

## **Human pancreatic islet-derived progenitors for cell replacement therapy in diabetes**

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### **Abstract:**

Diabetes is becoming a global epidemic, affecting millions of people worldwide. Cell replacement therapy using cadaveric islets has been shown to be successful for 1-5 years. However, scarcity of available donor pancreas limits this therapy from widespread use. Alternate replenishable cell sources such as embryonic stem cells, bone marrow stem cells, umbilical cord blood-derived progenitor cells and tissue-derived stem cells have been thought to be useful for cell replacement therapy in diabetes. We believe that stem / progenitor cells derived from pancreatic islets are “committed” to differentiate into insulin-producing cells. We assessed in vitro differentiation potential of 5 different pancreatic progenitors following a previously established in vitro differentiation protocol and observed that islet-derived progenitor cells show better differentiation to endocrine pancreatic lineage. Analysis of the insulin promoter region confirms a transcriptionally active conformation of insulin promoter region in islet-derived progenitor cells as compared to that in other cell types studied. Open chromatin conformation was assessed by using chromatin immunoprecipitation (ChIP) for H3K4me2, H3K4me3, H3Ac, H4Ac. Similarly silencing marks at insulin promoter were assessed by ChIP for H3K9me2 and H3K27me2. These epigenetic marks of active chromatin conformation are believed to be heritable and it is therefore reasonable to think that such islet-derived progenitors are better committed to differentiate into insulin-producing cells. Further studies on clonally expanded pancreatic islet cells will help us in generating endocrine lineage-specific progenitors for cell replacement therapy in diabetes.