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Identification of novel transcription factor genes for pancreas development by directed differentiation of embryonic stem cells

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Embryonic stem cells (ESCs), promising as a renewable source for regenerative mdicine, have yet been differentiated into insulin-secreting β cells for a replacement therapy in type 1 diabbetes, due at least partially to the knowledge gap of transcription factors (TFs) for pancreas development. We hypothesise here that the ESCs should provide a powerful model to identify novel pancreatic TF genes at the genomic level, provided the *in vivo* developmental process could be recapitulated *in vitro* by directed differentiation. Guided by knowledge of their normal development and RT-PCR and immunochemical analyses, we have established protocols for directed differentiation of mESCs into pancreatic progenitors. Indeed at day 15, a group of pancreatic progenitor marker genes including *Pdx1, Ptf1a, Nkx6.1, Pax4* and *Pax6* was up-regulated. Consistently, Pdx1-immunoreactive cells were detected on day 15. Most of these $Pdx1^+$ cells also expressed Nkx6.1. Microarray analyses of these differentiating ESC cells at days 0, 4, 8 and 15 confirmed their sequential differentiation and our bioinformatics algorithms for sequential datasets allowed us identified over 20 potential novel TF genes for pancreatic islet lineage development. The dynamic expression of representative known and novel genes was confirmed by quantitative real time RT-PCR analysis. This strategy may be modified to identify novel regulatory molecules for development of other tissue and organ systems.

Biography

Associate Prof Fang-Xu Jiang is Head of Islet Cell Development Program, The University of Western Australia. His research interest focuses mainly on proliferation, differentiation, self-renewal and regeneration of pancreatic insulin-secreting β-cell progenitors, including the molecular mechanisms of these biological processes. The ultimate aim is to generate unlimited number of β cells in vitro or stimulate patient's own progenitor/stem cells to become β cells in vivo to cure this disease.