

Ephoran Multi Imaging Solutions Platform

EPHORAN Multi-Imaging Solutions is a Contract Research Organization providing imaging expertise and knowledge to study, develop and promote the application of imaging technologies in pre-clinical drug research and development.

1) PRECLINICAL IMAGING

The preclinical imaging services cover all the imaging techniques from those extensively used in clinics (e.g. MRI, PET, CT, SPECT, US) to Optical Imaging (OI, visible light and Near Infra-Red – NIR) and Photoacoustic Imaging up to now limited to animal research.

Magnetic Resonance Imaging (MRI)

Instruments

- A 3 T system with a horizontal magnet (31 cm bore) equipped with two gradient bores ($\Phi > 21\text{cm}$, $> 11\text{cm}$); strength $> 200\text{ mT/m}$ and $> 400\text{ mT/m}$ at 200A, two transmitter and receiver channels for ^1H , ^{13}C , and ^{18}F imaging, two transmit and surface coils for brain and cardiac imaging of small and large animals.
- A 7T MR system with one gradient bore ($\Phi > 15$); strength 300 mT/m , RF coils mice and rats whole body, cardiac and respiratory gating.
- An 1 T MR system equipped with an innovative cryogen-free permanent magnet, Gradient strength of 450 mT/m , RF Coils for rats and mice, Integrated animal handling.
- MRI contrast agents both already used in clinical setting and experimental for preclinical imaging are available. Exclusive availability of a blood pool agent for intravascular, microvessel density, vessel permeability and tumor imaging.

Services

The activities include the set up of the service/instrumentation/animal models for MRI.

- Activities on 1, 3 and 7 Tesla equipments allowing from anatomical to functional imaging experiments in mice and rats and in animal models of human disease.
- Dynamic Contrast Enhanced (DCE) MRI for perfusion/blood flow/permeability studies
- Diffusion Weighted MRI (DWI) for cell membrane integrity/changes in cellularity
- Structural and functional MRI for morphology/blood flow and volume/vessel characterization
- Development of imaging post-processing tools and software

Description

The availability, in this platform, of three state-of-the-art magnetic resonance imagers allows to perform different kinds of experiments:

1. Oncology -> Imaging on Transgenic and Xenografts models (tumor growth, apoptosis, angiogenesis, drug efficacy evaluation)
2. Cardiovascular pathology -> Imaging on Transgenic and induced pathological models (plaque imaging , angiography, perfusion)
3. Cerebral pathology -> Imaging on induced pathological models (stroke, glioma , angiography, perfusion, EAE)
4. Inflammation -> Imaging on induced pathological models (arthritis, macrophage detection)

High frequency ultrasound and Photoacoustic imaging

- VisualSonics-VeVo2100 - High resolution micro-ultrasound system (spatial resolution < 30 μm) for mouse and rat
- Photoacoustic Mode (PA) is a new integrated feature built onto the Vevo LAZR platform to enhance high-resolution ultrasound-derived images with the sensitivity of optical imaging. Real-time, in vivo imaging of deep tissue (up to 1 cm), Integrated, 20Hz tuneable laser (680-970 nm), Resolution down to 45 μm , Imaging through endogenous haemoglobin signal , High optical contrast co-registered with high-resolution imaging.
- US contrast agents both already used in clinical setting and experimental for preclinical imaging are available.
- PA probes , nanoparticles.

Services

The activities include the set up of the service/instrumentation/animal models for US and PA.

- Activities on High resolution micro-ultrasound system equipment allowing from anatomical to functional imaging experiments from zebrafish to mice and rats.
- Vascular Imaging (Common Carotid Artery, Internal and External, Carotid Artery, Aorta, Inferior Vena Cava, Iliac Arteries, Femoral Arteries) mice and rats
- Abdominal Imaging (Inferior Vena Cava and Abdominal Aorta, Liver and Hepatic Vessels, Kidneys, Pancreas) in mice and rats
- Micro- Echocardiography Study in zebrafish
- Cancer Research Imaging (Visualization and 3D imaging reconstruction with Measurements of Tumor size) in mice and rats
- Oxygen saturation distribution , Haemoglobin content and quantification, 2D and 3D image capture and analysis with PA

Description

The availability, in this platform, of a state-of-the-art ultrasound instrument allows to perform different kinds of experiments:

1. Oncology -> Imaging on Transgenic and Xenografts models (tumor growth ,angiogenesis, drug efficacy evaluation)
 2. Cardiovascular pathology -> Imaging on Transgenic and induced pathological models (angiography, perfusion)
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Optical Imaging (OI)

Instruments

- Pearl Imager (Licor) designed for in vivo imaging in the near-infrared (NIR) spectral region
- IVIS® Spectrum (Caliper) High-sensitivity equipment for in vivo imaging of fluorescence and bioluminescence.
- OI contrast agents experimental for preclinical imaging are available. If necessary, labelling and/or smart probes are prepared on request.

Services

The activities include the set up of the service/instrumentation/animal models for OI.

- Activities on two OI equipments allowing functional imaging experiments in mice and rats and in animal models of human disease.
- Labelling of antibodies , proteins and chemicals
- Imaging of receptor-targeted fluorophore agents, blood pool imaging agents, smart probes
- Biodistribution and pharmacokinetics of fluorophore labelled compounds
- Stem cell labelling and tracking

Description

The availability, in this platform, of two state-of-the-art optical imaging instruments allows to perform different kinds of experiments:

1. Oncology -> Imaging on Transgenic and Xenografts models (tumor biology, apoptosis , angiogenesis, drug efficacy evaluation)
2. Drug absorption /distribution and metabolism
3. Cell migration
4. Gene expression and optical reporter proteins (luciferase, GFP)

5. Inflammation -> Imaging on induced pathological models (arthritis, macrophage detection)
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Nuclear Medicine (PET/SPECT)

Instruments

- Triumph GE is a fully integrated molecular imaging system PET/SPECT/CT for biomedical research and pharmaceutical development. Equipment providing high quality images and data for optimal resolution, contrast, noise-to-image quality and accurate 3D rendering with minimal x-ray dose. Triumph® pre-clinical PET/CT system scanner is an integrated imaging system that combines functional imaging with high-resolution anatomical imaging.
- The LabPET4 sub-system is an advanced digital system based on Avalanche Photodiodes (APDs). The system uses dual scintillator detection units in a phoswich architecture. The system provides an 11cm inner bore diameter with a 1.0mm resolution at the center of the FOV with an effective axial field of view of 3.7 cm and an imaging transverse field of view up to 10 cm.
- YAP-(S)PET Scanner provides a simple tool for Multimode Functional Imaging on Small Animals . The Scanner can be easily configured to perform studies either in PET or SPECT mode. The 4-head version of the scanner may work simultaneously in PET and SPECT mode.
- The in-house availability of a cyclotron for industrial production of clinical and research tracers provides both PET/SPECT agents and custom labeling of candidate molecules for pre-clinical studies.

Services

The activities include the set up of the service/instrumentation/animal models for PET and SPECT.

- Activities on Triumph PET/SPECT/CT scanner allowing for anatomical and functional imaging experiments in mice and rats and in animal models of human disease.
- Activities on YAP-(S)PET scanner allowing for functional imaging experiments in mice and rats and in animal models of human disease.
- Labelling of antibodies , proteins and chemicals both for PET and SPECT
- Imaging of receptor-targeted PET agents (new molecular imaging assays)
- Biodistribution and pharmacokinetics of labelled compounds (e.g.pharmacological agents in drug development)
- Identification/synthesis of PET/SPECT tracers for preclinical and clinical imaging (99-Tc, 18-

- F or 68-Ga)
- Human injectable solutions of Gluscan® (FluoroDeoxyGlucose or FDG), research PET tracers labeled (18-F or 68-Ga), and therapeutic radiopharmaceuticals labeled with Y-90 and Lu-177 are provided through the internal expertise and facility.
- PET/SPECT Molecular Imaging (custom labeling 18-F or 68-Ga , 99m-Tc) applied to drug discovery (for both pre-clinical and clinical research, new radiotracers for use in diagnostic imaging).

Description

The availability, in this platform, of a state-of-the-art PET/SPECT instrument allows to perform different kinds of experiments:

1. Oncology -> Imaging on Transgenic and Xenografts models (tumor metabolism, proliferation and growth, apoptosis , angiogenesis, drug efficacy evaluation)
2. Cardiovascular pathology -> Imaging on Transgenic and induced pathological models (plaque imaging)
3. Cerebral pathology -> Imaging on induced pathological models (stroke, glioma , degenerative pathologies)
4. Inflammation -> Imaging on induced pathological models (arthritis, macrophage detection)
5. Validation of new biomarkers of pharmacological activity as predictors of drug response in the clinical setting (novel drug delivery and gene therapy approaches).

X-ray

Instruments

- Triumph GE is a fully integrated molecular imaging system PET/SPECT/CT for biomedical research and pharmaceutical development.
- The X-O(TM) X-ray Computed Tomography (CT) sub-system provides high-quality CT images for whole body anatomical imaging. The system features a digital detector using a large area 5.3 mega pixel CMOS detector. The system includes an X-ray generator with a variable output of 40 to 80 kVp and a maximum energy output of 40W with a 75 um focal spot size. The resolution achievable ranges form 50 to 180 um. The system design permits changing the FOV with a maximum imaging volume of 9.3 cm in diameter by 9.7 axial FOV.

Services

The activities include the set up of the service/instrumentation/animal models for CT.

- Activities on Triumph PET/SPECT/CT scanner allowing for anatomical imaging experiments in mice and rats and in animal models of human disease.

Description

The availability, in this platform, of a state-of-the-art PET/SPECT instrument allows to perform different kinds of experiments:

1. Oncology -> Imaging on Transgenic and Xenografts models (bone imaging , proliferation, drug efficacy evaluation)
2. Contrast enhanced CT with iodinated contrast agent , nanoparticles, liposomes, dendrimers .

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2) PHARMACO-TOXICOLOGICAL AND ANALYTICAL TESTING

Pharmaco-toxicological activities part of the offers of Ephoran Service using a network of qualified partners.

PHARMA TOX

Pharmaco-toxicological activities performed under GLP rules and regulations fulfilling safety requirements.

Instruments

The instruments list includes small animal equipment (anaesthesia system, automated blood sampler, physiological monitoring equipment, ECG, respiratory, oxymeter), general research equipment (centrifuge, dose calibrator, HPLC systems) as well as computer hardware and software requirements for PK analysis , and Optical and Scanning Electron Microscopy .

Animal Facility

Restricted-access, air conditioned , continuously monitored for temperature and humidity to ensure full compliance to regulations on animal welfare .

Services

- Cardiovascular effects in rats and rabbits, anesthetized open chest pigs
- Neurotoxicity test including Irwin test, Rota Rod
- Single dose, expanded acute toxicity in mice and rats
- Repeated dose toxicity (up to 28 days)
- Maximum Tolerated Dose (MTD) and toxicokinetics in mice and rats
- In vitro effects on histamine release from rat peritoneal mast cells
- Testing on different cell lines for MTT, LDH, NR
- Blood/plasma kinetics in conscious rats (automated blood sampling)
- Urinary, biliary and fecal excretion (mice, rats)

Description

The Animal Facility is equipped to perform, help design and implement pilot and GLP-compliant pharmacology and toxicology in mice, rats and pigs. A flexible pre-clinical research and development service allows us to meet client's need for a comprehensive program or a single study.

- Single and repeated dose toxicity studies including toxicokinetics
- Analytical methods development (HPLC, Elisa)
- Pharmacokinetics (ADME)

3) ANALYTICS and CUSTOM SYNTHESIS

Analytics and Custom Synthesis are activities part of the offers of Ephoran Service using a network of qualified partners. Analytical activities performed under GLP rules and regulations including set-up, validation and application of bioanalytical methods and fulfilling safety requirements

Instrument and Services

SUPPORT FOR RESEARCH AND DEVELOPMENT

- In vitro target validation
- Signal Pathway/MOA investigation
- e-ADMET studies
- Biomarkers discovery and detection

Technologies and tools

- ✓ *Stable or transient cell transfection*
- ✓ *Gene silencing*
- ✓ *Protein/protein interaction*
- ✓ *Antagonist competition*
- ✓ *Cell uptake*
- ✓ *ICC/IHC/IF*
- ✓ *Phosphoproteomics*
- ✓ *Gene expression*
- ✓ *Adhesion, Migration*
- ✓ *Apoptosis, Necrosis, Cytotoxicity*
- ✓ *Angiogenesis*
- ✓ *Proliferation*
- ✓ *Differentiation*
- ✓ *Proteome analysis*
- ✓ *Gene expression analysis*
- ✓ *Quantitative detection method set up (Immunoenzimatic, mass spectrometry)*
- ✓ *Nuclear Magnetic Resonance Spectroscopy*
- ✓ *MALDI imaging*
- ✓ *Peptide mass fingerprinting*
- ✓ *Protein mapping*
- ✓ *Proteome and phospho-proteome qualitative and semi-quantitative analysis*
- ✓ *Phosphorilation and glycosilation sites determination*
- ✓ *Protein/Proteome Profiling*
- ✓ *ImmunoPrecipitation-Profilng*
- ✓ *Mass spectrometry*

BIOANALYTICS

- Preclinical and clinical studies
- ADME, PK/TK, and DM
- PD, Biomarkers quantification

- Bio-analytical methods for small and macro molecules quantification

Technologies and tools

- ✓ *Macromolecules quantification in complex matrices by Immunoenzymatic assays, qPCR*
- ✓ *Small molecules quantification in complex matrices by LC-MS/MS*
- ✓ *Solubility by LC-MS/MS*
- ✓ *Membrane permeability by CACO-2 and MDCK cells*
- ✓ *Drug stability by LC-MS/MS*
- ✓ *In vitro intrinsic clearance by LC-MS/MS*
- ✓ *Protein binding by LC-MS/MS*
- ✓ *CYPs inhibition/induction by q-PCR*
- ✓ *Cytotoxicity by Cell-based assays*
- ✓ *Biodistribution by MALDI Imaging*

CUSTOM SYNTHESIS

Scientific service focused on Organic Chemistry, delivering solutions and products for Chemical, Pharmaceutical and Biotech industries and for Universities and Research Institutions.

Based on skills and expertise in a wide range of synthetic reactions, Services are focused on the custom synthesis of Small Molecules including:

- Reference Standard
- Lead compounds and derivatives
- Intermediates
- Starting materials and building blocks
- Targeted molecules (eg.: with Biotin, Fluorescent probes, PEG...)

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