Introduction

Diabetes is a chronic disease characterized by a deficit in β-cell mass and a failure of glucose homeostasis, resulting in a variety of severe complications and an overall shortened life expectancy. Insulin deficiency leads to an increase in the level of glucose in the blood, which itself causes symptoms and may belief-threatening and, in the longer term, is associated with damage to blood vessels and nerves **(Gonez & Knight,2010)**.

There is a compelling need to develop novel therapies for diabetes mellitus Recent successes in the transplantation of islets of Langerhans are seen as a major breakthrough. However, there is huge disparity between potential recipients and the availability of donor tissue. Human embryonic stem cells induced to form pancreatic β-cells could provide a replenishable supply of tissue**(Docherty et al.,2007).**

Stem cells are defined as clonogenic cells capable of both self-renewal and multilineage differentiation. This mean that these cells can be expanded in vivo or in vitro and differentiated to produce the desired cell type. There exist several sources of stem cells that have been demonstrated to give rise to pluripotent cell lines:

1) embryonic stem cells .
2) embryonic germ cells.
3) embryonic carcinoma cells .
4) adult stem cells.

By using in vitro differentiation and selection protocols, embryonic stem cells can be guided into specific cell lineages and selected by applying genetic selection when a marker gene is expressed. Recently, differentiation and cell selection protocols have been used to generate embryonic stem cell

derived insulin-secreting cells that normalize blood glucose when transplanted into diabetic animals**(Berná et al,2001).**
The use of small specific molecules has been instrumental in the modulation of stem cell proliferation and differentiation to obtain insulin-containing cells.

Examples include nutrients (glucose, nicotinamide and retinoic acid), acids (butyrate), alkaloids (cyclopamine and conophylline) and pharmacological agents (LY294002 and wortmannin). These molecules, alone or in combination with specific growth factors and hormones, will likely provide key information to design specific culture media in order to obtain customized cells for implantation in diabetes **(Roche et al 2006).**

In order to become a realistic clinical issue transplantation of insulin producing cells derived from stem cells, it needs to over come multiple-experimental obstacles. The first one is to develop a protocol that may allow obtaining a pure population of functional insulin-secreting cells as close as possible to the pancreatic β-cell. The second problem should concern to the transplantation itself, considering issues related to immune rejection, tumour formation, site for implant, implant survival, and biosafety mechanisms **(Roche et al, 2005) .**