

## **Promotoren**

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**Prof. Zhidong Ling**  
**Prof. Daniel Pipeleers**

Diabetes Research Center  
Vrije Universiteit Brussel

JDRF Center  
for Beta Cell Therapy in Diabetes

## **Leden van de examencommissie**

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**Prof. Jens H Nielsen**

Department of Medical Biochemistry and  
Genetics, University of Copenhagen  
Denmark

**Prof. Jean-Christophe Jonas**

Unit of Endocrinology and Metabolism  
Université Catholique de Louvain

**Prof. Frans Schuit**

Gene Expression Unit  
Department of Molecular Cell Biology  
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**Prof. Ilse Smolders**

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Drug Analysis  
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**Prof. Karin Vanderkerken**

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Vrije Universiteit Brussel

FACULTEIT GENEESKUNDE EN FARMACIE

**Doctoraat in de Medische Wetenschappen**

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UITNODIGING

TOT DE OPENBARE VERDEDIGING VAN HET  
DOCTORAATPROEFSCHRIFT VAN

**Qidi WANG**

MAANDAG 5 OKTOBER 2009

Auditorium P. Brouwer  
Faculteit Geneeskunde & Farmacie  
Laarbeeklaan 103, 1090 Brussel

## **Qidi WANG**

### **'Regulation of Beta Cell Phenotype by Glibenclamide'**

maandag 5 oktober 2009 om **17 uur**  
auditorium P. Brouwer

#### **Situering van het proefschrift**

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Earlier studies from our department have shown that the phenotype of beta cells can be altered by environmental conditions leading to differences in the viability and function of the cells. Treatment with the hypoglycemic drug glibenclamide was found to increase the basal protein and insulin synthetic activity of the cells. The present work has identified the site and the mechanisms through which this effect is achieved. Both in vivo and in vitro exposure of beta cells to this therapeutic agent results in an activation of translation factors through a calcium-dependent pathway that involves mTOR-, PKA- and MEK-dependent signaling. This activation causes an up-regulation of genes that encode for enzymes in protein synthesis and in metabolic pathways that facilitate nutrient catabolism through mitochondrial metabolism and fatty acid oxidation. These effects occur in the subpopulation of beta cells that has been degranulated under influence of the insulin-releasing action of the drug. On basis of these observations, it is concluded that the sustained presence of the insulin secretagogue glibenclamide induces a functional adaptation in those beta cells that have been degranulated by administration of this drug. This adaptation consists in increasing hormone synthesis under basal conditions, and in decreasing the cellular susceptibility to toxic effects of fatty acid overload.

#### **Curriculum Vitae**

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Qidi Wang was born in Shanghai in December 1974. She obtained an MD degree at Shanghai Second Medical University in 1998, and a Master degree in Clinical Endocrinology in 2000, with research activities on the role of leptin in endocrine disease. She was subsequently appointed as Endocrinologist at the Shanghai Clinical Center for Endocrine & Metabolic Diseases of Ruijin Hospital that is affiliated to Shanghai Jiaotong University School of Medicine (director Prof Ning Guang). In this position she was selected by her hospital to perform Ph.D studies at the Diabetes Research Center of Vrije Universiteit Brussels (VUB) with which the Shanghai Center has long-standing interactions. During the first two years of her stay in Brussels she combined her research work with classes in Medical and Pharmaceutical Research which led to a second Master degree that she obtained with great distinction in 2003. She has opted for a training in several disciplines in the perspective of her further career in Shanghai and a collaboration with VUB.