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Doctoraat Medische Wetenschappen
PhD in Medical Sciences
2011-2012

Openbare verdediging van/*Public defence of*

Lina SUI

Voor het behalen van de academische graad van
'DOCTOR IN DE MEDISCHE WETENSCHAPPEN'
To obtain the academic degree of
'DOCTOR IN MEDICAL SCIENCES'

**Human embryonic stem cells as a source for
cell replacement therapy in diabetes**

Promotor: prof. Luc Bouwens

Co-promotor: dr. Josue K. Mfopou

Tuesday 11 September 2012

Auditorium Brouwer, 17:00

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

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Situering van het proefschrift/*Summary of the dissertation*

Type 1 diabetes is characterized by the loss of beta cells in the pancreas. Many possible ways of generating beta cells have been studied with the intention to relieve the shortage of donor pancreata as transplantable source to treat diabetes patients. Human embryonic stem cells (hESCs) represent a promising source for cell replacement therapy in diabetes. The generation of abundant functional beta cells from hESCs is not yet achieved in vitro, although derivation of PDX1 expressing pancreatic progenitor cells from hESCs in vitro and their differentiation potential towards mature beta cells in vivo have been demonstrated. In our study, we aimed at evaluating the potential of hESCs to be used as a source in beta cell replacement therapy. We studied the further differentiation of hESC-derived PDX1+ progenitors in vivo and their proliferation in a defined medium in order to fulfill the vast demand for cell replacement therapy. We also studied the signalling pathways that regulate definitive endoderm (DE) differentiation with the aim of eliminating undefined factors present in the culture media. We found that the PDX1+ progenitors have potential to further differentiate into pancreatic endocrine cells after transplantation in the subcutaneous space in mice. Furthermore, the pancreatic progenitors can be expanded in a serum free proliferation medium. Finally, we addressed the role of FGF signaling in the early stage of DE development. In conclusion, our findings allowed us to derive fully specified pancreatic progenitors in vitro and setup an efficient system for expansion of these progenitors. They pave the way for using hESC-derived pancreatic progenitors as a source in cell replacement therapy.

Curriculum Vitae

Lina Sui was born on November 19th, 1981 in Tianjin, China. She obtained her bachelor degree with high distinction in animal science on July 2004 and master degree with degree of honour in developmental biology on July 2007 at Northwest A&F University, Yangling, China. After that, she becomes a doctorate candidate in Medical Science at the Cell Differentiation Unit (DIFF) of Diabetes Research Center (DRC) of Vrije Universiteit Brussel (VUB) under the guidance of Prof. dr. Luc Bouwens and dr. Josue Kunjom Mfopou. Her Ph.D work focuses on the differentiation of pancreatic cells from human embryonic stem cells. The project generated four first-author articles. Two of them are in the submitted state, two are accepted and in press. She has presented her scientific works at international and national congresses.