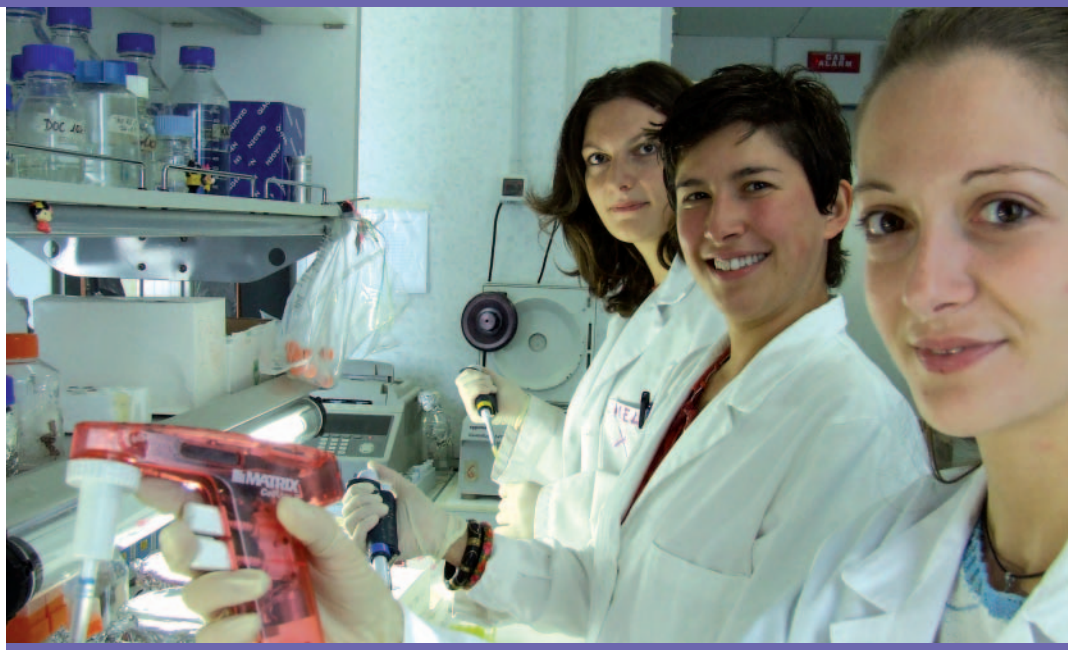
NEST
Pathfinder

SOLUTION FOR COMPLEX DISEASES

COBIOS



Diabetes is a chronic condition which afflicts over 19 million citizens across 25 Member States of the European Union, and poses a major health risk to millions of people worldwide. Changing dietary habits has resulted in a major increase in the number of people suffering from diabetes. Indeed, future projections estimate that current figures may double by 2030. The COBIOS consortium is undertaking revolutionary new research that may radically improve the treatment of diabetes.

COBIOS is a ground-breaking project that proposes to change the manner in which gene delivery and gene therapy are conducted. If successful, biological delivery systems will be able to detect changes of a pre-determined molecule and then proceed to deliver a biological compound in response.

New treatment for diabetes envisioned

The central aim of COBIOS is to develop synthetic biology devices for therapy in medicine. In particular, to create methods for the treatment of diabetes through the innovative use of novel biological delivery systems.

Among its objectives, COBIOS intends to deliver a systematic approach to developing well characterised, engineered biological devices in higher eukaryotes that will constitute re-usable 'building blocks' for future engineered systems design. The project will also provide computer-aided design tools for the building and simulation of synthetic gene circuits, tools that will be available to the scientific community.

The project will use yeast and mammalian systems to engineer stable synthetic oscillator networks. These systems will be able to express mRNA/protein levels with a pre-determined frequency and amplitude. The initial test bed will be conducted using the yeast system for the synthetic biology design strategies.

With regards to the mammalian tissue, individual cellular oscillators will be synchronised so as to fulfil the macroscopic function of an insulin delivery device. This means that the engineering of the synthetic network engages in additional inputs and outputs that would enable the resetting of the oscillators.

From an applicable therapeutic viewpoint, the desired outcome would be a system which would synchronise the insulin oscillations with the circadian rhythm.

"It will drastically change the way we think about gene delivery and gene therapy."

The project team, headed by Italy's Fondazione Telethon, will utilise methods from system dynamics and control theory to develop and implement modular control networks that enable oscillations in the connected networks.

In the course of the project, three problem areas will be addressed. Firstly, the robustness of controller dynamics and, secondly, suitable interfaces to the controlled networks.

The third problem area where the team will direct their energy is on the mechanisms for regulation of the controller's dynamic characteristics (such as period and amplitude) through external signals that can be exogenous or outputs of cellular signal processing at the level of individual cells and tissues.

Scientific diffusion and benefit

The success of COBIOS lies in the deep level of collaboration between a variety of disciplines. The high level of knowledge required for this project is almost impossible to find in one research institution. For that reason, a number of institutions from Europe and across the Atlantic, from the United States, will pool their knowledge for the project.

The COBIOS experience will afford the European partners the opportunity to learn from their American counterpart (Boston University). This will place the consortium, already respected in Europe, as a world leader in the area of synthetic biology for medicine.

A major milestone will be accomplished if the COBIOS project proves to be a success. It will drastically change the way we think about gene delivery and gene therapy.

This will be the first time the team's novel therapeutic approach will be applied *in vivo*. After initial tests in mammalian cells, it will then progress to *in vivo* testing with a mouse model of diabetes with the engineered synthetic device for stable production of insulin. The insulin production will be designed to synchronise with the circadian clock.

Future projections indicate commercial potential

All approaches developed over the course of the project will be patented and partners from industry will be approached for commercial development. For this reason, a managerial position has been created as part of the project to identify European based industries and small to medium-sized enterprises that would be interested in the outcomes of the project.

A website will be created, which will allow both the scientific and industrial communities to access up-to-date information, as well as the experimental methodologies and computational tools used in the project. Furthermore, results will be disseminated through the use of seminars, congresses, symposia, as well as through peer-reviewed publications.

AT A GLANCE

Official Title
Engineering and Control of Biological Systems: a New Way to Tackle Complex Diseases and Biotechnological Innovation

Coordinator
Fondazione Telethon (Italy)

Partners
- Delft University of Technology (The Netherlands)
- Institut National de Recherche en Informatique et en Automatique (France)
- Genostar (France)
- Swiss Federal Institute of Technology Zurich (Switzerland)
- Boston University (United States)
- Universita' degli Studi di Napoli 'Federico II' (Italy)

Further Information
Dr Diego di Bernardo
Fondazione Telethon
Telethon Institute of Genetics and Medicine
via G Saliceto 5
00161 Rome
Italy
email: dibernardo@tigem.it
fax: +39 081 6132 351

Project cost
€ 2 582 710

EU funding
€ 2 064 275

Project reference
Contract No 043379 (NEST)