1. Introduction to bio-artificial organs

The design and production of bio-artificial organs is one of the most challenging applications of a relatively new science: tissue engineering. Tissue engineering has been defined as "an interdisciplinary field which applies the principles of engineering and life sciences towards the development of biological substitutes that aim to maintain, restore or improve tissue function" [1].

In general, every organ that can be broken apart into single cells or cell clusters, without disrupting the original function is potentially suitable for generating a bio-artificial organ. However, it is generally difficult to preserve the functionality of cellular units placed in environmental conditions that usually are quite different from their native site. In addition, only few materials enable creation of a tissue/material interface that is fully biocompatible towards both the immobilised cells and the host's tissue. In particular, special care must be taken not only to assess the material's physical-chemical properties and biocompatibility, but also to select the tissue's sources, in compliance with physiological competence and safety principles. Finally, the overall suitability of the newly developed biohybrid devices for clinical application must also be carefully assessed.

2. Diabetes mellitus

Diabetes mellitus (DM) is the most common endocrine disorder; the pathology is associated to metabolic abnormalities such as elevated blood glucose levels and their biochemical consequences that may provoke acute illness or result during the time course of the disease into secondary chronic complications [2]. These mainly affect
eyes, kidney, nerves and blood vessels. Although it is not an immediate life-threatening disease anymore, in the majority of instances, provided that the patients are promptly and adequately treated, DM still represents a potentially lethal and certainly highly disabling disease. It is estimated that over 100 million people in the world actually suffer for either type 1 or type 2 DM. At the clinical onset of type 1 Diabetes mellitus (T1DM) that affects mainly, but not exclusively, adolescent/young individuals, the majority of islet $\beta$-cells has been completely destroyed by autoimmunity.

Since T1DM patients will require life-long, multiple daily insulin injections, they unfortunately represent a heavy burden to society. In fact, if these individuals have seen their life expectancy to gradually improve from the introduction of insulin therapy, their increased longevity has not resulted in elimination of the risk for developing chronic, often very serious complications of the disease, such as premature blindness, terminal renal insufficiency, vascular disease and disabling neuropathy. These complications may occur in spite of the selected insulin therapy regimens because it is very difficult to mimic performance of the glucose sensing apparatus incorporated in the normal $\beta$-cells. Consequently, the physiological stimulus-coupled insulin secretory response is far from being reproduced by subcutaneous exogenous insulin injections.

3. Application of bio-artificial pancreas

Bio-Artificial Pancreas (BAP), composed of insulin producing cells that are protected from the host's immune reaction by biocompatible, selective permeable and chemically stable artificial membranes, would ideally apply to the potential cure of T1DM by transplantation. In fact, BAP that contains insulin-producing cells would provide for continuous insulin delivery under strict regulation by the extra-cellular glucose levels. The goal of such a "totally automatic treatment" for T1DM could be also theoretically accomplished by creating an "artificial pancreas". In this instance, a glucose sensor [3] implanted subcutaneously, would continuously record extra-cellular glucose levels and convert the chemical information into an electronic signal, by a mini-computerised system. This would regulate, in turn, release of pre-stored insulin by a mini-pump, in order to maintain normoglycemia. This machinery, while able to reverse hyperglycemia, has been preliminarily proven to function, so far, for only very limited periods of time, due to still pending technical problems.

The most actual and effective way to prevent the onset of secondary complications in patients with T1DM is based on strict blood glucose control. This goal may be achieved by injecting either short- or long-acting insulin molecules, as frequently as 4 times a day. Unfortunately, this therapeutic option is associated with major drawbacks: (a) patients are exposed to high risk for developing severe hypoglycemia, (b) risk for developing secondary complications of the disease is attenuated, but not eliminated [4] and (c) patients' compliance with intensive insulin therapy may be quite poor, because of both, strict blood glucose monitoring that involve multiple finger pricks, and insulin injections. The imperfect blood glucose control achieved by subcutaneously-injected exogenous insulin lies on a fundamental pitfall consisting of the physical distance between the insulin injection site and the liver, that represents the first physiological site of insulin action.