

Calcitonin Gene Related Peptide signaling pathways *(CGRP)*	HDMEC	PF. 4.5

SKIN REGENERATION

Cell migration/Wound healing	HaCaT, NHEK, NHDF	PF. 3.14
Cell proliferation	HaCaT, NHEK, NHDF	PF 3.9
Total collagen formation	NHDF	PF. 4.3

IN VIVO

in vivo	Allergic Contact Dermatitis	Pig	DER 2
	Imiquimod-induced psoriasis-like skin inflammation	Mouse	DER 1
	Pruritogens-induced scratching behavior	Mouse – Rat	DER 3
	Wound healing	Mouse	DER 4

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BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
Histology *(IHC-P)*	Skin structure *(keratin10, loricrin, filaggrin, elastin, involucrin, e-cadherin, ZO-1)*	Human *(explant or RHE)*
	Cell proliferation (Ki67,...)	Human *(explant or RHE)*
	Immune cells (*macrophages, T-cells, Langerhans,...*)	Human *(explant or RHE)* Mouse, Rat
	α-SMA	Rat Kidney
Staining *(paraffin slices)*	Hematoxylin & Eosin, Sirius red, Masson's trichrome,...	Multiple species & tissues
Luminex/CBA	Inflammation pathway IL-6, IL-10, MCP-1or IL-8 IFN-γ or IL-1β ,TNF and IL-12p70	Human *(cell supernatant)*
ELISA	Inflammatory cytokine *(TNF-α , IL-6, IL-17)*	Mouse *(ear)*
PCR	IL-17a, IL-17f, IL-22, IL-23p19, IL-1β	Mouse skin

> New developments in progress ?

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Gastrointestinal System

Porsolt has extensive expertise and years of experience in gastrointestinal safety pharmacology and efficacy. Porsolt provides models that focus on different gastrointestinal indications and different parts of the gastrointestinal system. Porsolt also continues to develop and validate new and relevant models.

in vivo COLONIC MOTILITY

Anti-diarrhea *(castor oil)*	Mouse – Rat	GI 7
Colonic transit *(bead model)*	Mouse – Rat	GI 16
Fecal consistency	Mouse – Rat	GI 22

in vivo EMESIS - NAUSEA

Early and delayed emesis *(telemetry)*	Ferret	GI 15
Early anti-emetic activity *(morphine, cisplatin, emetine,...)*	Ferret	GI 10
Emesis induction	Ferret	GI 9
Pica behavior	Rat	GI 17

in vivo FOOD ALLERGY

Beta-lactoglobulin-induced allergy	Mouse	FA 2
Peanut-induced allergy	Mouse	FA 1

in vivo GASTRIC EMPTYING

Gastric emptying *(measurement of plasma acetaminophen levels)*	Rat	GI 23
Gastric emptying *(phenol red test)*	Mouse – Rat	GI 8

in vivo GASTROINTESTINAL TRANSIT

Charcoal meal test	Mouse – Rat	GI 1
Distribution pattern of phenol red	Mouse	GI 26

in vivo GASTROPARESIS

Clonidine-induced delayed gastric emptying *(liquid meal)*	Rat	GI 20
Clonidine-induced delayed gastric emptying *(solid meal)*	Rat	GI 21
Post operative ileus	Mouse	GI 25

in vivo INTESTINAL MUCOSITIS

Chemotherapy-induced intestinal mucositis	Mouse – Rat	GI 32

Gastrointestinal System

ULCEROGENIC ACTIVITY

in vitro	Indomethacin-induced gastric mucosal cell damage	Rat gastric mucosal cells	GI 29
in vivo	Colorectal distension (CRD model) after acetic acid sensitization	Rat	GI 13
	Colorectal distension (CRD model) after TNBS sensitization	Rat	GI 30
	Gastric acid secretion *(Shay's method)*	Mouse – Rat	GI 3
	Ulcerogenic activity *(acute and sub-chronic)*	Rat	GI 2
	Ulcerogenic activity prevention *(induced by ethanol)*	Rat	GI 19
	Ulcerogenic activity prevention *(induced by indomethacin)*	Rat	GI 27

VISCERAL SMOOTH MUSCLE

ex vivo

Isolated colon	Guinea-pig - Rat	VSM 6
Isolated duodenum	Rat	VSM 2
Isolated ileum	Guinea-pig	VSM 1

ADDITIONAL MODELS

in vivo

Conditioned taste aversion	Rat	GI 24
Pilocarpine salivation	Mouse – Rat	PNS 7
Salivation induction	Mouse – Rat	PNS 6

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
New! Staining *(paraffin slices)*	Hematoxylin & Eosin, Sirius red, Masson's trichrome, Toludine blue	Multiple species & tissues
Luminex	Inflammatory cytokines: IL-1α , IL-1β , IL-6, IL-10, MCP-1 and TNF	Mouse *(ileum, plasma)* *Mesentric lymph nodes and splenocytes*
Biochemical	MPO activity	Mouse, Rat *(serum, plasma)*
	Ammonia	Rat *(serum, plasma)*
	Lipid panel *(HDL, LDL, GGT, FFA, TG, cholesterol ...)*	Mouse, Rat *(serum, plasma)*
	Liver function panel *(ALAT, ASAT, ALP, bilirubin ...)*	Mouse, Rat *(serum, plasma)*
Elisa	Inflammatory cytokines: TNF-α /IL-1 , IL-6	Mouse, Rat *(serum, plasma, ileum)*
	Redox potential *(GSH)*	Mouse, Rat *(serum, plasma, ileum)*
	Allergy *(Total IgE, histamine, mMCP-1)*	*Mouse (plasma)*
Histology (IHC-P)	Neutrophils (MPO)	Mouse (intestine)

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Histology services

Porsolt has recently expanded its histology capabilities for multiple types of tissues in varied animal species, to support pre-clinical studies, investigative and safety assessment, and toxicology studies. These capabilities can be included as part of ongoing models or as separate stand-alone services.

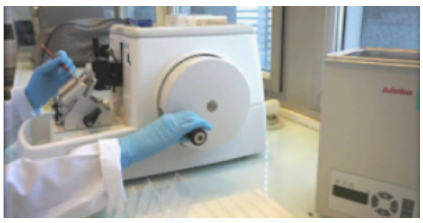
Tissue preparation
- Paraffin
- Frozen Sections

Staining
- Routine and Special Stains
- Immunohistochemistry
- Immunofluorescence

Digitalization
- Brightfield
- Fluorescence
- Whole Slide Scanning

Analysis
- Automated Image Analysis
- Pathologist review
- Machine learning

TISSUE PROCESSING



FFPE (Formalin fixed paraffin embedded) tissue

Frozen tissue embedding and cryosectioning

Decalcification of bone and hard tissues

Tissue Micro Array (TMA)

STAINING

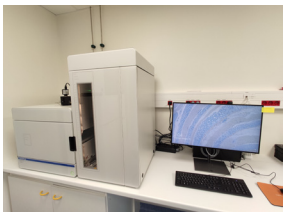
Routine stains (Hematoxylin and Eosin, Toluidin Blue, Sirius Red ...)

Special stains (Safranin-O / fast Green, Masson Trichrome ...)

Immunohistochemistry staining

Immunofluorescence staining (multiple colors)

SCANNING



Whole Slide Scanning

Brightfield and Fluorescence (multiple colors)

High resolution and high throughput imaging

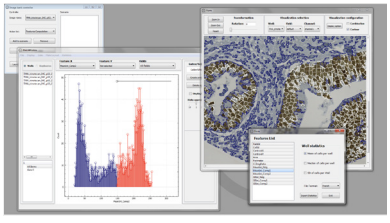
PATHOLOGY SERVICES

Microscopic observations and findings

Semi quantitative scoring

Reporting and image illustrations / annotations

AUTOMATED IMAGE ANALYSIS



Tailor-made image analysis algorithm development for staining / IHC / IF slides

Automated and semi automated image analysis

Machine learning / Deep learning approach

Cell population / Quantitative expression / Mapping analysis

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Inflammation

Inflammation is a response to a variety of stimuli, including damaged cells, irritants and pathogens, and is relevant for many different indications. Porsolt's varied capabilities and expertise, together with multiple *in vitro* and *in vivo* models used for screening, efficacy, and safety assessment of potential compounds, allows us to address the specific needs of the industry.

in vitro

IMMUNE RESPONSE

Basophile activation assay (CD200R)	Mouse whole blood	PF 5.11
Cell proliferation	Multiple cellular models	PF 3.9
Cytokine release (inflammation)	Mouse primary splenocytes and mesenteric lymph node hiPS microglia	PF 5.12
Cytolysis	Multiple cellular models	PF 3.4
Immune cell activation and proliferation	Primary mouse splenocytes	PF 5.8
Immune cell killing assay	Human T lymphocyte and tumor cells	PF 10.47
Immune check point inhibitor	*(PD1) - (PDL1)* biochemical assay *(HTRF)*	ONC 11.2
Immune check point inhibitor	*(CTLA-4) - (B7-1)* biochemical assay *(HTRF)*	ONC 11.2
Lipid peroxidation	Multiple cellular models	PF 3.18
Mitochondrial membrane potential	Multiple cellular models	PF 3.3
Phagocytosis	Mouse – Rat Human macrophages	PF 5.10
Sensitization	Monocytes *(THP-1 cell line)*	PF 4.20

in vivo

IN VIVO MODELS

12-tetradecanoylphorbol-13-acetate *(TPA)* - induced ear edema	Mouse	PI 18
Air pouch	Mouse	PI 24
Arachidonic acid-induced ear edema	Mouse	PI 31
Carrageenan-induced edema	Mouse – Rat	PI 9.17
Peanut-induced allergy	Mouse	FA 1

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Inflammation

New!	Bleomycin-induced lung injury	Guinea-pig	RES 8
	Lipopolysaccharide (LPS) Lung Injury (acute)	Mouse	RES 9
	Yeast-induced hyperthermia	Mouse	PI 11

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
Immunophenotyping *(flow cytometry)*	*Leukocytes (Treg,Tc), neutrophils, monocytes, macrophages*	*Mouse, Human (blood, bloodbags, buffy coat, bone marrow, tumors...)*
Histology *(IHC-P)*	Immune cell detection *(CD8, CD3, CD68, CD45,...)*	Rat, Mouse, multiple organs
Luminex	Inflammation pathway IL-6, IL-10, MCP-1or IL-8 IFN-γ or IL-1β ,TNFα and IL-12p70	Human *(cell supernatant)*
Flow cytometry *(ICC)*	STAT pathway *(STAT1, STAT2, STAT3, STAT6...)*	Human *(blood)*
	Cell signaling *(Erk, NFkB, C-jun)*	Human *(blood)*
ELISA	Inflammatory cytokines *(TNFα ,IL-1β ,IL-6,IL-10)*	Mouse *(air pouch exsudat, plasma)*
	Inflammatory protein *(CRP)*	Rabbit *(plasma, serum)*
Hematology	WBC *(White Blood Cell count)*: neutrophils, macrophages, lymphocytes, eosinophils, basophils	Guinea-pig, Mouse *(air pouch exsudat, Bronchoalveolar lavage fluid, plasma)*
qPCR	IL-1β, IL-6, IL-8, IL-12α, IL-12β, MCP-1, TNF-α and INF-γ	Guinea-pig (lung)

> New developments in progress ?

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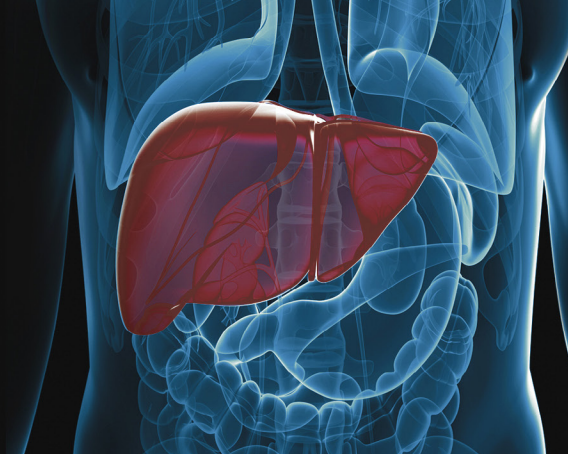
Liver & Hepatic System

Porsolt's experience in preclinical safety and efficacy has led to the development of models that focus on the liver and hepatic system. This is an important part of the process to better understand the effects of compounds on the liver and hepatic system.



in vitro	Acetaminophen (acute model)	Primary hepatocytes, Mouse	PF 6.03
	Cholestasis/Bile canaliculi network	Primary hepatocytes sandwich configuration, Rat	PF 3.16
	Glutathione (GSH), intracellular GSH content	Primary human and rat hepatocytes	PF 3.28
	Steatosis/Lipid, intracellular accumulation: neutral lipids	Primary human and rat hepatocytes	PF 3.29
	Cytolysis	Primary human and rat hepatocytes	PF 3.4
	Lipid, intracellular accumulation: phospholipids	Primary human and rat hepatocytes	PF 3.30
	3D Hepatotoxicity (Viability)	Primary human hepatocyte spheroids	PF 6.02
in vivo	Acetaminophen (acute model)	Mouse	LI 2
	Bile Duct Ligation (BDL) (chronic model)	Rat	CV 2.7
	Carbon tetrachloride (CCl4) (acute model)	Rat	LI 1

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
Histology *(IHC-P)*	Hepatic transporters *(MRP-2, ZO-1,...)*	Rat *(liver)*
	Hepatocellular ballooning *(H&E, p62)*	Rat *(liver)*
Staining *(paraffin slices)*	Hematoxylin & Eosin, Sirius red, Masson's trichrome,...	Multiple species & tissues
Biochemical	Lipid panel *(HDL, LDL, FFA, TG, cholesterol...)*	Mouse, Rat *(plasma, serum)*
	Liver function panel *(ALAT, ASAT, ALP, bilirubin...)*	Mouse, Rat *(plasma, serum)*
ELISA	Inflammatory cytokines *(TNF-α /IL-1β /IL-6)*	Mouse, Rat *(plasma, serum)*

Medical Devices

Porsolt's vast array of models and technical capabilities that have been acquired and validated over many years, enable us to provide testing services for Medical Devices that follow ISO and OECD guidelines and include *in vitro* and *in vivo* models for sensitization, toxicity and safety.

CYTOTOXICITY

in vitro	MTT colorimetric cell viability assay	L929 cells	TOX 18
	Neutral Red colorimetric cell viability Assay	3T3 cells	TOX 19

IRRITATION

in vitro	Reconstituted human epidermis irritation assay	Episkin	TOX 21
in ovo	HET-CAM *(Hen's Egg Test Chorio Allantoic Membrane)* - alternative to occular irritation assay	Chicken egg	TOX 24
in vivo	Acute dermal irritation *(topical application)*	Rabbit	TOX 22
	Intradermal reactivity test *(intracutaneous injection)*	Rabbit	TOX 16
	Skin irritation test	Rabbit	TOX 3

SKIN SENSITIZATION

in vivo	Guinea-pig Maximization Test *(GPMT)*	Guinea-pig	*In development*
	Local Lymph Nodes Assay *(LLNA)*	Mouse	TOX 14

TOXICITY

in vitro	Skin sensitization	Monocyte cell line (THP1)	PF11.2
in ovo	Acute systemic toxicity *(or repeated doses)* alternative to embryotoxicity in mammals	Chicken egg	TOX 23
in vivo	Acute systemic toxicity	Mouse – Rat	TOX 11
	Repeated doses systemic toxicity	Mouse – Rat	TOX 12

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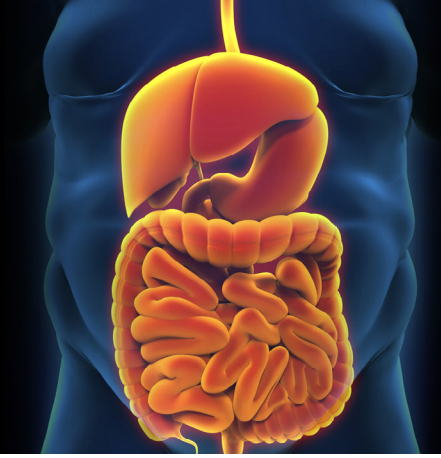
Obesity & Metabolic Disorders

Obesity and metabolism related disorders are key therapeutic areas that have attracted a global focus in recent times. Porsolt has a comprehensive range of models available for obesity, impaired glucose tolerance, and diabetes, to assist with the development of novel therapeutic agents and treatment and reduction of risk factors associated with metabolic diseases.



DIABETES | METABOLIC DISORDERS | OBESITY

DIABETES

in vitro	Type 1 diabetes: Cytokine induced pancreatic cell death (ATP content)	Rat insulinoma INS-1 cells	PF 7.3
	Glucose stimulated insulin secretion	Rat insulinoma INS-1 cells	PF 7.2
in vivo	**Chemically-induced animal models** Alloxan-induced type 1diabetes single injection of alloxan	Rat	MET 17
	HFD/STZ-induced type 2 diabetes high fat diet and single injection of streptozotocin	Rat	MET 15
	Streptozotocin *(STZ)*-induced type 1 diabetes single injection of streptozotocin	Mouse – Rat	MET 16
	Genetic Animal Models Zucker Diabetic Fatty *(ZDF)* type 2 diabetes, glucose intolerance, hyperinsulinemia...	Rat	MET 12
	Leptin-deficience ob/ob - db/db obesity, type 2 diabetes	Mouse	MET 7
	Nutritional Animal Models Diet-induced obesity *(DIO)* special diets	Mouse	MET 18
	Assessments Insulin tolerance test *(ITT)*	Mouse – Rat	MET 2
	Intravenous glucose tolerance test *(IVGTT)*	Rat	MET 1
	Oral glucose tolerance test *(OGTT)* HOMA-IR, QUICKI and ISI calculation	Mouse – Rat	MET 12

METABOLIC DISORDERS

in vivo	Insulin tolerance test *(ITT)*	Mouse – Rat	MET 2

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Obesity & Metabolic Disorders

in vivo

OBESITY

Genetic Animal models Leptin-deficience ob/ob - db/db obesity, type 2 diabetes	Mouse	MET 7
Zucker Fatty obesity, hyperlipidemia...	Rat	MET 7
Nutritional Animal models Diet-induced obesity *(DIO)* special diets	Mouse	MET 18
Assessments Acute 24-hr feeding	Rat	MET 14
Fast-induced feeding *(over 4 hours)*	Mouse	MET 13
Food/water intake and body weight gain *(3-hr schedule-fed over10 days)*	Rat	MET 6
Food/water intake and body weight gain *(over 28 days in pathologic animals)*	Mouse – Rat	MET 7

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
ELISA	Pancreas activity *(insulin, glucagon)*	Mouse, Rat *(plasma)*
	Adipocytes (adiponectin, leptin)	Mouse, Rat *(plasma)*
	Sexual hormone (testosteron)	Mouse, Rat *(plasma, serum)*
	GI hormones (acyl ghrelin)	Mouse, Rat *(plasma, serum)*
Biochemical	Lipid panel *(HDL, LDL, FFA, TG, cholesterol...)*	Mouse, Rat *(plasma)*
	Liver function panel *(ALAT, ASAT, ALP, bilirubin...)*	Mouse, Rat *(plasma)*
	Renal function *(creatinin, urea, electrolytes...)*	Mouse, Rat *(plasma, urine)*
	Diabetes *(HbA1c)*	Mouse, Rat *(total blood)*
	Pancreas activity *(amylase, lipase)*	Mouse, Rat *(plasma, serum)*

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Oncology

Oncology is an area that commands a larger proportion of the research world's resources. Porsolt can provide *in vitro* oncology screening and efficacy testing as well as testing in specific *in vivo* models.

Biochemistry	*in vitro*		*in ovo*	*in vivo*		*ex vivo*
Bioanalysis	2D screening	3D screening	CAM Assay	Hollow Fiber Assay	Tumor Graft	Proteomic Cytometry Histology

Complexity / Relevance

in vitro

RECEPTOR PHARMACOLOGY AND SIGNALING PATHWAYS

High-content imaging

AKT phosphorylation	Multiple cellular models	PF 10.7
Androgen receptor nuclear translocation	LNCaP cell line	PF 10.1
Calcium homeostasis	Multiple cellular models	PF 3.33
cAMP quantification	Multiple cellular models	PF 3.40
ERK activation *(pERK1/2)*	Multiple cellular models	PF 3.27
NFkB activation	Multiple cellular models	PF 3.23
Prostate Specific Antigen *(PSA)* expression	LNCap cell line	PF 10.15

TARGETING ANGIOGENESIS

in ovo

HET-CAM assay *(screening – 3R approach)*	Chicken eggs	ONC 13.1

TARGETING THE IMMUNE SYSTEM: IMMUNO-ONCOLOGY

Biochem.

Binding assay of immune check points inhibitors *(HTRF)*	Multiple inhibitors	ONC 11.2

in vitro

Immune T-cell infiltration assay *(cytometry)*	3D co-culture multiple cells	ONC 10.6
Immune T-cell killing assay (high-content imaging)	2D co-culture multiple cells	PF 10.47
T-cell activation assay (high-content imaging)	Human peripheral mononuclear blood cell and CD3+ T cells	PF 10.50

Oncology

in vivo

Syngeneic models of:

Breast cancer (anti-PD-1/CTLA-4)	**4T1 cells** Mouse	ONC 3.1
Colon cancer (anti-PD-1/CTLA-4)	CT26.WT cells Mouse	ONC 3.2
Glioblastoma (anti-PD-1/CTLA-4)	GL261 cells Mouse	ONC 3.3
Renal cancer (anti-PD-1/CTLA-4)	RenCa cells Mouse	ONC 3.4

TARGETING METASTASIS

in vivo

Experimental lung metastasis syngeneic model of breast cancer		ONC 1.1
Experimental lung metastasis syngeneic model of colon cancer		ONC 1.2
Experimental lung metastasis xenograft model of breast cancer	MDA-MB-231 cells (Mouse)	ONC 8.1

in vitro

Invasion assay (high-content imaging)	Multiple 3D cellular models	PF 3.15
Migration assay (high-content imaging)	Multiple 2D cellular models	PF 3.1

TARGETING TUMOR-ASSOCIATED SIDE EFFECTS

in vivo

PAIN

Chemotherapy - induced intestinal mucositis	Mouse	GI 32
Chemotherapy - pain - Vincristine model	Rat	PI 21
Chemotherapy induced Pain: Cisplatin model	Rat	PI 41

in vivo

CACHEXIA

Drug-induced cachexia model	Rat	ONC 9.2
Tumor-induced cachexia model	AH-130 cells (Rat)	ONC 9.1
Tumor-induced cachexia model	C26 cells (Mouse)	ONC 9.3
Tumor-induced cachexia model	LLC1 cells (Mouse)	ONC 9.4

TARGETING PRIMARY TUMOR

in vitro

Cell cycle (cytometry)	Multiple 2D or 3D cellular models	PF 3.8
Cell proliferation/cytolysis assay (high-content imaging)	Multiple 2D cellular models	ONC10.2

	Cell viability (colorimetric assay)	Multiple 2D cellular models	ONC 10.1
	Clonogenicity assay anchorage-independent	Multiple 3D cellular models	ONC 10.4
	Spheroid proliferation/cytolysis assay (high-content imaging)	Multiple 3D cellular models	ONC 10.3
	Organoid models of Glioblastoma	Multiple patient sample	*In development*
in ovo	Tumor chicken ChorioAllantoic Membrane (TCAM) xenograft assay (screening – 3R approach)	Multiple cellular models Chicken eggs	ONC 4
in vivo	Hollow fiber assay (screening – 3R approach)	Multiple cellular models (Mouse - Rat)	ONC 5
	Orthotopic syngeneic models of:		
	Breast cancer	4T1 cells (Mouse)	ONC 3.1
	Colon cancer	CT26.WT/C26 cells (Mouse)	ONC 3.2
	Glioblastoma (brain tumor)	GL261 cells (Mouse)	ONC 3.3
	Kidney cancer	RenCa cells (Mouse)	ONC 3.4
	Orthotopic xenograft models of:		
New!	Breast cancer	MDA-MB-231/BT 20 (Mouse)	ONC 7.1
New!	Glioblastoma (brain tumor)	U87MG cells (Mouse)	ONC 7.2
	Pancreatic cancer	BxPC-3/PANC-1 cells (Mouse)	ONC 7.3
	Subcutaneous syngeneic models of:		
	Breast cancer	4T1 cells (Mouse)	ONC 2.1
	Colon cancer	CT26.WT/C26 cells (Mouse)	ONC 2.2
	Glioblastoma (brain tumor)	GL261 cells (Mouse)	ONC 2.3
	Lung cancer	LLC1/KLN205 cells (Mouse)	ONC 2.4
	Renal Cancer	105K cells (Mouse) (TSC Alliance)	ONC 3.4
	Subcutaneous xenograft models of:		
	Bladder cancer	SW780 cells (Mouse)	ONC 6.13
	Breast cancer	MDA-MB -231/BT-20 cells (Mouse)	ONC 6.1
	Colon cancer	HCT-8/HCT-116 cells (Mouse)	ONC 6.2
	Fibrosarcoma	HT-1080 cells (Mouse)	ONC 6.9

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Glioblastoma (brain tumor)	U118MG/U87MG/ U138MG cells (Mouse)	ONC 6.3
Kidney cancer	ACHN cells (Mouse)	ONC 6.4
Liver cancer	Hep3B2.1-7/HepG2 cell (Mouse)	ONC 6.6
Lung cancer	A549/PC-9/H69 cells (Mouse)	ONC 6.5
Pancreatic cancer	BxPC-3/CFPAC-1/ PANC-1 cells (Mouse)	ONC 6.11
Prostate cancer	LNCaP/PC-3 (Mouse)	ONC 6.10

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	MATRIX
Immunophenotyping	Regulatory T-cells *(CD4, FoXP3)* Cytotoxic T-cells *(CD8)*	Mouse
Histology	Breast cancer *(ER, PR, HER-2)*	*Mouse*, Human Tumor xenograft
	Epithelial to mesenchymal transition *(E-cadherin,Vimentin)*	Mouse, Human Tumor xenograft
	Immune cells *(T-cells, macrophages,...)*	Rat, Mouse
New!	Tumor microenvironment *(Apoptosis, proliferation, hypoxia, angiogenesis)*	Rat, Mouse, Human
Staining	Hematoxylin & Eosin, Sirius red, Masson's trichrome...	Multiple species
Luminex/CBA	Th1/Th2/Th17 pathway *(IL-2, IL-4, IL-6, IFN-γ , TNF α, IL-17A, IL-10)*	Mouse, Human
	Inflammation pathway *(IL-6, IL-10, MCP-1, IL-8, IFN-γ , IL-1β , TNF, IL-12p70)*	Mouse, Human
Western Blot	Ubiquitin, Lamin B1, ERK1/2, P-ERK1/2, P-S6k1, *S6K1* AKT, P-AKT, GSK3, P-GSK3, GAPDH, PSMA, *EGFR, H3, HIF-1a, CA9*	Mouse, Rat, Human *(multiple cells and tissues)*
Multimodal acquisition	Cell metabolism *(DHFR, protein synthesis)*, Cell stress *(ROS, lipid peroxidation, intracellular phospholipid accumulation, mitochondrial membrane potential, GSH)*, Hypoxia *(Pymonidazole)*, Autophagy *(LC3B)*, Signaling *(ERK1/2, NfKB, AKT, AR, PSA, cAMP, calcium homeostasis)*	

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Pain

Pain is a growing area of interest in the industry and Porsolt is perfectly placed to provide services with recognized expertise and many years of experience. Porsolt offers a variety of models, from *in vitro* screening, to *in vivo* acute, neuropathic, and chronic pain, addressing pain therapeutics and pain associated symptoms and side effects.

in vivo

ACUTE PAIN

Cold plate	Mouse – Rat	PI 36
Hot plate	Mouse – Rat	PI 1
Modified hot plate	Mouse	PI 28
Pain after local administration	Mouse – Rat	PI 40
Pinchmeter	Mouse – Rat	PI 22
Tail flick	Mouse – Rat	PI 2

in vivo

INFLAMMATORY PAIN

Capsaicin paw	Mouse – Rat	PI 30
Carrageenan-induced acute inflammatory pain *(reversal & prevention protocol)*	Mouse - Rat	PI 14
Complete Freund Adjuvant *(CFA)* - induced acute inflammatory pain	Mouse – Rat	PI 20
Complete Freund Adjuvant *(CFA)* - induced chronic inflammatory pain: monoarthritis model	Mouse - Rat	PI 15
Formalin paw *(early phase)*	Mouse – Rat	PI 7
Formalin paw *(late phase)*	Mouse – Rat	PI 8
Migraine model	Mouse – Rat	*In development*
Mono-iodoacetate *(MIA)* - induced chronic inflammatory pain: osteoarthritis model	Rat	PI 19
Mono-iodoacetate (MIA) - induced low back pain	Rat	PI 43
Osteoarthritis	Guinea-pig	*In development*

in vivo

NEUROPATHIC PAIN

Chemotherapy - induced neuropathic pain: Cisplatin	Rat	*PI 21*
Chemotherapy - induced neuropathic pain: Vincristine model	Rat	PI 21
Chronic Constrictive Injury - induced neuropathic pain: CCI/Bennett model	Rat – Mouse	PI 12
Diabetic - induced neuropathy	Rat	PI 23
New! Spared nerve injury	Rat	PI 42
Spinal Nerve Ligation - induced neuropathic pain: SNL/Chung model	Rat - Mouse	PI 13

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Pain

POST-OPERATIVE PAIN

in vivo

Brennan model post-operative pain	Rat – Guinea-pig	PI 16

VISCERAL PAIN

in vivo

Acetic acid writhing	Mouse	PI 6
Colorectal distension *(CRD)*	Rat	GI 30
New! Dextran Sodium Sulfate *(DSS)*-induced colitis	Mouse	PI 37
Parabenzoquinone writhing	Mouse	PI 27
TNBS-induced colitis	Guinea-pig - Rat	*In development*

NON-EVOKED PAIN ENDPOINTS

Home Cage Observation	Locomotor Activity	Rotarod
Dynamic Weight Bearing	Gait Score	Ptosis

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Pharmacokinetics

Pharmacokinetic *(PK)* studies are a key component of drug development programs, that help determine the appropriate modes of administration, dose ranges and treatment timing.

Porsolt has many years of experience, performing pK studies, as standalone services, or as part of larger studies involving established models. Our varied capabilities and expertise enable us to use multiple routes of administration, in different species and collect a variety of tissues for analysis.

PK studies in multiple species:

- Mouse
- Rat
- Guinea-pig
- Ferret
- Rabbit
- Dog
- Mini-pig
- Pig (incl. piglet)

Routes of administration

Standard	intracerebroventricular (i.c.v)
	intramuscular (i.m.)
	intranasal (i.n.)
	intraperitoneal (i.p.)
	intraplantar (i.pl.)
	intravenous (i.v., caudal, cephalic, saphenous, ear)
	nebulization
	oral: per os (p.o.), capsule
	subcutaneous (s.c.)
	topical application (ex: ear, skin, ocular)
	transdermal, transmucosal (using patch)
Under Anesthetic	intra-lesion
	intra mammary fat pad
	intraarticular (knee, ankle, facet joint)
	intracardiac (with or without thoracotomy)
	intracaecal
	intracerebroventricular (i.c.v), intracerebral (using stereotaxy)
	intracolonic
	intradermic
	intrapancreatic
	intrarenal
	intrathecal (i.t.), intraspinal
	intratibial
	intratumoral
	oropharyngeal aspiration
	perineural (ex : perineural)

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Catheterization	intracaecal, intrajejunum, intravesical
Intravenous catherization (iv. slow bolus or infusion)	caudal, femoral, jugular, cephalic, saphenous, veins
Mini-pump implantation (i-precio, osmotic) for infusion	s.c. i.v. i.p

Types of tissue and fluid collected

Adipose Tissue	Diaphragm	Paw
Adrenal Gland	Ear	Skin
Ascitic Fluid	Ganglia	Spinal Cord
Bladder	Heart	Spleen
Blood (Plasma, Serum, Whole)	Intestines	Stomach
Bone	Kidney	Testis
Brain (Cerebral Structures)	Liver, Lymph nodes	Thymus
Bronchoalveolar Liquid	Lung	Tumor
Caecum	Muscle	Urine
Cerebrospinal Fluid	Nerve	Vesicular Gland
Colon	Ovary	

Contact us for specific requests

Clinical Chemistry | Coagulation | Hematology | ELISA

> *Read the detailed chapter "Biomarker Assays" (in Capabilities section) on page 44 > 45 at the end of this catalog.*

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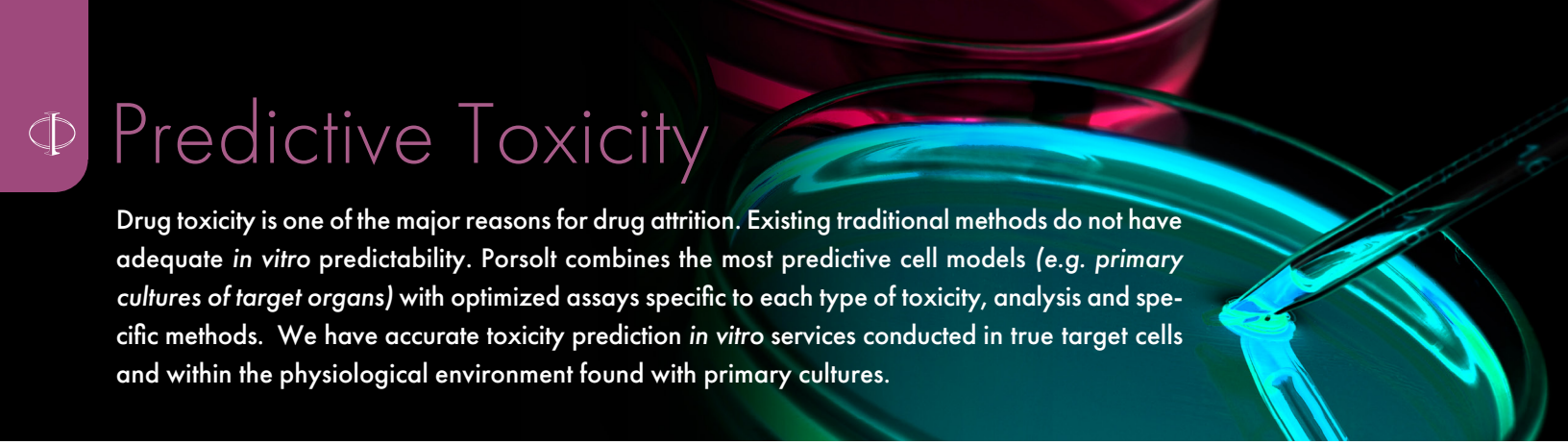
Predictive Toxicity



Drug toxicity is one of the major reasons for drug attrition. Existing traditional methods do not have adequate *in vitro* predictability. Porsolt combines the most predictive cell models *(e.g. primary cultures of target organs)* with optimized assays specific to each type of toxicity, analysis and specific methods. We have accurate toxicity prediction *in vitro* services conducted in true target cells and within the physiological environment found with primary cultures.

in vitro

CARDIOTOXICITY

** Read the detailed list of these tests on page 10*

COMPREHENSIVE *IN VITRO* PROARRHYTHMIA ASSAY *(CIPA):*		
Electrophysiology measurement *(conventional manual patch-clamp)*	Cardiac ion channels	CV 5.6 to CV 5.9*
Cardiotoxicity	iPSC-derived cardiomyocytes: iCell2®	PF 1.08
Proarrhythmic risk assessment *(MEA & Calcium transient assay)*	human-induced pluripotent stem cell-derived cardiomyocytes *(hiPSC-CMs)*	CV 5.14 PF 1.7

in vitro

DRUG INDUCED VASCULAR INJURY *(DIVI)*

Cell toxicity	HUVEC	PF 11.1
Coagulation impairment Tissue Factor and Thrombomodulin	HUVEC	PF 11.1
Leucocyte recruitment VCAM-1, E-Selectin and ICAM-1	HUVEC	PF 11.1

in vitro

GASTROINTESTINAL SYSTEM

Gastric mucosal cell damage	Primary Rat gastric mucosal cells	GI 29

in vivo

GENERAL TOXICITY

Acute toxicity	Rat – Mouse – Dog – Mini-pig	TOX 11
Preliminary chronic toxicity	Rat – Mouse	TOX 12

in vitro

HEPATOTOXICITY

Cholestasis & bile canaliculi network	Primary hepatocytes *(R)* sandwich configuration	PF. 3.16
Cytolysis *(2D & 3D)*	Primary hepatocytes *(H,R & M)* and HepG2	PF. 3.4
Oxidative stress: Glutathione *(GSH)* depletion	Primary hepatocytes *(H & R)* and HepG2	PF. 3.28
Phospholipidosis	Primary hepatocytes *(H & R)* and HepG2	PF. 3.30
Steatosis: intracellular lipid	Primary hepatocytes	

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Predictive Toxicity

in vitro NEPHROTOXICITY

Cytolysis	Primary human renal proximal tubule epithelial cells Human renal proximal tubule epithelial cell line *(HK-2)* *MDCK-II, CRFK,...*	PF 3.4
Lysosomal activity	Primary human renal proximal tubule epithelial cells Human renal proximal tubule epithelial cell line *(HK-2)*	PF 3.7
Mitochondrial membrane potential	Primary human renal proximal tubule epithelial cells Human renal proximal tubule epithelial cell line *(HK-2)*	PF 3.3

in vitro NEUROTOXICITY

Cytolysis	Primary neurons (R,M) cell lines	PF 3.4
Excitotoxicity Calcium measurement	Primary neurons *(R, M)* cell lines	PF. 3.33
Mitochondrial membrane potential	Primary neurons *(R, M)* cell lines	PF. 3.3
Neurite outgrowth	Primary neurons (R,M) cell lines	PF 3.6

in vitro SKIN TOXICITY

Cytotoxicity - Cell viability	3T3 & L929 fibroblasts	TOX 18&19
Ocular irritation *(HET-CAM)*	Chicken egg	TOX 24
Skin irritation	Reconstituted human epidermis	TOX 21
Skin sensitization	Monocyte cell line *(THP1)*	PF 11.2

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Respiratory System

The effects of compounds and therapies on the respiratory system can be assessed using a variety of models, and species, with which Porsolt has extensive experience. These models can be used for assessing the efficacy and/or safety of compounds, and include models for airway function, asthma, cough, fibrosis, bronchospasm, etc.

ex vivo	Isolated pulmonary artery	Rat	RES 10
	Isolated trachea	Rat – Guinea-pig	RES 4
in vivo	Airway function (whole body plethysmography)	Mouse – Rat Guinea-pig	RES 1
	Airway function in large animals	Dog	RES 7
	Airway function under hypercapnia (whole body plethysmography)	Rat	RES 2
New!	Bleomycin-induced pulmonary fibrosis	Guinea-pig - Mouse	RES 8
	Citric acid-induced cough	Guinea-pig	RES 6
	Histamine bronchospasm	Guinea-pig	RES 3
	LPS-induced pulmonary injury	Guinea-pig - Mouse	RES 9
	Ovalbumin-induced asthma	Guinea-pig	RES 5

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
Staining *(paraffin slices)*	Hematoxylin & Eosin, Sirius red, Masson's trichrome...	Multiple species & tissues
Luminex/CBA	TNF, IL-6, IL-1β , IL-10 and MCP-1	Mouse *(BAL)*
Biochemical	MPO activity	Mouse *(whole lung)*
Hematology	WBC *(White Blood Cell count)*: Neutrophils, Macrophages, Lymphocytes, Eosinophils,Basophils	Guinea-pig - Mouse *(BAL)*
ELISA	TNF, IL-6, IL-1β	*Mouse (BAL)*
qPCR	IL IL-6, IL-10,TNF-a, IL-1β, IL-6, IL-8, IL-12a, IL-12β, MCP-1, TNF-a and INF-yα	Guinea-pig - Mouse

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Safety Regulatory Package

Porsolt's broad expertise and years of preclinical pharmacology experience makes us the ideal partner to conduct your GLP Safety Pharmacology experiments. Porsolt offers safety studies in both *in vitro* and *in vivo* models with facilities, procedures, materials and software, that are validated to GLP standards.

BEHAVIORAL PHARMACOLOGY STUDIES FOR INVESTIGATING ABUSE AND DEPENDENCE POTENTIAL

Conditioned place preference	Rat	CNS 7.5
Drug discrimination	Rat	CNS 7.8
Non-precipitated withdrawal *(option: telemetry)*	Rat	CNS 7.3
Self-administration *(initiation)*	Rat	CNS 7.6
Self-administration *(substitution)*	Rat	CNS 7.7

CORE BATTERY [ICH S7]

CARDIOVASCULAR ACTIVITY RECORDING

hERG channel	HEK 293 cells	CV 5.6

CARDIOVASCULAR STUDIES IN CONSCIOUS ANIMALS

Arterial blood pressure, heart rate and ECG	Mouse – Rat – Dog Guinea-pig – Mini-pig	CV 1.4

CENTRAL NERVOUS SYSTEM STUDIES

Activity meter	Mouse – Rat	CNS 1.2
Primary observation *(Irwin)*	Mouse – Rat	CNS 1.1
Rotarod	Mouse – Rat	CNS 1.5

RESPIRATORY STUDIES

Airway function *(whole body plethysmography)*	Mouse – Rat Guinea-pig	RES 1

FORMULATION ANALYSIS

> *Read this detailed content in "Capabilities Section" on page 46 at the end of this catalog.*

SUPPLEMENTAL STUDIES

Autonomic nervous system	Rat	CV 6
Cardiovascular studies in anesthetized animals	Multiple species	CV 1*

** Read more in 'Hemodynamics' section on page 10*

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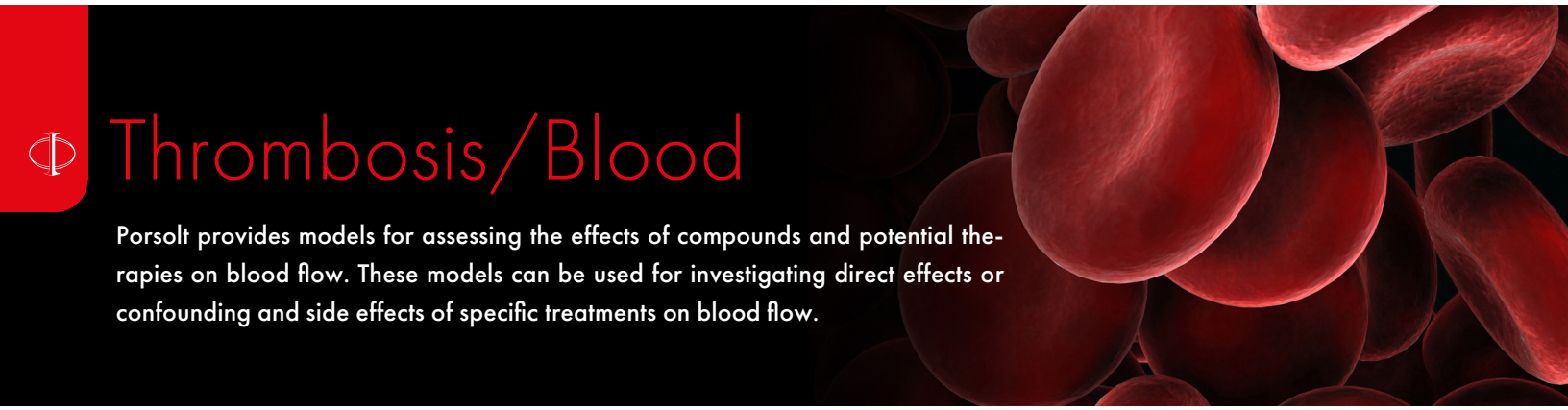
Safety Regulatory Package

	Gastrointestinal system	Multiple species	GI
	Renal function	Mouse – Rat	REN
in vitro	Cardiomyocytes	iCell²®	CV5.14



Thrombosis/Blood

Porsolt provides models for assessing the effects of compounds and potential therapies on blood flow. These models can be used for investigating direct effects or confounding and side effects of specific treatments on blood flow.

in vitro	Endothelial cell activation/ Drug-Induced Vascular Injury (DIVI)	HUVECs cells	PF 2.1
in vivo	Arterial thrombosis (FeCl2)	Rat	BL 3
	Arterio-venous shunt (silk thread model)	Rat	BL 5
	Bleeding time (anesthetized animal)	Rat	BL 2
	Venous thrombosis (FeCl2)	Rat	BL 4

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
Coagulation	APTT *(Activated Partial Thrombin Time)*	Multiple species
	Prothrombin time	Multiple species
	Fibrinogen	Multiple species
Hematology	Complete Blood Count: - Red blood cells: hemoglobin, hematocrit, mean cell volume, mean cell hemoglobin concentration, platelets - White blood cells: lymphocytes, neutrophils, eosinophils, basophils, monocytes	Multiple species

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Urogenital System

Porsolt offers a range of models that address complications specific to, or are associated with, the urogenital system, including the assessment of renal function, bladder function and the genital system.

ex vivo BLADDER FUNCTION

Isolated bladder strip	Rat	VSM 4

in vivo GENITAL SYSTEM

Isolated uterus	Rat	VSM 3
Isolated vas deferens	Guinea-pig	VSM 5
Penile erection	Rat	UG 1

in vitro *IN VITRO* NEPHROLOGY

Cytolysis	RPTECs, HK-2, MDCK-II and CRFK	PF 3.4
Lysosomal activity	RPTECs	PF 3.7
Mitochondrial membrane potential	RPTECs and HK-2	PF 3.3

in vivo RENAL FUNCTION

Diuresis and urinary electrolytes	Mouse – Rat	REN 1
Unilateral ureteral obstruction-induced renal fibrosis	Rat	REN 4

HYPERTENSION MODELS

5/6 nephrectomy	Rat	REN 3
Chronic *(2K1C)* Goldblatt hypertension *(high renin model)*	Rat	CV 2.5
Chronic DOCA – salt hypertension *(low renin model)*	Rat	CV 2.3

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Urogenital System

BIOMARKER ASSAYS

PLATFORM	BIOMARKER	SPECIES *(SAMPLE)*
Histology *(IHC-P)*	Urothelium structure & thickness *(E-Cadherin)*	Rat
Fibrosis	αSMA	Rat
Staining *(paraffin slices)*	Hematoxylin & Eosin, Sirius red, Masson's trichrome...	Multiple species & tissues
Biochemical	Renal function *(creatinin,urea, electrolytes, total protein, albumin)*	Mouse, Rat *(urine, serum, plasma)*
	Glomerular filtration *(creatinin clearance)*	Mouse, Rat *(serum, plasma)*
	Blood Urea Nitrogen *(BUN)*	Mouse, Rat *(urine, serum, plasma)*
qPCR	αSMA, TNF-α αFibronectin, CCL-2 and TGF- β1	Mouse

> New developments in progress ?

Follow us on LinkedIn/company/porsolt and on our website: *www.porsolt.com*

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Capabilities

BIOMARKER ASSAYS

CELL & TISSUE BANKS

FORMULATION ANALYSIS

IMAGE PROCESSING & DATA ANALYSIS

TECHNICAL SKILLS

TECHNICAL CAPABILITIES

Biomarker Assays

Clinical chemistry

< PARAMETERS MEASURED ON SERUM/PLASMA SAMPLES

Calcium *(total)*

Magnesium, Phosphorus, Sodium, Potassium

Chloride/Triglycerides/Creatinine

Total Bilirubin

AST *(Aspartate Aminotransferase)*/ALP *(Alkaline Phosphatase)*/ALT *(Alanine Aminotransferase)*

GGT *(Gamma Glutamyl Transferase)*

Cholesterol/HDL cholesterol/LDL cholesterol/Glucose

NEFA *(Non Esterified Fatty Acids)*

Total proteins/Urea/Albumin

Amylase *(pancreatic)*/Lipase

Insulin/Glucagon

Adiponectin/Leptin

< PARAMETERS MEASURED ON URINARY SAMPLES

Creatin

Sodium, Potassium, Chloride

Albumin *(microalbumin)*/Total proteins/Semi-quantitative parameters

< PARAMETERS MEASURED ON CELL CULTURE SUP.

LDH *(lactate deshydrogenase)*

< PARAMETERS MEASURED ON TOTAL BLOOD

HbA1c *(glycated hemoglobin)*

Coagulation

< PARAMETERS MEASURED ON PLASMA SAMPLES

APTT *(Activated Partial Thrombin Time)*

Prothrombin Time/Fibrinogen

Hematology

< PARAMETERS MEASURED ON TOTAL BLOOD SAMPLES

Complete blood count including red blood cell, hemoglobin,hematocrit, mean cell volume, mean cell, hemoglobin, mean cell hemoglobin concentration, platelets, white blood cell, neutrophils, lymphocytes, monocytes, eosinophils, basophils.

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Biomarker Assays

Immuno assays:

- ELISA / AlphaLISA
- HTRF *(Homogeneous Time Resolved Fluorescence)*
- Immunostaining of cell surface and intracellular biomarkers
- Multiplexed immunophenotyping & biomarker detection by automated 5-laser flow cytometry
- Multiplexed analysis of soluble and intracellular protein expression by the Luminex and BD™ Cytometric Bead Array *(CBA)* technique
- High-throughput flow cytometry
- FLIPR Tetra high-throughput cellular screening system
- High-content histology:
  - tissue sections
  - 3D microtissues
  - tissue microarray
- High-throughput image acquisition of IF/IHC-stained tissue sections or tissue microarrays

Cell & Tissue Banks

Fresh blood from healthy donors through an agreement with the French blood bank.

Primary cell cultures:

- Cryopreserved primary cells *(rodents and human)*
- Freshly isolated rodent primary cell cultures:
  - neurons, astrocytes, oligodendrocytes, microglia
  - pituitary cells
  - hepatocytes
  - splenocytes

Human Induced Pluripotent Stem Cells *(hIPSC)* derived cells:

- hiPSC derived dopaminergic neurons
- hiPSC derived Microglia
- iCell[2®] *(Cardiomyocytes)*
- iCell[2®] Microglia

Cell lines:

- Cancer cell lines: liquid and solid tumors
- Normal immortalized cell lines
- Cell lines expressing our proprietary specific biosensors

Artificial 3D microtissues

Human & animal tissue access & processing
(commercial and tailor-made Tissue Micro Arrays)

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Formulation Analysis

Porsolt's vast portfolio of models and services for different indications also allows us to provide a comprehensive follow-up analysis of your project as part of a larger development program.

Method transfer or development

Method validation:

- specificity
- linearity
- accuracy
- precision

Stability and homogeneity evaluation
(stock and dosing formulations)

Adsorption evaluation
(for in vitro studies)

Formulation analysis:

- concentration verification
- homogeneity of formulations

Image Processing & Data Analysis

Image processing and data analysis provide very useful tools for biological applications.

Firstly,acquired images are described based on adapted and customized features *(texture, color, grey-level, shape, etc.)* The obtained image information is classified using data analysis and visualization methods.

Image acquisition:

- High image resolution
- Tissue preview and ROI selection
- Brightfield and fluorescence for IHC and IF

Quantitative image analysis:

- Intensity of labeling
- Subcellular target characterization
- Event counting
- ROI detection
- Tissue structure description *(shape, tissular organization, etc.)*
- Features linked to neuronal biology
- Indices to assist pathologists with their diagnoses *(e.g. in oncology)*

> ***Clients can send their own images for quantitative image & data analysis and pathology review.***

Technical Skills

Stereotaxic surgery
Cystometry
Induction of cognitive deficits
Induction of neuropathic pain
Induction of arthritis and osteo-arthritis
Ligation models
Medical device implantation
Microdialysis
Nephrectomy
Post-operative pain
Pump administration
Spinal surgery
Telemetry device implantation

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Routes of administration

Standard	intracerebroventricular intramuscular (i.m.) intranasal (i.n.) intraperitoneal (i.p.) intraplantar (i.pl.) intravenous (i.v., caudal, cephalic, saphene, ear) nebulisation oral: per os (p.o.), capsule subcutaneous (s.c.) topical application (ex: ear, skin, ocular) transdermal, transmucosal (using patch)
Under Anesthetic	intra-lesion intra mammary fat pad intraarticular (knee, ankle, facet joint) intracardiac (with or without thoracotomy) intracaecal intracerebroventricar, intracerebral (using stereotaxy) intracolonic intradermic intrapancreatic intrarenal intrathecal (i.t.), intraspinal intratracheal intratibial intratumoral oropharyngeal aspiration perineural (ex : perineural)
Catheterization	intracecal, intrajegunum, intravesical
Intravenous catheterization (iv. slow bolus or infusion)	(caudal, femoral, jugular, cephalic, saphenous, veins)
Mini-pump implantation (i-precio, osmotic) for infusion	s.c i.v i.p

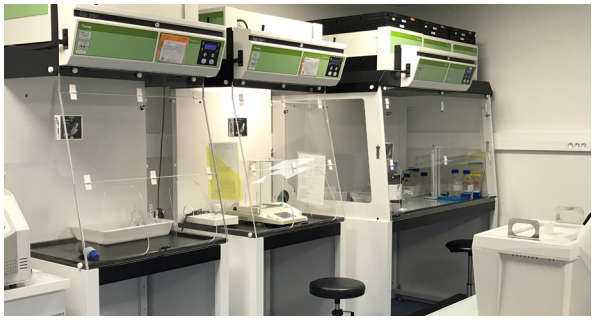
Biological Specimen Collection

Adipose Tissue	Diaphragm	Paw
Adrenal Gland	Ear	Skin
Ascitic Fluid	Ganglia	Spinal Cord
Bladder	Heart	Spleen
Blood (Plasma, Serum, Whole)	Intestines	Stomach
Bone	Kidney	Testis
Brain (Cerebral Structures)	Liver	Thymus
Bronchoalveolar Liquid	Lung	Tumor
Caecum	Muscle	Urine
Cerebrospinal Fluid	Nerve	Vesicular Gland
Colon	Ovary	

Technical Capabilities

Facilities

Conventional animal facility | IVC housing | Biosafety level 2 *(BSL2)* facilities



Equipment

HPLC

High-throughput Fluorometric Luminometric Imaging Plate Reader *(FLIPR)*

Automated multipurpose plate reader *(e.g. for HTRF, Absorbance, Luminescence, Fluorescence measurements)*

QuantStudio™ 5 Real-Time PCR System

High-content imaging

Immunohistology processing platform

Live-content imaging

Automated flow cytometry

Automated video detection

In vivo telemetry systems

High-throughput label-free and image-based cytometry

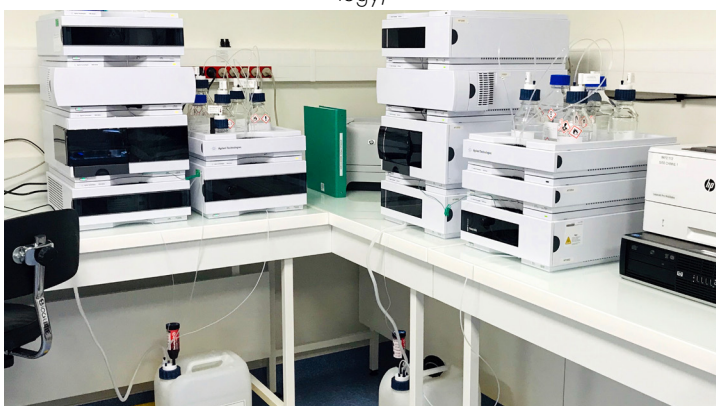
Biochemistry analyzer

Hematology analyzer

Non-invasive multimodal *in vivo* imaging *(e.g. for luminescence, fluorescence, and X-ray)*

Ultrasound imaging

Automated Immunoassay multiplex array Bio-Plex 200 System (Luminex® technology)



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Porsolt Global Offices ■ Regional Representatives ■ Research Facility

Global Headquarters & Main Research Facility
Le Genest-Saint-Isle - France

- 70,500 sq.ft. Research Center including *in vitro* specialized laboratories
- Housing facilities for mice, rats, gerbils, guinea-pigs, hamsters, rabbits, ferrets, pigs, mini-pigs, dogs
- Close proximity to principal animal and tissue suppliers
- Experimentation | Surgery | Archiving
- Data Analysis | Imaging

aaalac INTERNATIONAL

GRADE A GLP Compliance GRADE A

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