



PREDECT: a powerful new European Consortium addressing novel laboratory models for cancer target validation

The Animal Cell Technology Unit at IBET/ITQB-UNL, Oeiras, is part of PREDECT, an European consortium of 26 principal investigators, managed by Servier, AstraZeneca and the University of Helsinki, which brings together academic laboratories, biotechs and the pharmaceutical industry. This research network aims to develop innovative models and technologies for the preclinical evaluation of cancer therapy targets. The program of work should eventually improve the clinical success of therapies designed for the treatment of cancer.

There has been an explosion, in the last decade, of the knowledge regarding the genetic changes that are associated with cancer. This knowledge provides great opportunities for improved, selective treatments through the design of new drugs and antibodies that are targeted specifically to those changes in tumour cells responsible for the survival, proliferation and spread of the cancer. A challenge for drug discovery is to establish which of the many molecular changes associated with a particular cancer type, in a particular patient subgroup, are responsible for the pathology and which are associated “bystanders” playing a minimal or no role. Accumulating information suggests that an alarmingly high proportion of new drugs, targeted to recently-identified molecular changes in cancer, lack efficacy when tried in patients. One reason for this lack of efficacy may reflect the use of over-simplified laboratory models of cancer that do not represent the complexity and heterogeneity of tumours. In these “reductionist” models promising drug targets may not work as they would in a cancer patient and consequently drug inhibition has only a modest or no effect clinically.

PREDECT sets out to provide new laboratory models of human cancer that better reflect the complexity and heterogeneity of cancers. Working in teams investigating breast, prostate and lung cancers, PREDECT will use advanced mouse models of cancer, some of which will be genetically engineered and matched to particular groups of patients with these cancers, to progressively “deconstruct” the complex tumours into simpler forms for use on the laboratory bench. Examples are thin slices of tumour tissue and tumour cells growing in three-dimensions together with supporting cells, rather than the simple, conventional two-dimensional models. At each stage of the reduction of complexity, the tumour cells will be profiled to establish how closely they represent the tumour of origin, growing *in vivo*, and thus how closely they represent a human tumour. Novel complex models with the appropriate profiles can eventually be used to validate that a new, potential target for cancer treatment is worth pursuing.



The PREDECT project will provide robust technologies permitting the biotechnology and pharmaceutical industry to take early decisions on whether or not to invest in and pursue an intensive drug discovery programme on a new target, reducing wasted effort. If the technologies suggest the target is valid, these PREDECT platforms will also permit early validation of biomarkers indicating which cohorts of patients would be suggested to benefit from the drug, increasing the likelihood of success for the patient in clinical trial, and decreasing trial duration and expense. Additionally, laboratory models that better represent cancer pathologies will permit academic researchers to perform investigations of tumour biology with greater fidelity.

Professor John Hickman, Coordinator for Servier of the PREDECT consortium comments: *"The Innovative Medicines Initiative has allowed cancer researchers in Industry to come together to determine which are the bottlenecks in the drug discovery process that limit the emergence of more effective cancer therapies. We believe that inadequate laboratory models to investigate and validate potential targets have contributed to the failure of recent clinical trials where the drugs lacked efficacy. To create innovative technologies and platforms, more representative of the complexities associated with human tumours, we need top-flight academic expertise in cancer cell biology, bioinformatics and systems biology to complement our efforts in drug discovery. Having experienced in my own career both academic and industrial cultures, it has been exciting to create a programme which demonstrates to partners that the cultural differences between us are minimal and that we are united in trying to fulfil the urgent medical need for better cancer treatments."*

"At IBET/ITQB-UNL we will develop three-dimensional cultures of tumour cells together with supporting cells following a systematic technological approach based on bioreactors which allow fully controlled environment", explains Dr Catarina Brito, PREDECT's Principal Investigator at the Animal Cell Technology Unit, at IBET/ITQB-UNL.

Dr Paula Alves, Scientific Coordinator of the Animal Cell Technology Unit at IBET/ITQB-UNL and Director of IBET adds: *"To fully accomplish the Consortia objectives it will be critical to establish robust and standardized methods that allow for the widespread implementation of the developed models, both in academic and industrial settings."*

The five-year PREDECT project, providing new tools for target validation to improve drug efficacy, integrates a group of pharmaceutical companies composed of Hoffmann-La Roche, Bayer Schering Pharma, AstraZeneca, Boehringer Ingelheim International, Orion Pharma, Sigma-Tau and Servier whose total in-kind contributions to the project are matched by funding from the IMI Joint Undertaking, resulting in a total of 17.2 Million Euros.

The Animal Cell Technology Unit at IBET/ITQB-UNL is the only Portuguese team to integrate a Consortia funded by the 2nd call of the IMI Joint Undertaking.

The academic and biotechnology company expertise essential to the programme is provided by The University of Helsinki, Biomedicum Genomics Ltd and VTT Turku (Finland), University of Tartu (Estonia) Radboud University Nijmegen and Erasmus University Rotterdam (Netherlands), Institute of Cancer Research (UK), Oncotest GmbH and the Margarete Fischer-Bosch Institute (Germany), Ecole Polytechnique Fédérale Lausanne (Switzerland), Weizmann Institute (Israel) and Instituto de Biologia Experimental e Tecnológica (Portugal).

PREDECT Website is at www.predect.eu





About the Innovative Medicines Initiative (IMI)

The five-year PREDECT project is funded by IMI (www.imi.europa.eu), a unique public-private partnership between the European Federation of Pharmaceutical Industries and Associations, EFPIA and the European Union, represented by the European Commission.

IMI aims to put Europe at the forefront of biopharmaceutical innovation and to support more efficient discovery and development of better medicines for patients.

IMI's innovative funding scheme has a budget of Euro 1 billion provided by the European Commission. That amount will be matched by in-kind contributions of at least another 1 billion euro from EFPIA members.

The **Animal Cell Technology Unit of iBET/ITQB-UNL**, coordinated by Dr Paula Alves, is a research group combining knowledge and competences of scientists from a wide range of disciplines (Biochemistry, Biology and Engineering). Our know-how in terms of biopharmaceuticals spans from the initial expression vector design and cell line establishment through all stages of process development and scale-up (production, purification, stability and storage). Additionally, the recognized potential of cell- and gene-based therapies led us to develop expertise in both areas. In recent years, the ACTU has been dedicating substantial effort in the development of new in vitro models for pre-clinical research. <http://tca.itqb.unl.pt>

iBET is a private non profit institution created in 1989. As a Biotechnology Research Organisation iBET acts as an interface between academic institutions while also creating and organising autonomous knowledge and expertise in Chemistry, Biology and associated areas with applications to Health/ Pharmaceuticals, Agroindustry, Forestry, Agrochemistry and Environment. Since 2001, iBET with ITQB (Instituto de Tecnologia Química e Biológica) and Instituto Gulbenkian de Ciência (IGC) an Associate Laboratory of the Ministry of Science and Technology. www.ibet.pt

O **Instituto de Tecnologia Química e Biológica (ITQB)**, in Oeiras, is a research and advanced training institute of the Universidade Nova de Lisboa and is one of the major Research Centres in Portugal dedicated to fundamental research in chemistry and life sciences. With a highly multidisciplinary nature, ITQB is a centre for the advanced training in chemistry, biology and associated technologies.

