Differentiation of Pluripotent Stem Cells into Pancreatic Progenitors

Alkabbi, Sara

Pluripotent stem cells have a great potential to proliferate in the lab and differentiate into all cell types. Pancreatic progenitor cells generated from PSCs can be transplanted directly into the patient's body, where they are converted inside human body into functional mature beta cells expressing insulin to adjust the blood glucose level, where it can be used to treat type 1 diabetic patients and advanced cases of type 2 diabetic patients. Therefore, our aim in this project was to generate pancreatic progenitors from human embryonic stem cells that may be used in the near future to treat diabetic patients in our region. hESCs were differentiated into definitive endoderm (DE) with a high efficiency, where the cells expressed high percentages of SOX17 and FOXA2 (more than 95%) and lost the pluripotency markers (OCT4 and SOX2). The DE was further differentiated into two distinct types of pancreatic progenitors expressing specific transcription factors (TFs). These two types were 1) progenitors expressing PDX1 and NKX6.1 (PDX1+/NKX6.1+) and 2) other progenitors expressing only PDX1 (PDX1+/NKX6.1-). We used a protocol, which was more efficient than the recently established one. Interestingly, it has been shown that the presence of NKX6.1 is crucial to obtain fully functional pancreatic beta cells. These findings indicate that we were able to generate the correct pancreatic progenitors that can further differentiate into functional beta cells after their transplantation into diabetic patients. We believe that this study is important because it provides a reproducible protocol that can generate progenitors for treating diabetic patients.