Cover Page



Universiteit Leiden



The handle <u>http://hdl.handle.net/1887/32608</u> holds various files of this Leiden University dissertation.

Author: Ellenbroek, Johanne Hendrike (Rianne) Title: Pancreatic β - and α -cell adaptation in response to metabolic changes Issue Date: 2015-25-03

Pancreatic β - and α -cell adaptation in response to metabolic changes

Rianne Ellenbroek

Pancreatic $\beta\text{-}$ and $\alpha\text{-}cell$ adaptation in response to metabolic changes 2015, Johanne Hendrike Ellenbroek

All rights are reserved. No part of this publication may be reproduced, stored, or transmitted in any form or by any means, without permission of the copyright owners.

ISBN: 978-94-6108-929-8

Cover: Maarten Ellenbroek, illustration by Polygon animation, reprinted with permission from Great Ormond Street Hospital for Children, London, United Kingdom. Layout and printed by: Gildeprint - Enschede.

The research described in this thesis was performed at the department of Nephrology of the Leiden University Medical Center, Leiden, The Netherlands.

The research presented in this thesis was supported by the Diabetes Cell Therapy Initiative consortium, the Dutch Diabetes Research Foundation, the DON foundation, the Bontius Foundation and an unrestricted research grant from Novo Nordisk.

The printing of this thesis was kindly supported by Novo Nordisk B.V.

Pancreatic β - and α -cell adaptation in response to metabolic changes

Proefschrift

ter verkrijging van de graad van Doctor aan de Universiteit Leiden, op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker, volgens besluit van het College voor Promoties te verdedigen op woensdag 25 maart 2015 klokke 15.00 uur

door

Johanne Hendrike (Rianne) Ellenbroek

geboren te Zwolle in 1985

Promotiecommissie

Promotores	Prof. dr. E.J.P. de Koning Prof. dr. T.J. Rabelink
Copromotor	Dr. F. Carlotti
Overige leden	Prof. dr. J.A. Romijn <i>Academisch Medisch Centrum, Amsterdam</i> Prof. dr. H. Pijl Prof. dr. P.C.N. Rensen

Contents

Chapter 1.	General introduction	7
Chapter 2.	Topologically heterogeneous β -cell adaptation in response to high-fat diet in mice	35
Chapter 3.	β -Cell adaptation in response to dexamethasone-induced insulin resistance is topologically heterogeneous in rats	51
Chapter 4.	Topologically heterogeneous $\beta\text{-}$ and $\alpha\text{-}cell$ adaptation with maintenance of $\alpha\text{-}$ to $\beta\text{-}cell$ ratio in obesity	63
Chapter 5.	Glucagon like peptide-1 receptor agonist treatment reduces β -cell mass in normoglycaemic mice	75
Chapter 6.	Long-term ketogenic diet causes glucose intolerance and reduced β – and α -cell mass but no weight loss in mice	89
Chapter 7.	A high-throughput screening platform using primary human islets to assess β -cell function	103
Chapter 8.	Summary and general discussion	117
Chapter 9.	Nederlandse samenvatting Curriculum vitae List of publications	133 141 143