



**iBET****OVERVIEW**

MISSION AND OBJECTIVES

Created in 1989, the Instituto de Biologia Experimental e Tecnológica (iBET) is a private non profit institution. A Biotechnology Research Organisation, iBET interfaces between academic institutions and the economy while creating and organizing autonomous knowledge and expertise.

iBET fosters the competitiveness of its customers and partners, by creating wealth out of knowledge of Chemistry, Biochemistry and Biology.

iBET's targeted areas are biopharmaceuticals and novel therapies; protein stability, structures and drug design; water, energy and the environment; food and wellness; agro-forestry; pilot plant services and analytical services.

The objectives of iBET are:

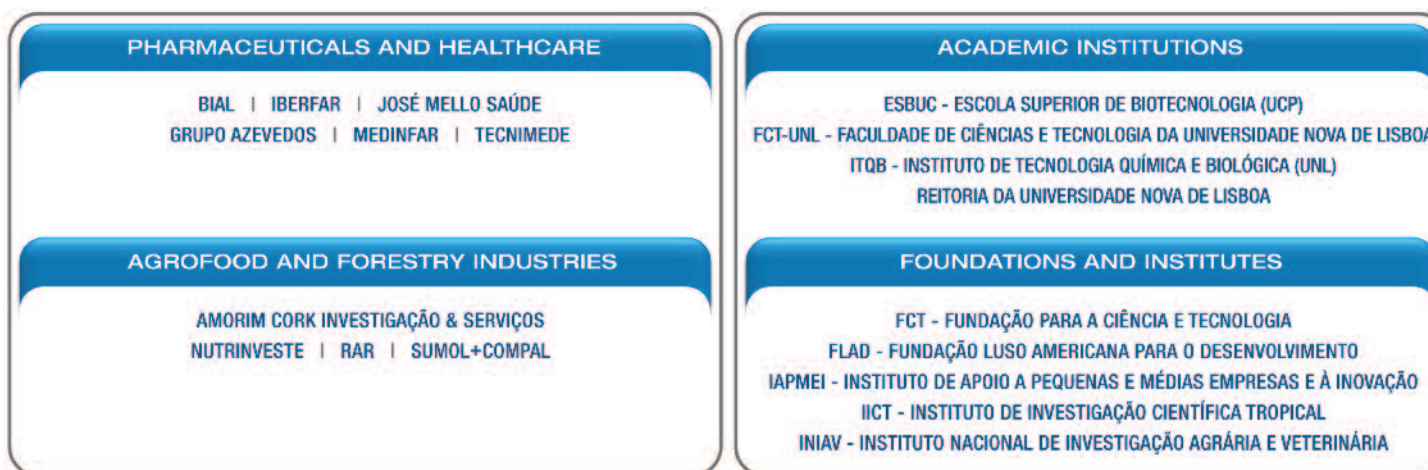
- To create and sustain excellence in all its teams and collaborations, ensuring economic competitiveness;
- To push for faster utilization of the new biotechnological tools in business activities;
- To train interdisciplinary, creative researchers and project managers for biotechnological development;
- To provide a support infrastructure for companies starting or reinforcing biotechnological processes and manufacturing;
- To support incubation of start up/spin off companies;
- To attract foreign companies to carry out R&D in Portugal.



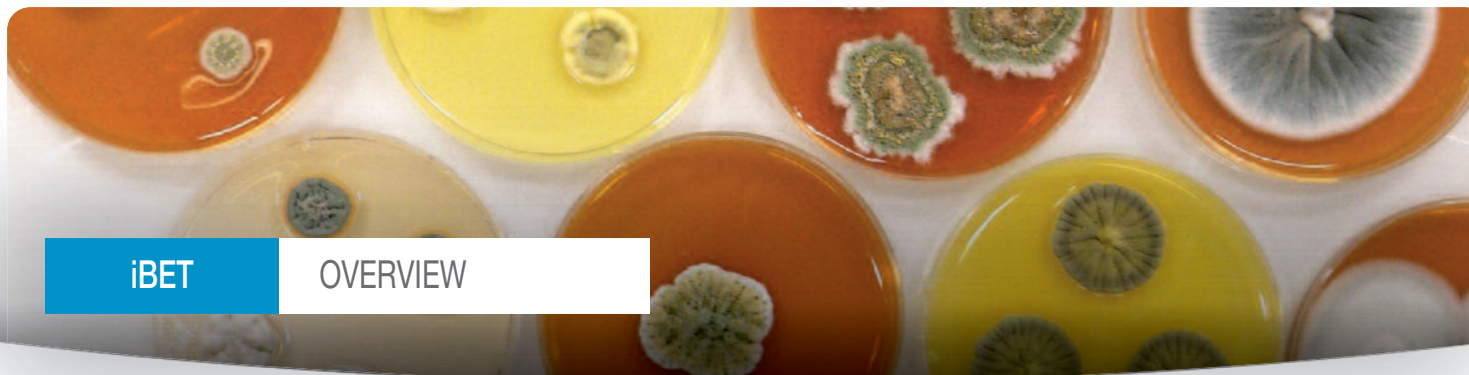
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iBET's SHAREHOLDERS AND THEIR AREAS OF ACTIVITY

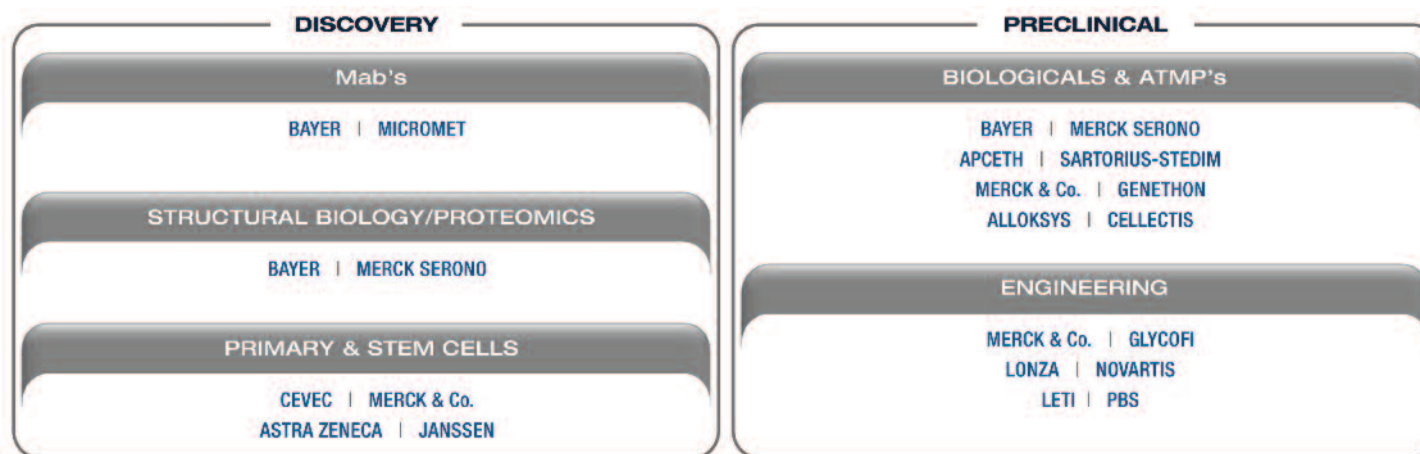


Altogether private partners hold 60% and public partners hold 40% of iBET's capital.


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iBET's CLIENTS

Over its twenty years of existence, iBET has had projects with more than fifty Portuguese and sixty foreign companies (including Boehringer-Ingelheim, Glaxo SmithKline, Novo Nordisk and Unilever).



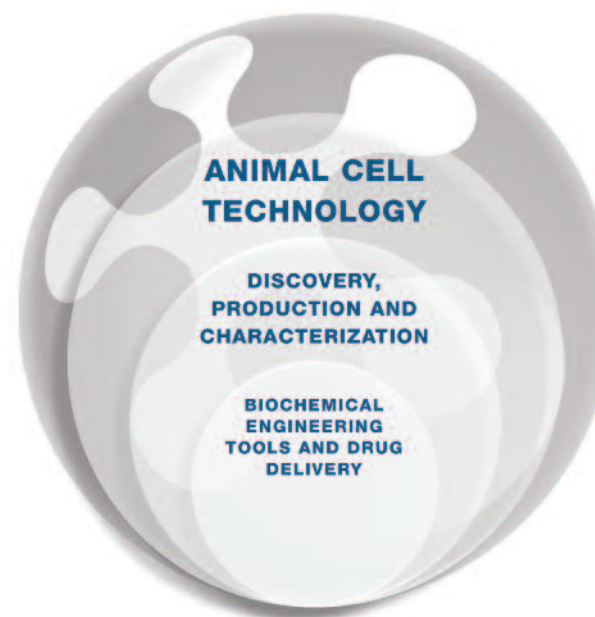


BIOPHARMACEUTICALS AND NOVEL THERAPIES

iBET's main activities target Biopharmaceuticals and ATMP's Discovery, Development and Clinical Trials, up to cGMP production at Genlbet.

Essential capabilities are orchestrated around the Animal Cell Technology Unit, also organizing the expertise available at Pilot Plant and Analytical Service Units, or Protein Structure, Drug Delivery and Systems Biology for Bioprocessing groups.

Recombinant proteins, virus like particles, vaccines, viral vectors and cells for gene and cell therapy using different biological platforms (bacteria, yeast, insect and mammalian cells) complemented with purification, formulation and stability studies. Biologicals and *in vitro* model systems for discovery and preclinical development are key service areas.





ANIMAL CELL TECHNOLOGY UNIT - ACTU

At the ACTU, the biology and biochemistry of cells and viruses is intertwined with the “synthetic” physico-mathematical tools needed to understand complex phenomena, optimize process integration or link systems biology to bioprocess engineering modeling.

Development of biopharmaceuticals at ACTU encompass the design of the appropriate expression vector(s) and/or cell line establishment all the way to process optimization, scale-up and technology transfer – production, purification, formulation and storage.

The accumulated knowledge on the mechanisms underlying cell growth and metabolism as well as product biosynthesis permit a rational and fast development of recombinant therapeutic proteins (including MAb's), viral vaccines and vectors for gene therapy. Recombinase mediated cassette exchange to reduce screening in cell development, fluorescence and chemometric techniques used for real time monitoring facilitating PAT (Process Analytical Technology) requirements or surface plasmon resonance to design purification membranes constitute core skills.

Expertise in expansion, differentiation and cryopreservation of human stem cells (adult, embryonic and induced pluripotent stem cells) and handling of primary cultures of patient-derived cells (liver and cancer) guarantees excellence in cell therapy and 3D in vitro models process design. Integrative approaches, including proteomics platforms, are applied for stem cells bioprocess characterization and elucidation of molecular pathways regulating cell survival, cell cycle progression and/or differentiation.



PROTEIN STABILITY AND STRUCTURE AND DRUG DESIGN

This area at iBET is widely experienced in 3D protein structure determination by X-ray crystallography, limited proteolysis for protein construct design, and differential fluorimetry assays for protein stability studies.

These skills are complemented with adjacent competences within iBET, e.g., mass spectrometry, protein sequencing, and protein production and purification at pilot plant level. State-of-the-art diffraction data measurement facilities exist in-house or can be accessed at Synchrotron Radiation facilities in Europe.

As an alternative to X-ray crystallography in cases where small target proteins fail to crystallize, structural NMR is available, benefiting from access to a wide range of spectrometers located at CERMAX in ITQB. NMR spectroscopy can also be used for drug screening and hit optimization, mapping of protein-ligand interactions during drug discovery process, structure-activity relationships and studies of protein-protein complexes.

Through close collaboration with ITQB, molecular modeling of protein structures, protein-ligand and protein-protein interactions is also available, with access to in-house state-of-the-art computing facilities.

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RESEARCH AND SERVICES

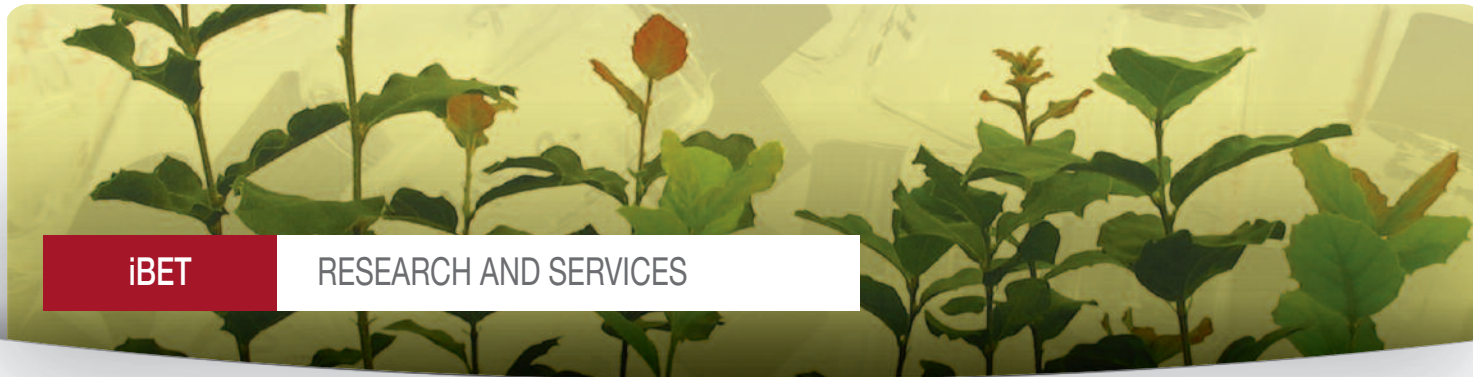
FOOD AND WELLNESS

The Food and Wellness area at iBET joins competences of several interdisciplinary groups with the common objective of answering questions related to food characterization and food safety, development of Nutraceuticals, including functional ingredients and formulation of functional food, valorization of agro-food wastes and development of renewable biopolymers for packaging.

Food Safety is approached as biological risk with studies taking place on the interface between basic science and risk analysis, aiming at anticipating safety problems during manufacturing or distribution and contributing to improving preservation of food products.

iBET Nutraceuticals's area include confidential contract research projects together with the food and ingredient industry for the recognition and isolation of natural health-promoting ingredients from several botanical sources and formulation of new functional products. Bioactivity evaluation can be performed from *in vitro* chemical and cell-based assays to human intervention trials.

iBET is a favored partner for providing support in the construction of Scientific Dossiers to defend health claims, for submission to the EC and EFSA.



WATER ENERGY AND THE ENVIRONMENT

The Energy, Water and the Environment area is seeking, through a range of scientific and practical initiatives, evenly distributed in several interface and infrastructural research groups, to solve critical problems of environmental safety. In doing so, it enhances the environmental and economic sustainability of a wide diversity of areas namely, waste water treatment and reuse, drinking water quality and treatment, waste valorization and biorefinary, gas and energy research studies and process sustainability.

AGRO-FORESTRY

Plant-based Bio-economy is an increasing reality in which sustainability requires the use of renewable resources. Aiming to support agriculture and forestry and contribute to better food and health, we develop and use biotechnology and genomic tools in economically important plant species including forest and fruit species, cereals, legumes and medicinal plants.

Exploiting complementary expertises of our teams, state-of-the-art tools are used to identify regulators, genes and strategies responsible for resistance to pests and diseases and for tolerance to water deficit, salinity and temperature stresses.



PILOT PLANT

The Pilot Plant has expertise in bioprocess development, optimization and production using different biological systems (bacterial, yeasts, mammalian cells, insect cells / baculovirus system). The main area of activities is the pharmaceutical industry (human and veterinary), in the development of production processes for new vaccines, diagnostics and therapeutic products.

Upstream processing equipment includes stirred tank bioreactors (2 to 500L) and disposable systems. Downstream processing equipments includes sterilizable disk and tubular centrifuges, Ultra/Microfiltration units, high pressure homogenizers, preparative and pilot scale chromatographic units and freeze dryer. All equipments are connected through a CAN field-BUS network to a centralized control system (UBICON) so that all operations can be fully controlled and documented as a basis for cGMP dossiers.

The Pilot Plant offers also a production service of pre-clinical grade products (mainly proteins and MAb's) at the *gram* scale for structural and pre-clinical studies.

Clinical grade material, produced under cGMP, can be provided by our partner Genlbet, with production facilities located in the same building.



ANALYTICAL SERVICES UNIT

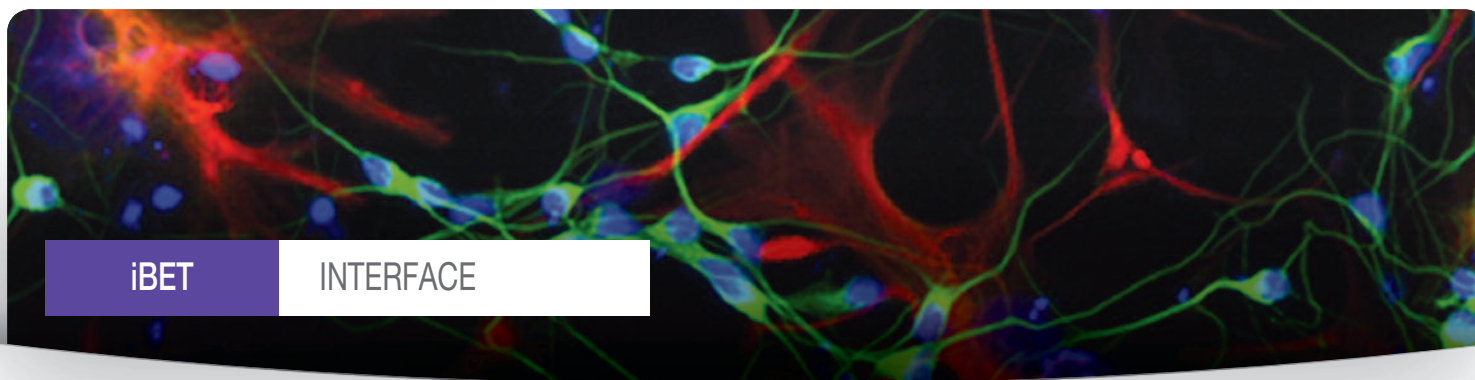
The Analytical Services Unit (ASU) is a joint department of iBET and ITQB-UNL under the executive management of iBET.

ASU is certified by the INFARMED (Portuguese Pharmacy and Medicines Agency) as compliant with OECD Good Laboratory Practices Principles (GLP). The services provided involve the expertise of three laboratories.

The Analytical Laboratory has a long track record of development and validation of chromatographic (HPLC, UPLC and GC, GC-MS), capillary electrophoresis and FTIR methodologies for the analysis of pharmaceutical products (e.g. raw materials, API's and related compounds), biopharmaceuticals (e.g. vaccines), analysis of components of food and natural products.

The Microbiology and Bioassays Laboratory performs *in vitro* bioassays for activity/potency determination and analysis of master cells banks, master virus seed stocks, biopharmaceuticals or food products by microbiological, biochemical and molecular biology methods.

The Mass Spectrometry Laboratory provides services of molecular mass determination, identification and characterization of proteins, peptides, small molecules, among others, using soft-ionization mass spectrometry (ESI- and MALDI-MS/MS) and HPLC-MS/MS.



THE CONCEPT

iBET started as an interface to the society and economy of the research carried out by our academic partners. Thus, whenever one team of researchers from our academical partners is carrying out a project, with the participation of companies, they are iBET researchers.

This implies that the interface areas of work change according to the projects that are taking place at each moment. Currently, these are some of the areas operating at the interface of IBET.

- Antibiotic Stress and Virulence of Enterococci
- Applied and Environmental Mycology
- Biochemical Engineering Laboratory
- Biomolecular Diagnostics Laboratory
- Bioseparation Laboratory
- Control of Gene Expression
- Laboratory of Membrane Processes
- Microbial and Enzyme Technology Laboratory
- Pharmacokinetics and Biopharmaceutical Analysis
- Systems Biology and Engineering



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R&D PARTNERS

MAIN RESEARCH AND DEVELOPMENT PARTNERS

As an interface between academic institutions and the industry, iBET's main R&D partners are:

- ITQB, a postgraduate research institute of Universidade Nova de Lisboa (UNL), provides advanced training and carries interdisciplinary research in Chemistry, Biology, Biochemistry and neighboring technological areas. Sharing the building with iBET, ITQB is responsible for the strongest collaborations of all the academic partners;
- The Faculdade de Ciências e Tecnologia/UNL adds biotechnological and engineering competences;
- Instituto Gulbenkian de Ciência (IGC), supported by the Fundação Calouste Gulbenkian (FCG), carries on biomedical research and education, operating as a "host institution", offering excellent facilities to foreign and Portuguese research groups;
- GenIbet is a cGMP biopharmaceutical Contract Manufacturing Organization, partially owned by IBET (45%). GenIbet's core activity is the manufacture of biopharmaceuticals for early stage drug development, pre-clinical studies and cGMP manufacturing for Phase I and II clinical trials.

iBET, with ITQB, IGC and the Research Center of Faculdade de Ciências Médicas/UNL (CEDOC), constitute an Associate Laboratory of the Ministry of Science and Technology. This laboratory is devoted to Biologically Active Molecules, Molecular Medicine, Developmental Biology, Biological Risk and Plant Biotechnology.



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