

biogem

**QUALITY  
AND  
EXCELLENCE**

**R&D, pre-clinical and  
customized services**





## About Biogem Service

Biogem Service is the Area that offers highly specialized and integrated R&D services to Pharmaceutical Industries, Biotech Companies and Academic Institutions.



We work with your goals  
in our mind



Biogem's research activities include both Client oriented Research Platforms, centered on Drug Discovery and Preclinical Studies, and Proprietary Research Platforms, aimed at developing novel therapeutics and diagnostic tools.

## Our services

**In vivo studies** in animal models covering various therapeutic areas (oncology, diabetes, arthritis, ocular pathologies, etc.): drug testing and data elaboration for preparation of IND/IMPd; exploratory PK/PD; generation and characterization of genetically modified models.

**Customized analyses** of drug metabolism, toxicology, histopathology, pharmaceutical preclinical development of new compounds, chromatographic analyses and mass spectrometry.

Production of **Recombinant Protein** and **Antibodies**, identification and validation of novel biomarkers, and set up of diagnostic kits.

Evaluation of gene function, gene expression and DNA alterations by **NGS, microarrays** and avant-garde Knock-Out/Knock-Down and Knock-In tools; all activities are supported by our **Bioinformatics Core**.

Biogem activities are performed according to our internal Quality Assurance System and Standard Operating Procedures as dictated by UNI EN ISO 9001:2015. In addition, the Preclinical Test Facility, which is part of Biogem, is waiting for GLP (Good Laboratory Practice) Certification by the Italian Ministry of Health. The high quality standards applied ensure an higher success rates.

## Animal Facility

Biogem Animal Facility can host **mice, rats, rabbits, guinea pigs and zebrafish.**

With an extension of over **1 000 sqm**, the Animal Facility comprises:

- Barrier zone, with a **Specific Pathogen-free (SPF)** area.
- Transgenesis area, to apply traditional or innovative techniques to generate genetically modified mice.
- Experimental areas, equipped with instruments for **in vivo imaging**, surgery rooms and necropsy room.
- Quarantine area, with rederivation laboratory for embryo transfer.
- Conventional animal house.
- Zebrafish Area.



AF is accredited by the Ministry of Health and has an **Internal Ethical Committee**, which evaluates the applications and monitors and inspects the standards of animal care, welfare and accommodation. Biogem is committed to the 3Rs principle. Housing and management of animals are done according to FELASA guidelines.

## Our expertise in Translational Medicine

**Cancer models:** more than 70 xenografts among subcutaneous, metastatic and orthotopic (i.e. mesothelioma and glioblastoma) and we also have a large collection of **PDX/PDOX** models.

**Ocular pathologies** models: Glaucoma, keratoconjunctivitis sicca (KCS), retinitis pigmentosa, Diabetic Retinopath.

**Infammatory Models:** IBDs (infammatory bowel diseases), acute colitis induced by TNBS, rheumatoid arthritis, and cystitis.

**Diabetic nephropathy** model.

**Metabolic diseases** models: type 1 and type 2 diabetes, obesity, and hypercholesterolemia.

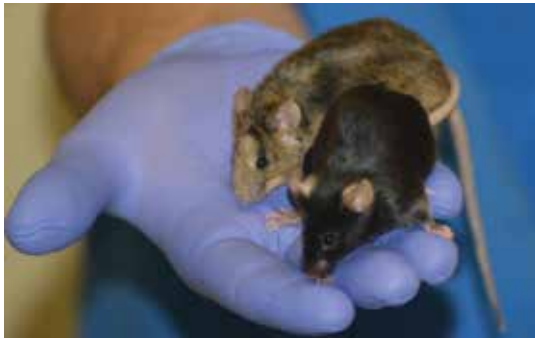
**Customized mouse models can be generated upon request.**



In-house technical and veterinarian assistance to define experimental protocols in order to monitor and keep animal welfare.

## Transgenic Animal Facility

Biogem offers quality custom generation of a wide range of mouse models using advanced molecular biology techniques, to obtain the precise models you need.



### Type of Engineered Mouse Models:

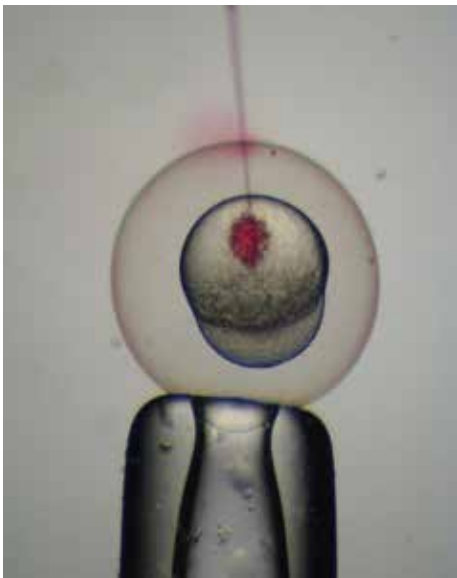
- ◆ Constitutive and Conditional knock-out
- ◆ Constitutive/Conditional Point mutation
- ◆ Rosa26 knock-in (constitutive and/or conditional)
- ◆ Humanization
- ◆ Reporter fusions
- ◆ Constitutive/Inducible Cre- or FLP-driver mouse strains

### Our services:

Design of targeting strategies, drafting for Ministerial authorization, vector construction, CRISPR/Cas9 system, electroporation of mouse embryonic stem (ES) cells, ES cells homologous recombination assessment, chimeric mice generation by morula or blastocyst injection, assessment of germline transmission, breeding chimeric mice to heterozygosity, genotyping, in vivo Cre or Flp modification, phenotypical characterization, sample collection, sperm freezing cryopreservation, in vivo sperm fertilization (IVF), SPF mice riderivation.

## Zebrafish Core Facility

The zebrafish (*Danio rerio*) is an important model for developmental biology, for modelling a wide variety of human diseases, and for screening small molecules, as well. The zebrafish model has key attributes, including the rapid embryological external development and the possibility to “easily” perform targeted mutagenesis, transgenesis and/or transient gene knock-down by microinjection into fertilized eggs.



Our services:

- ◆ Animal housing and care
- ◆ Breeding and maintenance
- ◆ Strain propagation and genotyping
- ◆ Embryo production and microinjection
- ◆ Transgenesis by CRISPR/Cas9 technology
- ◆ Morpholino oligonucleotide-mediated antisense knock-down
- ◆ mRNA and cDNA mediated misexpression
- ◆ Gene expression analysis (RNA in situ hybridization)
- ◆ Phenotyping
- ◆ Treatments for long-term toxicology studies
- ◆ Samples collections

## Pathology Unit

The Pathology Unit (PU) provides expertise and equipment for the examination of tissues and organs. In pre-clinical studies, PU activities contribute to accomplish a comprehensive interpretation on the toxicological and safety profiles of the investigated compounds.

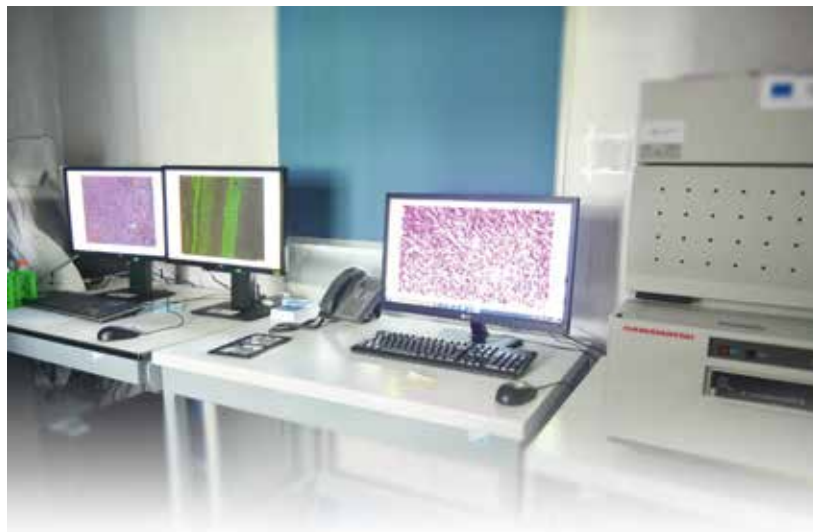
The PU welcomes collaborations and can also assist users in experimental design.

### **Our services:**

Dissection, macroscopic evaluations of organs/tissues, microtomy, embedding, routine staining, special histochemical and immunohistochemical stainings, frozen section histology, morphometric evaluations, in-situ hybridization, and image processing with dedicated softwares.

The main applications of PU activities:

- ◆ Identification of treatment-related lesions, distinguishing adverse versus adaptive changes
- ◆ Characterization of long-term outcome or regression after treatment discontinuation
- ◆ Determination of the causes of unscheduled deaths and their relation to the treatment
- ◆ Recognition of organs susceptible of toxicity





## Pharmacokinetics & Pharmacodynamics (PK/PD)

PK/PD unit supports pharmaceutical industry and Academic Institutes across all stages of drug development, including pharmacokinetic (PK), pharmacodynamic (PD) and toxicokinetic (TK) studies.

This unit is specialized in bioanalytical High Performance Liquid Chromatography Mass Spectrometry (HPLC-MS/MS)



### **Our services:**

Analytical method development and validation  
Method transfer, optimization and cross-validation  
Quantitative sample analysis in human and animal matrices  
Long-term sample storage.

PK/PD unit applies high quality standards utilizes leading industry software such as WinNonlin® to provide the most accurate and time-saving assessment of key parameters from the different studies.

## Experimental Pharmacology & Analytical Biochemistry

This unit supplies biochemical and cell-based screenings aimed to assess the biological activity and toxicity profile of small molecules and/or biologics.

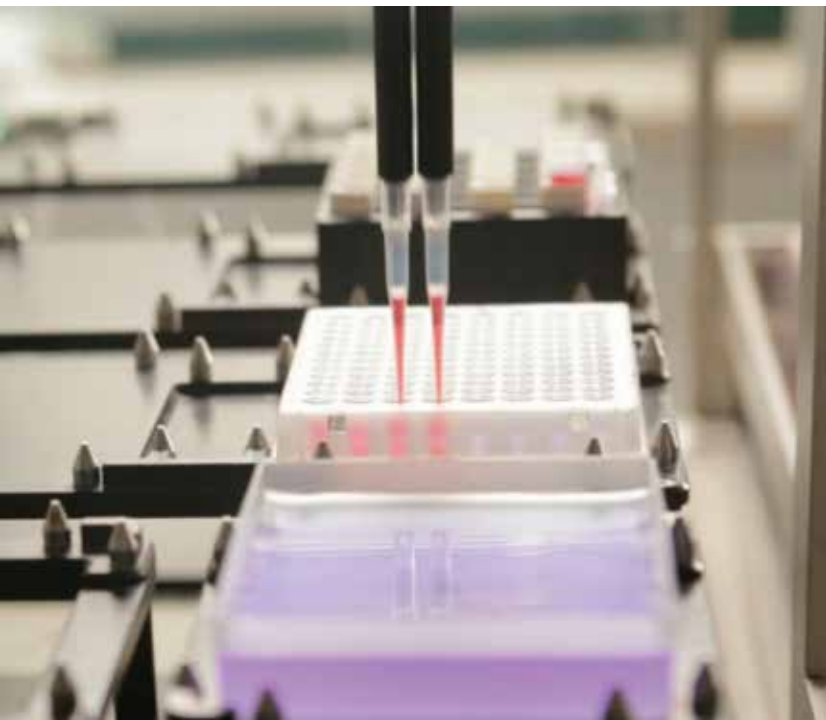
The custom cell-based assays and the high-throughput screening (HTS) platforms allow to rapidly characterize the test compound in terms of mechanism of action, cytotoxicity, and other properties.

On the basis of the experimental requirements it is possible to choose between more than 100 cellular models, including:

- ◆ stabilized cell lines
- ◆ primary cells from different tumour types
- ◆ unique pre-clinical models of malignant mesothelioma
- ◆ engineered cell lines expressing GFP or Luciferase reporter genes.

### Our services include:

- Cell culture (maintenance and storage, tests for pathogens and toxins identifications)
- Isolation of new primary cell lines
- Cytotoxicity and proliferation assays
- XC50 testing and confirmations
- Signal transduction assays
- Reporter gene assays
- Cytokine release assays
- FACS
- Chemotaxis, migration and angiogenesis
- Live Cell Imaging (Operetta High-Content Imaging System)
- Evaluation of ligand-receptor affinity by SPR (Biacore T200)



## Functional Genomics (FG)

The FG unit is equipped with forefront technologies for the Next-Generation Sequencing (NGS) and functional studies aimed to define the role of one or more genes in a specific context.

FG activities allow to assess the effects of a specific pharmacological treatment, to identify and validate novel therapeutic targets and/or diagnostic biomarkers. Our Bioinformatic core facility has an outstanding expertise in FG-derived data analysis.

### Our services:

Our Services:

Analysis of gene expression through Affymetrix microarrays, RNA-seq and qRT-PCR

Sequencing of DNA through Sanger Sequencing, pyrosequencing and NGS technologies

Determination of Single Nucleotide Polymorphism (SNP) and Copy Number Variation (CNV)

Functional studies based on over-expression, gene silencing, gene knock-out and/or gene-editing through CRISPR/Cas9 system.



## Protein Factory

The Protein Factory Unit (PF) helps research institutes and pharmaceutical industries in production, purification and characterization of Recombinant Proteins and monoclonal antibodies.



We provide assay design flexibility, by using either reagents provided by the sponsor or commercially accessible ones.

The PF unit is specialized in the production of recombinant proteins, biosimilars, monoclonal antibodies, ELISA and standards for immunoassays.

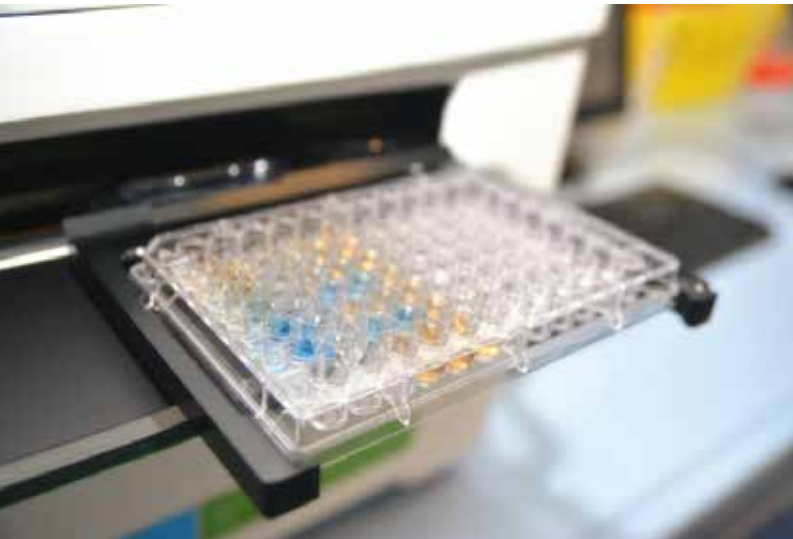
### Our services

- Experimental design and constructs' choice
- Cloning and expression of proteins in disposable bioreactors
- Extraction and purification on a small, medium and large scale (Akta FPLC system)
- Development and validation of analytical tests
- Structural, biochemical and biological characterization

**PF unit develops customized antibodies and ELISA kits.**

**mAb related services:**

- Antigen-design and production
- Immunization (protein, peptide and/or cellular Ag)
- Serum Titration
- Somatic Fusion Primary Screening of hybridomas
- Subcloning Reconfirmation screening
- Hybridoma stabilization and cell banking
- Antibody Purification
- Characterization (mAb isotyping, epitope mapping, WB, ELISA, HPLC, IEF, SDS-PAGE)
- Large-scale production and purification





## GLP Test Facility

The GLP Test Facility includes the following labs and areas:

- Pharmacokinetics/Pharmacodynamics;
- Histopathology (including Clinical Pathology and Anatomy & Pathological Histology labs)
- Cell Cultures;
- Formulation lab and compounds storage (e.g., test items)
- Animal Facility for Rodents and Rabbits;
- Central Archive;

The test facility offers services to companies focused on pharmaceutical, biotech and medical devices business.

In details:

- *in vivo* experimental toxicology on Rodents (*short term and long term studies*),
- toxicokinetics, pharmacokinetics/pharmacodynamics and metabolic studies (ADM studies) on samples from *in vivo/in vitro* investigations;
- studies on medical devices.

The Animal Facility can give support for *in house* generation of transgenic lines on behalf of the Sponsors.





Biogem has several research collaborations with pharmaceutical and biotechnology companies and with academic institutions. Beside offering fee-for-service contracts, we are also open to co-development preclinical research projects through joint venture collaborations.



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