INTRODUCTION
Diabetes is a disease that affects millions of people and is associated with serious complications and a shortened life span. Type 1 diabetes (T1D) is characterized by a marked deficiency of insulin-producing pancreatic beta cells, which have been destroyed by autoimmunity. The high blood glucose levels cause devastating complications including kidney failure, blindness, amputations, and cardiovascular disease. There have been great advances in reducing the toll from these complications through improvements in exogenous insulin treatment, but the ideal treatment will be replacement of the missing insulin-producing pancreatic beta cells. The proof-of-principle for this type of therapy was established with whole organ pancreas transplants and later success with transplants of islets. More recently, there has been great progress in generating beta cells from embryonic stem cells (ESCs) and induced pluripotent stem (iPS) cells, which could be used for beta cell replacement therapy, thus providing what would essentially be a cure if they can be successfully transplanted into patients. There are also hopes that transplantation of other types of cells such as mesenchymal stromal cells may provide some general protection against the autoimmune component of this disease through an unknown mechanism(s).

RATIONALE AND EXPERIMENTAL EVIDENCE OF CELL-BASED THERAPIES FOR DIABETES
In the 1980s it was shown that islet cells isolated from pancreases obtained from cadaveric donors could be transplanted into the livers of people with T1D resulting in normal blood glucose levels. As with other types of allogeneic transplantation, this treatment requires the patient to undergo lifelong immunosuppression. Although exciting, this approach is far from perfect because so few cadaveric pancreases are available, immunosuppressive drugs are required, and the cells usually fail after a few years. The two main challenges are finding an adequate supply of insulin-producing cells and protecting these cells from attack by the immune system. There has been impressive progress in solving the beta cell supply problem in that it is now possible to generate insulin-producing cells from human ESCs and iPS cells. With respect to protecting the cells, immunologists and bioengineers are working on a range of strategies to protect the transplanted cells from immune attack. One approach is to use cellular engineering to make the cells more resistant to such an attack and another is to encapsulate the cells within semi-permeable membranes to protect them from the cells of the immune system.

WHAT IS THE CLINICAL STATUS OF CELL-BASED THERAPIES FOR DIABETES?
At present, clinical cell-based therapies in the form of islets obtained from cadaveric pancreases can provide benefit for only a very small number of people with diabetes. New cell-based therapies being developed must be tested in rigorous clinical trials that comply with regulatory standards, such as those by the US Food and Drug Administration. Some clinical trials which have been approved by regulators are underway in which insulin-producing cells derived from ESCs are being placed into encapsulation devices and transplanted into human subjects with T1D, but clinical benefit has not yet been reported. There have been a variety of claims in recent years of beneficial results from unregulated transplants using a patient’s own adult stem cells, but these approaches are not supported by a current understanding of science and lack independent and objective efficacy data. These treatments and the clinics offering them should be avoided.

WHAT DOES THE NEAR FUTURE HOLD?
There continue to be high hopes and expectations that cells derived from stem cells will succeed for beta cell replacement therapy and thus essentially cure T1D. We know that insulin-producing cells derived from ESCs and iPS cells can reverse diabetes in experimental animals. A great deal of work on this problem is going on in companies and academic research centers. The calendar for successful clinical application is uncertain but progress toward this goal continues to be exciting.

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